GM26 · GOLD MEDAL MD / DNB MEDICINE

BASIC SCIENCE MODEL ANSWERS SERIES

Chapter 3
Renal Physiology

Part A — 12 PYQ essay answers (Doc 1)

Part B — 6 unique short notes (Doc 2)

Ready Reckoner — rapid revision tables

5 M short note = 1 page **10 M LAQ = 2 pages** **Cornell + Pareto**

Exam target: MD Medicine Final · DNB Medicine Theory · Bedside Viva · NEET-SS

Evidence-verified · India-focused · Harrison 22e, Brenner & Rector, KDIGO 2024

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Index — Part A (Doc 1)

Part B — how it fits with Part A

Part A answers the 12 **Doc 1** PYQ essays (nephron segments, loop of Henle, concentrating mechanism, bladder, GFR, potassium, casts, AKI biomarkers, metabolic–hormonal functions). Part B adds the **6 unique short-note topics from Doc 2** not covered in Part A — duplicated topics are omitted and cross-referenced. Same Cornell layout, Pareto highlighting and colour-coded boxes throughout.

Already in Part A (not repeated): counter-current multiplier (= concentrating mechanism, Q3) · loop of Henle & Bartter's (Q2) · metabolic & hormonal functions (Q12) · potassium homeostasis (Q9).

How to use this chapter

Element	What it is	How to use it in the exam
Mark distribution bar	The stacked bar under every question banner. **Segment width = marks**; each segment is one Cornell cue row, so the bar maps exactly onto the notes beside it	Budget your **writing time in proportion to segment width**. A 3 M block deserves three times the ink of a 1 M block — most candidates lose marks by writing all blocks the same length.
Pareto tier	The colour of each segment, repeated as a chip in the cue column: ■ **CORE** · ■ **ADDS** · ■ **DIST** · ■ **INDIA**	**CORE carries 60–80% of every answer** — the vital few. Under time pressure write CORE + INDIA + the summary band and stop. ADDS lifts a good answer; DIST is the gold-medal differentiator; **INDIA is 5–20% of every answer and is the mark nobody writes.**
Examiner box	The **magenta** band opening every answer: **Tests · Earns the marks · Loses the marks**	**Read this before the notes.** It decodes what the stem is actually asking — most marks are lost by answering a question adjacent to the one that was set. The 'Loses' line is the error the examiner is watching for.
Cornell layout	Three true Cornell elements: **cue column** (left, teal) · **notes column** (right) · **summary band** (gold, full width). Each answer runs **magenta = what is asked** → notes → **gold = what to write** → **black = what to memorise**	Cover the notes column and recall from the cue + tier + marks alone. Then check. This is active recall — re-reading is not studying.
Cornell summary band	The gold full-width band closing every answer	**Write it verbatim as your conclusion.** It is built to stand alone as a 3–4 line answer if you run out of time completely.
Cram box	The **black** strip at the very bottom of every answer — **naked facts only**: numbers, genes, transporters, doses, trials, eponyms. Deliberately not prose	**The night before, read only the cram boxes.** If you can recite one you can rebuild that whole answer from it. It is the last pass, not the first.
Page budget	Every 5 M short note is **exactly 1 page**; every 10 M LAQ is **exactly 2 pages**	This is your writing target in the hall. If you cannot reproduce the page in 8–10 min (5 M) or 18–22 min (10 M), you are over-writing.
Cornell cue column	The teal column on the left	Cover the right side and recall from the cue alone — this is the recall test, not re-reading.
Pareto highlight	Yellow highlight	The 20% of facts that earn 80% of the marks. If time is short, revise only these.
Colour-coded boxes	Navy = definition/criteria · Green = management · Amber = investigation · Purple = examiner pearl · Crimson = red flag or trap · Orange = drug dose / □□□□ India · Teal = basic science / recent advance · Gold = conclusion	Reproduce the **navy box first** and the **gold box last** in every answer — examiners mark the opening definition and the conclusion.
Flowchart panels	Monospaced, plain-arrow diagrams	Drawable in ~2 minutes. Draw at least one in every 10 M answer.
□□□□ boxes	Indian epidemiology, guidelines and practice	One India line per answer is the cheapest mark on the paper.

■ **CORE** ■ **ADDS** ■ **DIST** ■ **INDIA** *CORE = the vital few you cannot pass without · ADDS = separates good from average · DIST = gold-medal differentiator · INDIA = Indian relevance*

COMMON MISTAKE / TRAP

Evidence discipline used throughout: guideline positions carry the issuing body and year; trials are named only where they change practice; each recent advance is labelled **standard / optional / emerging / investigational**. Where nationally representative Indian data do not exist, the text says so explicitly rather than inventing a figure. All diagrams are original schematics — no copyrighted textbook figure is reproduced.

Q1 Nephron segments; RFTs for TIN

10 M | PYQ 2×

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 10 M

Open with this 1 M	Segments & function 3 M	What is TIN? 1 M	RFTs for TIN 3 M	Traps 1 M	Indian relevance 1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: not anatomy for its own sake — whether you can build the chain **segment → transporter → function** and then **use that map** to explain why tubulointerstitial nephritis wrecks tubular function long before GFR falls.
Earns the marks: the segment/transporter table, and the one sentence that unlocks the second half — **in TIN, tubular dysfunction is out of proportion to the fall in GFR**, so the tests you choose are tubular, not glomerular. Group the RFTs **segment-wise**.
Loses the marks: writing a pure anatomy essay and never answering the 'RFTs for TIN' half (worth 3 M on its own); listing investigations randomly; quoting urine eosinophils.

■ CORE 1 M

Open with this

Definition + numbers in the first two lines.

The **nephron** is the structural and functional unit of the kidney — a glomerulus plus its tubule — with ~1 million nephrons per kidney (range 0.2–2.5 million). Nephron number is fixed at birth (nephrogenesis ends at 34–36 weeks); low birth weight → low nephron endowment is a validated Indian risk factor for later CKD and hypertension (Brenner hyperfiltration hypothesis).

DEFINITION / CRITERIA

Cortical nephrons (85%) — short loops, peritubular capillaries → excretion and reabsorption.
Juxtamedullary nephrons (15%) — long loops + vasa recta → **urine concentration**.

■ CORE 3 M

Segments & function

Draw the nephron and label transporters — this table is the answer.

Segment	Reabsorbs / secretes	Key transporter	Clinical correlate
Glomerulus	Ultrafiltration, 180 L/day	Size + charge barrier	Proteinuria, haema casts
PCT (S1–S3)	65% Na^+ & H_2O, 100% glucose & AA, 80–90% HCO_3^-, PO_4, urate; secretes organic anions/cations	NHE3, SGLT2 (S1–S2)/SGLT1 (S3), NaPi-IIa, URAT1, OAT1/3	Fanconi syndrome, glycosuria
Thin descending limb	Water only (solute-impermeable)	AQP1	Countercurrent mu
Thick ascending limb	25% Na^+; water-**impermeable** → **diluting segment**; paracellular Ca^{2+}/Mg^{2+}	NKCC2, ROMK, ClC-Kb/barttin, claudin-16/19	Bartter syndrome; diuretics
DCT	5–10% Na^+; Ca^{2+} reabsorption	NCC, TRPV5	Gitelman; thiazides syndrome
CNT / collecting duct	Final 3% Na^+, K^+ secretion, H^+ secretion, water	ENaC, ROMK/BK, AQP2, H^+-ATPase, pendrin	Liddle, dRTA, neph PHA

■ CORE 1 M

What is TIN?

Define before you list tests — examiners give a mark for this line.

Tubulointerstitial nephritis (TIN) = inflammation of the tubules and interstitium with relative sparing of glomeruli and vessels. The physiological signature is tubular dysfunction out of proportion to the fall in GFR — so renal function tests are chosen to expose each segment.

■ CORE 3 M

RFTs for TIN

Segment-wise logic wins marks. Group, never list randomly.

Test	Abnormality in TIN	Segment localis
Early-morning urine osmolality; water deprivation ± DDAVP	Fails to concentrate (<600 mOsm/kg); nephrogenic DI pattern	Medullary CD / in
Urine pH on acidaemia; furosemide-fludrocortisone test (safer than NH_4Cl load)	Urine pH >5.5 despite acidosis → **distal (type 1) RTA**	α-intercalated cel
Urine anion gap (Na+K−Cl); urine osmolal gap	Positive UAG / low NH_4^+ → renal acidification defect	Distal nephron
Fractional excretion of HCO_3^-	>15% during alkali load → **proximal (type 2) RTA**	PCT
Tubular (LMW) proteinuria — β_2-microglobulin, α_1-microglobulin, RBP	Raised with low albumin:total protein ratio (<0.4); sub-nephrotic (<1–2 g/day)	PCT
Glycosuria with normoglycaemia, generalised aminoaciduria, TmP/GFR, uricosuria	Fanconi pattern	PCT
Serum K^+, Mg^{2+}, PO_4; FE_mg	Hypokalaemia/hyperkalaemia (type 4), Mg^{2+} & PO_4 wasting	TAL / DCT
Urinalysis + microscopy	Sterile pyuria, **WBC casts**, no RBC casts	Interstitium
Injury markers — urinary NAG, KIM-1, NGAL, MCP-1	Raised; research/tertiary use only in India	Tubular epitheliu
Imaging ± renal biopsy	Normal/small kidneys, lost cortico-medullary differentiation; biopsy is **confirmatory**	Whole interstitiu

■ DIST 1 M

Traps

COMMON MISTAKE / TRAP

- **Urine eosinophils are obsolete** — sensitivity ~30%, specificity ~68% (Muriithi, CJASN 2013). Do not offer this as a 'test for AIN'.
- Do not perform an ammonium chloride load in a sick or acidotic patient — use the furosemide–fludrocortisone test.
- Nephrotic-range proteinuria excludes pure TIN *except* NSAID-induced AIN with concurrent minimal change disease.

■ INDIA 1 M

Indian relevance

One India line converts a good answer into a gold-medal answer.

INDIAN RELEVANCE

- **CKDu (Uddanam, coastal Andhra/south Odisha)** — chronic interstitial nephritis in agricultural communities; bland urine, small kidneys, low-grade tubular proteinuria; heat stress ± agrochemical/silica hypotheses (ICMR studies ongoing).
- **Drugs:** OTC NSAIDs and analgesic combinations, PPIs, intermittent rifampicin, anti-tubercular drugs, herbal/Ayurvedic preparations with lead/cadmium.
- **Tropical infections:** leptospirosis, scrub typhus, hantavirus, snake envenomation — common causes of acute TIN in eastern India.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

The nephron is a serial arrangement of segments with unique transporters; each disease is best understood as **failure of one segment's transporter**. In TIN, GFR falls late while tubular functions fail early — hence concentrating ability, urinary acidification and low-molecular-weight proteinuria, not creatinine alone, are the renal function tests that make the diagnosis, with biopsy as confirmation.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

~1 million nephrons/kidney, fixed at 34–36 wk · cortical 85% / juxtamedullary 15% · **PCT 65% Na^+** (NHE3, SGLT2) · **TAL 25%** (NKCC2) · **DCT 5–10%** (NCC) · **CD 3%** (ENaC) · **TIN = tubular dysfunction out of proportion to the fall in GFR** · urine osm <600 · urine pH >5.5 · UAG positive · FE-HCO_3^- >15% = type 2 · LMW proteinuria, albumin:total protein <0.4 · **urine eosinophils obsolete** · CKDu Uddanam · tenofovir, rifampicin, NSAIDs

Q2 Loop of Henle; Bartter's syndrome

10 M | STD

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 10 M

Anatomy first 1 M	Countercurrent multiplier 3 M	TAL transport 2 M	Bartter syndrome 2 M	Clinical & DDx 1 M	Management 1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: countercurrent multiplication as a **mechanism** you can derive, plus whether you can reason forward from **loss of NKCC2 → the whole Bartter phenotype**. This is a physiology question wearing a clinical coat.
Earns the marks: distinguishing the **single effect (200 mOsm)** from its **multiplication along the loop**; the line '**Bartter is a genetic loop diuretic**'; and **urine calcium** as the one test that separates Bartter (high) from Gitelman (low).
Loses the marks: describing the gradient without ever naming the single effect; confusing the **multiplier** (loop) with the **exchanger** (vasa recta); omitting urine calcium and magnesium.

■ CORE 1 M

Anatomy first

Two sentences — then move to mechanism.

The **loop of Henle** connects the PCT to the DCT and consists of the thin descending limb, thin ascending limb and thick ascending limb (TAL). Only the 15% juxtamedullary nephrons have long loops with accompanying vasa recta, and these generate the medullary osmotic gradient (300 → 1200 mOsm/kg from cortex to papilla).

BASIC SCIENCE

Functions: (1) countercurrent multiplication → medullary hypertonicity; (2) reabsorbs ~25% of filtered Na^+; (3) the water-impermeable TAL is the **diluting segment** — it makes urine hypotonic (~100 mOsm/kg); (4) paracellular reabsorption of Ca^{2+} and Mg^{2+}; (5) site of macula densa → tubuloglomerular feedback.

■ CORE 3 M

Countercurrent multiplier

Draw this — 4 arrows, 2 minutes, guaranteed marks.

```
NKCC2 in TAL pumps Na-K-2Cl out (water CANNOT follow)
        |
        v  'SINGLE EFFECT' = 200 mOsm gradient at any level
Interstitium hypertonic  <-->  Tubular fluid hypotonic (~100 mOsm)
        |
        v  Countercurrent flow MULTIPLIES it axially
Cortex 300  ->  Outer medulla 600  ->  Papilla 1200 mOsm/kg
        |
        +-- UREA RECYCLING (UT-A1/A3, ADH-driven) = ~half the gradient
        +-- VASA RECTA = countercurrent EXCHANGER (passive; preserves gradien
t)
        v
ADH -> V2 -> AQP2 in collecting duct -> water exits -> CONCENTRATED URINE
```

■ CORE 2 M

TAL transport

The lumen-positive PD is the single most examined concept here.

NKCC2 brings Na^+-K^+-$2Cl^-$ in; K^+ **recycles back into the lumen through ROMK**, creating a lumen-positive transepithelial potential (+8 mV) that drives paracellular reabsorption of Na^+, Ca^{2+} and Mg^{2+} through claudin-16/19. Cl^- exits basolaterally via ClC-Kb, which requires the β-subunit **barttin** (also expressed in the inner ear → deafness in type 4).

■ CORE 2 M

Bartter syndrome

Define → classify → contrast with Gitelman. Never skip the genes.

DEFINITION / CRITERIA

Bartter syndrome = a group of autosomal recessive salt-losing tubulopathies caused by loss of function of TAL transporters, producing a 'loop-diuretic-like' state: hypokalaemic hypochloraemic metabolic alkalosis, hyperreninaemic hyperaldosteronism with **normal or low blood pressure**, and hypercalciuria.

Type	Gene / protein	Distinguishing feature
1	SLC12A1 (NKCC2)	Antenatal: polyhydramnios, prematurity, hypercalciuria, nephrocalcin
2	KCNJ1 (ROMK)	Antenatal; **transient neonatal hyperkalaemia** then hypokalaemia
3	CLCNKB (ClC-Kb)	Classic; presents later; Gitelman-like overlap, hypercalciuria often ab
4a / 4b	BSND (barttin) / digenic CLCNKA+CLCNKB	**Sensorineural deafness** + renal failure
5	MAGED2 (X-linked)	Severe but **transient** antenatal form
Bartter-like	*CASR* gain of function	Autosomal dominant hypocalcaemia + hypokalaemic alkalosis

■ ADDS 1 M

Clinical & DDx

The BP + urine Cl^- + urine Ca^{2+} triad separates every mimic.

Presentation: polyuria, polydipsia, salt craving, failure to thrive, growth retardation, muscle weakness, constipation, tetany (if hypomagnesaemic); nephrocalcinosis and stones in types 1–2.

Feature	Bartter	Gitelman	Vomiting / diuretic abuse
Defect	TAL (NKCC2 etc.)	DCT — *SLC12A3* (NCC)	Acquired
Diuretic mimicked	Furosemide	Thiazide	—
Age at onset	Antenatal / infancy	Adolescence / adult	Any
Urine Ca^{2+}	**High** (nephrocalcinosis)	**Low**	Variable
Serum Mg^{2+}	Normal / mildly low	**Markedly low**; chondrocalcinosis, tetany	Normal
Urine Cl^-	High	High	**<25 mEq/L in vomiting**; high with diuretics
Blood pressure	Normal / low	Normal / low	Low

■ INDIA 1 M

Management

Doses — write at least three.

DRUG DOSE

- **Potassium chloride** 1–3 mmol/kg/day in divided doses (KCl, not citrate — alkalosis already present).
- **K^+-sparing:** spironolactone 2–5 mg/kg/day *or* amiloride 0.3–0.5 mg/kg/day.
- **Indomethacin 1–3 mg/kg/day** — blocks the PGE_2 excess that drives renin; most effective in antenatal Bartter. Monitor for GI bleeding, NEC in neonates and NSAID nephrotoxicity.
- **Magnesium** supplementation (essential in Gitelman); liberal salt and water intake; growth-hormone therapy if growth failure persists.

INDIAN RELEVANCE

- Reliable contemporary nationally representative Indian data on Bartter prevalence are limited; case series are from tertiary paediatric nephrology units.
- **Commonest mimic in Indian practice:** surreptitious furosemide use, chronic vomiting, laxative abuse, and **heat-stress salt depletion** in outdoor labourers — exclude these before invoking a genetic tubulopathy.
- Genetic confirmation (NGS tubulopathy panels) is now available in India but out-of-pocket; diagnosis remains largely biochemical.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

The loop of Henle creates the medullary gradient by countercurrent multiplication, driven by NKCC2 and the lumen-positive potential in the TAL. Bartter syndrome is the genetic knockout of this segment — a hypokalaemic alkalosis with hypercalciuria and **normal blood pressure**. The bedside discriminators are blood pressure, urinary calcium and urinary chloride; treatment is potassium, a potassium-sparing agent and indomethacin.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

TDL = AQP1, water only · **TAL = NKCC2, water-impermeable = diluting segment** · **single effect 200 mOsm × countercurrent multiplication → 1200** · **urea ≈ 50% of the gradient** (UT-A1/A3) · **vasa recta = exchanger, NOT multiplier** · **Bartter = a genetic loop diuretic**, 5 types (NKCC2 / ROMK / ClC-Kb / barttin / CaSR), **urine Ca^{2+} HIGH**, nephrocalcinosis, deafness (type 4) · **Gitelman = NCC, urine Ca^{2+} LOW, Mg^{2+} very low**, adult, tetany · Rx: KCl 1–3 mmol/kg/day, spironolactone/amiloride, **indomethacin 1–3 mg/kg/day**, Mg^{2+}

Q3 Urinary concentrating mechanism

5 M | STD

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

Definition 1 M	Three requirements 1.5 M	Key numbers 1 M	When it fails 1 M	Test & India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: the **three requirements** for concentrated urine — and, in the viva, which one has failed in the patient in front of you.
Earns the marks: naming all three (hypertonic medulla · preserved vasa recta · ADH-responsive collecting duct), giving **urea's ~50% contribution** to the gradient, and converting the physiology into a differential diagnosis.
Loses the marks: drawing the loop of Henle and stopping there; forgetting urea; not stating the numbers (50 → 1200 mOsm/kg).

■ CORE 1 M
Definition

DEFINITION / CRITERIA

The **urinary concentrating mechanism** is the ability of the kidney to excrete solute in a minimal volume of water by generating a hypertonic medullary interstitium (300 → 1200 mOsm/kg) and then equilibrating collecting-duct fluid with it under ADH control. It allows urine osmolality to range from 50 to 1200 mOsm/kg.

■ CORE 1.5 M
Three requirements

State these three — they are the marking scheme.

(1) A hypertonic medulla (countercurrent multiplier, TAL). **(2)** Its preservation (countercurrent exchanger, vasa recta). **(3)** A water-permeable collecting duct (ADH → AQP2). Failure of any one abolishes concentration.

```
TAL: NKCC2 pumps NaCl out, water impermeable  ->  'single effect' 200 mOsm
                    |  multiplied by countercurrent flow
                    v
Papillary interstitium 1200 mOsm  <--  UREA recycling (UT-A1/A3) ~50%
                    |
                    |  vasa recta = countercurrent EXCHANGER (does not wash out)
                    v
ADH -> V2 receptor -> Gs -> cAMP -> PKA -> AQP2 (Ser256-P) to apical membrane
                    v
Water leaves CD down the gradient  ->  urine up to 1200 mOsm/kg
```

■ CORE 1 M
Key numbers

Parameter	Value	Why it matters
Max / min urine osmolality	1200 / 50 mOsm/kg	Obligatory urine volume ≈ 500 mL/day
Medullary gradient contributors	NaCl ~50%, **urea ~50%**	Protein malnutrition → low urea → poor concentration
ADH osmotic threshold	280–285 mOsm/kg	Thirst threshold is higher (290–295)
Diluting segment	TAL (water-impermeable)	Loop diuretics abolish **both** concentration and dilution

■ ADDS 1 M
When it fails

Convert physiology into a differential — this is where marks are won.

Defect	Mechanism	Example
Loss of gradient (medullary washout)	TAL transport blocked or medulla damaged	Loop diuretics, chronic TIN, sickle-cell (papilla), high-flo
ADH deficiency	Central AVP-D	Trauma, tumour, granuloma, TB hypophysitis
ADH resistance	V2 / AQP2 failure	**Lithium**, hypokalaemia, hypercalcaemia, obstruction, A mutation
Low urea delivery	Reduced gradient	Protein malnutrition, excess water intake
Osmotic diuresis	Solute drags water	Uncontrolled diabetes, mannitol, high-protein feeds

■ INDIA 0.5 M
Test & India

INVESTIGATION

Bedside test: **early-morning urine osmolality** — >600 mOsm/kg effectively excludes a concentrating defect. Formal: **water deprivation test** ± desmopressin; modern practice prefers **arginine- or hypertonic saline-stimulated copeptin** (Fenske, *NEJM* 2018), which outperforms the classic test. Nomenclature updated 2022: central DI → **AVP-deficiency**, nephrogenic DI → **AVP-resistance**.

INDIAN RELEVANCE

Loss of concentrating ability is the **earliest functional abnormality** in the chronic interstitial nephritis of **CKDu (Uddanam belt, coastal Andhra/south Odisha)**, and in chronic lithium therapy — both present as nocturia with a bland urinary sediment long before creatinine rises. Copeptin assays are not widely available in India; the water deprivation test remains standard.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

Concentration = **a hypertonic medulla** (TAL countercurrent multiplier + urea recycling), **preserved by the vasa recta**, **exploited by ADH via AQP2**. Nocturia and an early-morning urine osmolality <600 mOsm/kg are the earliest clinical footprints of its failure.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

3 requirements: hypertonic medulla · preserved vasa recta · ADH-responsive CD · urine osm **50 → 1200 mOsm/kg** · gradient = **50% NaCl + 50% urea** · max/min urine 1200/50 · obligatory urine volume **500 mL/day** · ADH threshold 280–285 · **V2 → cAMP → PKA → AQP2 (Ser256)** · **early-morning urine osm >600 excludes a concentrating defect** · earliest defect in CKDu and lithium

Q4 Bladder innervation; dysfunction

10 M | PYQ 2×

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 10 M

Open with this 1 M	Innervation 3 M	Reflex arc 2 M	Classification 2 M	Red flags 0.5 M	Evaluation 0.5 M	Management 1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: three nerves with their **segments and receptors**, then whether you can convert a **lesion level into a bladder type**. The examiner is checking you can localise, not recite.
Earns the marks: the triad — **pelvic S2–S4 (M3) · hypogastric T10–L2 (α₁, β₃) · pudendal S2–S4 (Onuf's nucleus)** — and a classification **by lesion level** (suprapontine / suprasacral / sacral / infrasacral), each with its urodynamic signature.
Loses the marks: reciting nerves without mapping them to a bladder type; classifying by eponym instead of by level; never separating **storage** from **voiding** failure.

■ CORE 1 M
Open with this

Micturition is a spino-bulbo-spinal reflex under voluntary cortical control. Continence and voiding require reciprocal (synergic) activity of the detrusor and the two sphincters, coordinated by the **pontine micturition centre (Barrington's nucleus)**. Any lesion of this axis produces a **neurogenic bladder**, whose pattern is predicted by the *level* of the lesion.

■ CORE 3 M
Innervation

Draw this table — it answers half the question.

Nerve	Origin	Transmitter / receptor	Action
Pelvic (parasympathetic)	S2–S4 (sacral micturition centre)	ACh → **M3** (>M2)	Detrusor **contraction** =
Hypogastric (sympathetic)	T10–L2 (intermediolateral column)	NA → **α₁** at bladder neck; **β₃** on detrusor	Internal sphincter contrac detrusor relaxes = **stora**
Pudendal (somatic)	S2–S4 (**Onuf's nucleus**)	ACh → nicotinic	External urethral sphincte contraction (voluntary)
Afferents	Aδ (stretch) via pelvic; **C-fibres** (nociceptive, normally silent)	→ PAG → PMC	C-fibres become active af injury → detrusor overact

■ CORE 2 M
Reflex arc

Two-minute diagram.

```
Filling  ->  A-delta stretch afferents (pelvic n.)  ->  sacral cord S2-S4
         ->  PAG  ->  PONTINE MICTURITION CENTRE  ->  medial frontal cortex
STORAGE : sympathetic T10-L2 ON (alpha1 neck contracts, beta3 detrusor relaxe
s)
          + pudendal ON  = 'GUARDING REFLEX'
VOIDING : cortex permits -> PMC fires -> sympathetic + pudendal OFF
          -> parasympathetic S2-S4 ON -> detrusor contracts, sphincters relax
          = DETRUSOR-SPHINCTER SYNERGY
```

■ CORE 2 M
Classification

Level of lesion → bladder pattern. This is the examiner's favourite.

Lesion level	Example	Bladder type	Clinical picture
Suprapontine	Stroke, Parkinson's, dementia, tumour	Uninhibited / detrusor overactivity, **synergic** sphincter	Urgency, frequency, urge inc sensation preserved; low res
Suprasacral cord (above conus)	SCI, transverse myelitis, MS, **Pott's spine**	**Automatic (reflex, UMN) bladder** — detrusor overactivity + **detrusor-sphincter dyssynergia**	Reflex voiding, incomplete e high pressures → upper tract autonomic dysreflexia if ≥T6
Sacral / infrasacral	Conus, cauda equina, pelvic surgery, diabetic cystopathy	**Autonomous (atonic, LMN) bladder** — detrusor areflexia	Retention with **overflow inc** large residual, absent reflexe
Sensory (afferent) lesion	Tabes dorsalis, diabetes, B_{12} deficiency	Sensory atonic bladder	Painless huge-capacity inser bladder, overflow

■ DIST 0.5 M
Red flags

RED FLAG / EMERGENCY

- **Cauda equina syndrome** — saddle anaesthesia, painless retention, lax anal tone: emergency MRI + decompression <48 h.
- **Autonomic dysreflexia** (lesion ≥T6): severe hypertension, pounding headache, bradycardia, flushing/sweating above the level. **Sit the patient up, remove the trigger (drain the bladder first), then nifedipine 10 mg bite-and-swallow or GTN** — never nitrates if a PDE-5 inhibitor was taken in 24 h.
- **Detrusor leak-point pressure >40 cmH_2O** predicts hydronephrosis and reflux — the single most important urodynamic number.

■ ADDS 0.5 M
Evaluation

INVESTIGATION

Bladder diary + post-void residual (USG) → urinalysis/culture → serum creatinine → **USG KUB for upper tracts** → **urodynamics/video-urodynamics** (the definitive test; do at ~3 months after SCI once spinal shock resolves, then annual surveillance) → MRI spine to define the lesion → cystoscopy if haematuria or long-term catheter.

■ INDIA 1 M

Management

Principle: protect the kidney first, continence second.

MANAGEMENT

- **Clean intermittent catheterisation (CIC)** 4–6 times/day — the gold standard; indwelling catheter only if CIC is impossible.
- **Antimuscarinics:** oxybutynin 5 mg TDS, solifenacin 5–10 mg OD, tolterodine 2 mg BD (dry mouth, constipation, cognitive effects — avoid oxybutynin in the elderly).
- **Mirabegron** 25–50 mg OD (β_3 agonist) — fewer anticholinergic effects; check BP.
- **α-blocker** (tamsulosin 0.4 mg OD) for dyssynergia and bladder-neck obstruction.
- **Refractory neurogenic detrusor overactivity:** intradetrusor onabotulinumtoxinA **200 U** (repeat ~6-monthly) — counsel that CIC may become necessary.
- Areflexic bladder: CIC ± Credé/Valsalva only if outlet is low-pressure (never with dyssynergia).
- Surgery: sphincterotomy, augmentation cystoplasty, sacral neuromodulation, urinary diversion.

INDIAN RELEVANCE

- Commonest Indian causes: **road traffic accidents and fall from a height/tree** (SCI), **Pott's spine and tubercular myelitis**, transverse myelitis, and **diabetic cystopathy** — test post-void residual in every long-standing diabetic with recurrent UTI.
- **Reusable catheters** cleaned and re-used are standard Indian practice: single-use hydrophilic catheters are unaffordable for most; clean (not sterile) technique has acceptable UTI rates and remains preferable to an indwelling catheter.
- Do **not** treat asymptomatic bacteriuria in patients on CIC — a major driver of antimicrobial resistance.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

Storage is sympathetic (T10–L2, α_1 and β_3) plus pudendal; voiding is parasympathetic (S2–S4, M3); the pons ensures synergy. Suprapontine lesions cause an overactive but synergic bladder, suprasacral lesions cause an automatic bladder with dyssynergia that **threatens the kidneys**, and sacral lesions cause an atonic bladder with overflow. Management is CIC plus detrusor relaxation, guided by urodynamics, with upper-tract protection as the overriding aim.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Pelvic S2–S4, M3 → VOID · **Hypogastric T10–L2: α_1 neck + β_3 dome → STORE** · **Pudendal S2–S4 (Onuf's nucleus) → EUS, voluntary** · PMC = Barrington (M-region void, L-region store), PAG, cortex · **Suprapontine** = DO, sphincter **synergic** · **Suprasacral** = DO + **DSD** · **Sacral/conus** = areflexic · storage vs voiding failure · Rx: **CIC** + antimuscarinic / β_3-agonist (mirabegron) / botulinum · Pott's spine = commonest Indian cause

Q5 Bladder nerve supply; automatic bladder

10 M | STD

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 10 M

Definition 1 M	Nerve supply 3 M	Evolution after SCI 2 M	Automatic vs autonomous 2 M	Complications 1 M	Management 1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: the same anatomy as Q4, but the examiner now wants the **time course after spinal cord injury** and the precise meaning of the term '**automatic bladder**'.
Earns the marks: the sequence **spinal shock → areflexic bladder → automatic (reflex) bladder** with its timeline; the **automatic vs autonomous** distinction (lesion **above** the conus vs **at/below** it); and **autonomic dysreflexia** above T6.
Loses the marks: using 'automatic' and 'autonomous' as synonyms — the examiner is specifically testing this; omitting autonomic dysreflexia, which is a lethal, and therefore unforgivable, miss.

■ CORE 1 M

Definition

Give this definition first — most candidates cannot.

DEFINITION / CRITERIA

Automatic (reflex / UMN) bladder = reflex emptying of the bladder mediated entirely by the intact sacral (S2–S4) micturition reflex arc, occurring below a **complete suprasacral spinal cord lesion** after spinal shock has passed, with loss of both sensation and voluntary control, and loss of pontine coordination → detrusor-sphincter dyssynergia.

■ CORE 3 M

Nerve supply

Recall in one table, then spend your time on the clinical part.

Component	Nerve / segment	Receptor	Function
Detrusor	Pelvic n. — parasympathetic **S2–S4**	M3 (ACh)	Contraction → voiding
Detrusor (storage)	Hypogastric n. — sympathetic **T10–L2**	β_3 (NA)	Relaxation → filling
Internal (smooth) sphincter	Hypogastric n. — sympathetic T10–L2	α_1 (NA)	Contraction → continence
External (striated) sphincter	Pudendal n. — somatic S2–S4 (**Onuf's nucleus**)	Nicotinic (ACh)	Voluntary contraction
Afferents	Aδ stretch (pelvic); C-fibres (silent)	→ PAG → PMC → cortex	Sensation of fullness; C-fib drive the reflex after SCI

■ CORE 2 M

Evolution after SCI

Draw this timeline — it *is* the answer to 'automatic bladder'.

```
COMPLETE SUPRASACRAL CORD LESION (e.g. T6 traumatic SCI, Pott's spine)
        |
        v  PHASE 1 - SPINAL SHOCK  (2-12 weeks)
  Areflexia: flaccid, ATONIC bladder -> painless RETENTION -> overflow
  Management: indwelling catheter first days -> switch to CIC early
        |
        v  PHASE 2 - RECOVERY OF REFLEXES (C-fibre afferents emerge)
        v  PHASE 3 - AUTOMATIC (REFLEX) BLADDER
  Reflex void at ~200-300 mL, no sensation, no voluntary control
  Triggered by suprapubic tapping / thigh stroking / anal stretch
  BUT pons is disconnected -> DETRUSOR-SPHINCTER DYSSYNERGIA
        |
        v
  HIGH intravesical pressure + incomplete emptying
  -> VUR -> hydronephrosis -> stones, UTI -> CKD  (the real killer)
```

■ CORE 2 M

Automatic vs autonomous

The examiner will ask exactly this contrast.

Feature	Automatic (reflex, UMN)	Autonomous (atonic, LMN)
Lesion	Above the conus (suprasacral)	Conus / cauda equina / pelvic nerves
Reflex arc	**Intact**	**Destroyed**
Detrusor	Overactive, small capacity	Areflexic, large capacity
Sphincter	Dyssynergic (spastic)	Flaccid
Voiding	Reflex, triggered	By straining / Credé / CIC
Residual urine	Moderate–high	Very high
Incontinence	Reflex incontinence	Overflow (dribbling)
Bulbocavernosus / anal tone	Present / increased	**Absent** / lax
Upper tract risk	**High** (dyssynergia, DLPP >40 cmH_2O)	Lower unless outlet obstructed

■ ADDS 1 M

Complications

RED FLAG / EMERGENCY

- **Autonomic dysreflexia** (lesions ≥T6): paroxysmal severe hypertension, throbbing headache, reflex bradycardia, flushing and sweating *above* the lesion, pallor and piloerection *below*. Trigger is usually a distended bladder or bowel. **Sit up → loosen constrictions → drain the bladder/relieve the trigger → nifedipine 10 mg bite-and-swallow or GTN if SBP stays >150 mmHg.** Can cause intracerebral haemorrhage, seizures and death.
- Recurrent UTI and urosepsis; struvite and calcium stones (immobilisation hypercalciuria); VUR and hydronephrosis; **CKD — historically the leading cause of late death after SCI**; squamous carcinoma with long-term indwelling catheter (>10 y).

■ INDIA 1 M

Management

MANAGEMENT

- **CIC 4–6 times/day** aiming to keep volumes <400–500 mL — the single most important intervention.
- **Antimuscarinic** (solifenacin 5–10 mg OD / oxybutynin 5 mg TDS) or **mirabegron** 25–50 mg OD to convert a high-pressure reflex bladder into a low-pressure reservoir.
- **Tamsulosin** 0.4 mg OD for dyssynergia; **intradetrusor onabotulinumtoxinA 200 U** if refractory.
- **Urodynamics at ~3 months, then annual** upper-tract USG + creatinine surveillance for life.
- Refractory: sphincterotomy or urethral stent (male, condom drainage), augmentation cystoplasty, sacral neuromodulation, Mitrofanoff, or diversion.
- Avoid: chronic indwelling catheter, treating asymptomatic bacteriuria, Credé/Valsalva in the presence of dyssynergia.

INDIAN RELEVANCE

- Aetiology in India: **fall from height/tree and road traffic accidents** dominate traumatic SCI; **tuberculous (Pott's) paraplegia** is the leading non-traumatic cause — always image the spine and start ATT under NTEP.
- Reusable (clean, not sterile) catheters are the norm; teach the patient or a family member. Ensure supply and hand hygiene.
- Lifelong urological surveillance is poorly implemented outside tertiary centres — build it into the discharge plan; PMJAY covers urodynamics and botulinum toxin at empanelled centres.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

The bladder is stored by the sympathetic (T10–L2) and pudendal nerves and emptied by the parasympathetic (S2–S4); the pons provides synergy. After a complete suprasacral lesion, spinal shock gives an atonic bladder, and its resolution gives an **automatic bladder** — reflex emptying without sensation, control or synergy. Because dyssynergia generates high pressures, the aim of treatment is not continence but **preservation of the upper tracts**: CIC, detrusor relaxation, and lifelong urodynamic surveillance.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Spinal shock → areflexic bladder → automatic bladder · **AUTOMATIC = lesion ABOVE the conus** — reflex, DSD, empties to a trigger · **AUTONOMOUS = conus / cauda equina** — areflexic, overflow, needs Credé / CIC · **Autonomic dysreflexia: lesion ≥T6** — BP surge + pounding headache + **bradycardia**, flushing above / pallor below · **Rx: sit patient UP, remove the trigger (blocked catheter, faecal impaction), nifedipine/GTN** · CIC is the standard of care; reusable clean catheters in India

Q6 Estimation of GFR

5 M | PYQ 2×

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

Definition 1 M	Methods 2 M	Caveats 1 M	Guideline & India 1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: that you understand eGFR is an **estimate**, and — more importantly — **when it lies**. A short note that only lists formulae scores 2/5.
Earns the marks: CKD-EPI 2021 (race-free) as the current equation with **cystatin C** to confirm when accuracy changes management (KDIGO 2024); the **falsely high** scenarios (low muscle mass, cirrhosis, amputee, **vegetarian/low-protein Indian diet**); and drugs that **raise creatinine without touching GFR**.
Loses the marks: quoting Cockcroft–Gault as the current standard; not knowing CrCl overestimates GFR by 10–20%; reporting a G stage without the A (albuminuria) stage.

■ CORE 1 M

Definition

DEFINITION / CRITERIA

GFR = the volume of plasma cleared of a substance by the glomeruli per unit time; normal 120 ± 25 mL/min/1.73 m². The ideal marker is freely filtered, and neither reabsorbed, secreted, metabolised nor protein-bound — hence **inulin clearance is the gold standard**. GFR = (U × V)/P.

■ CORE 2 M

Methods

Classify — never list randomly.

Method	How	Comment
Exogenous (measured GFR)	Inulin (gold standard); iohexol, ^{99m}Tc-DTPA, ^{51}Cr-EDTA, iothalamate	Accurate; used for donor evaluation, chemotherapy research. Costly, needs infusion/isotope.
Creatinine clearance	24-h urine; (U_{Cr} × V)/P_{Cr}	**Overestimates GFR by 10–20%** (tubular secretio errors are the main problem
Cockcroft–Gault	[(140−age) × wt] / (72 × S_{Cr}) × 0.85 if female	Gives **creatinine clearance, not indexed to BSA** for many **drug dose** labels (e.g. DOACs)
MDRD	4-variable	Validated only for GFR <60; underestimates at high
CKD-EPI 2021	Creatinine-based, **race-free**	Current recommended equation for reporting eGFR
Cystatin C	CKD-EPI$_{Cys}$ or combined creatinine–cystatin C	**Most accurate** when combined; independent of m affected by steroids, thyroid disease, obesity, smok

■ ADDS 1 M

Caveats

Every one of these is a viva question.

COMMON MISTAKE / TRAP

- eGFR equations assume a **steady state** — **invalid in AKI** (use kinetic eGFR or trends).
- **Falsely high eGFR:** low muscle mass — elderly, cirrhosis, amputees, malnutrition, and the Indian vegetarian/low-protein diet (low creatinine generation).
- **Falsely low eGFR:** high muscle mass, creatine supplements, cooked-meat meal before sampling.
- **Creatinine rises without any fall in GFR** (blocked tubular secretion): **trimethoprim, cimetidine, dolutegravir, cobicistat, ritonavir** — do not label this AKI.
- Confirm CKD with a repeat eGFR after ≥90 days; always report eGFR **with albuminuria (ACR)** — KDIGO staging is G×A.

■ INDIA 1 M

Guideline & India

INDIAN RELEVANCE

KDIGO 2024 CKD guideline: report creatinine-based eGFR (CKD-EPI 2021) as standard; use **cystatin C to confirm** when creatinine-based eGFR is likely to be inaccurate or when the result will change management. Race-based coefficients have been removed.
Indian relevance: validation studies in Indian cohorts show a modest bias with CKD-EPI, and a widely accepted India-specific coefficient is **not established** — reliable nationally representative validation data remain limited. Cystatin C is available in India but costly and not standardised across laboratories; **24-h creatinine clearance remains widely used**, and ^{99m}Tc-DTPA is the practical measured-GFR method for living-donor workup.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

Inulin clearance is the gold standard but is a research tool; in practice GFR is **estimated** with **CKD-EPI 2021 creatinine**, confirmed by **cystatin C** when accuracy matters, and measured with iohexol or ^{99m}Tc-DTPA when it must be exact. Always interpret eGFR alongside albuminuria, the clinical steady state and the patient's muscle mass.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Inulin = gold standard; measured GFR = iohexol, ^{99m}Tc-DTPA, ^{51}Cr-EDTA · **CKD-EPI 2021 (race-free)** · **cystatin C confirms when accuracy changes management (KDIGO 2024)** · Cockcroft–Gault gives **CrCl, not indexed** · **24-h CrCl overestimates GFR by 10–20%** · **Falsely HIGH eGFR**: low muscle, elderly, cirrhosis, amputee, **vegetarian/low-protein diet** · **Cr ↑ without GFR fall**: trimethoprim, cimetidine, dolutegravir, cobicistat, ritonavir · **G1–G5 × A1–A3, always report both**; CKD needs ≥90 days

Q7 GFR; tubular transport; acidosis mgmt

10 M | STD

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 10 M

Part 1 — GFR	Part 2 — Tubular transport	Part 3 — Acidosis	RTA at a glance	Emergency & CKD	Indian relevance
2 M	2 M	2 M	2 M	1 M	1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: three linked parts carrying roughly equal marks. This is a time-management question as much as a knowledge question — most candidates answer part 1 beautifully and never reach part 3.
Earns the marks: allocating time to all three parts; the algorithm **anion gap → urine anion gap → serum K^+ → RTA type**; and **exact alkali doses** (1–2 mEq/kg/day distal vs 5–15 mEq/kg/day proximal — the difference is itself a favourite question).
Loses the marks: writing a long GFR essay and running out of time before acidosis management, which carries the same marks; using the urine anion gap when ketones or hippurate are present instead of the **urine osmolal gap**.

■ CORE 2 M

Part 1 — GFR

Definition + determinants + autoregulation. Keep it to 6 lines.

GFR is the volume of plasma filtered per unit time (120 ± 25 mL/min/1.73 m²). **GFR = Kf × [(P_{GC} − P_{BS}) − (π_{GC} − π_{BS})]**; with P_{GC} 45–50, P_{BS} 10–15 and π_{GC} 25–30 mmHg, the net ultrafiltration pressure is only ~10–15 mmHg. Renal blood flow is 20–25% of cardiac output; RPF ~600 mL/min; **filtration fraction = GFR/RPF ≈ 0.2**.

```
AUTOREGULATION (MAP 80-180 mmHg)
  1. MYOGENIC reflex   : stretch -> afferent arteriolar constriction
  2. TUBULOGLOMERULAR FEEDBACK :
       high NaCl at MACULA DENSA -> NKCC2 uptake -> ADENOSINE
       -> A1 receptor -> AFFERENT constriction -> GFR falls
  3. Angiotensin II  -> EFFERENT constriction -> maintains GFR when RPF low
     (hence the acute eGFR 'dip' with ACEi/ARB and with SGLT2 inhibitors)
```

■ CORE 2 M

Part 2 — Tubular transport

Segment → transporter → drug → disease. One table.

Segment	Transport	Drug acting here	Disease
PCT	65% Na^+/H_2O; 100% glucose; 80–90% HCO_3^- (NHE3 + carbonic anhydrase); PO_4, AA, urate	Acetazolamide, **SGLT2 inhibitors**, mannitol (osmotic)	Type 2 RTA, Fanco
TAL	25% Na^+ via NKCC2; lumen-positive PD → paracellular Ca^{2+}/Mg^{2+}	Furosemide, torsemide	Bartter
DCT	5–10% Na^+ via NCC; Ca^{2+} via TRPV5	Thiazides	Gitelman, Gordon
CNT/CD	Na^+ via ENaC; K^+ via ROMK/BK; H^+ via H^+-ATPase; H_2O via AQP2	Amiloride, spironolactone, tolvaptan	Liddle, dRTA, PHA, nephrogenic DI

Carrier-mediated transport shows **saturation (T_m)**, competition and specificity: glucose T_m ≈ 375 mg/min, renal threshold ~180 mg/dL, with **splay** due to nephron heterogeneity — the basis of glycosuria in diabetes and of SGLT2-inhibitor glycosuria at normal glucose levels.

■ CORE 2 M

Part 3 — Acidosis

Define → classify → localise with the urine anion gap → treat.

DEFINITION / CRITERIA

Metabolic acidosis = primary fall in HCO_3^- with compensatory fall in $PaCO_2$ (**Winter's formula:** expected $PaCO_2$ = 1.5 × HCO_3^- + 8 ± 2). Classify by **anion gap** = Na^+ − (Cl^- + HCO_3^-), **corrected +2.5 per 1 g/dL fall in albumin**.

```
METABOLIC ACIDOSIS -> Anion gap?
  HIGH AG ('GOLD MARK'): Glycols, Oxoproline, L-lactate, D-lactate,
         Methanol, Aspirin, Renal failure, Ketoacidosis
  NORMAL AG (hyperchloraemic) -> URINE ANION GAP (Na+K-Cl)
         NEGATIVE ('neGUTive') -> GI loss: diarrhoea, ureteric diversion
         POSITIVE -> RENAL TUBULAR ACIDOSIS -> check serum K+
               K+ LOW  -> type 1 (urine pH >5.5) or type 2 (FE-HCO3 >15%)
               K+ HIGH -> type 4 (urine pH <5.5, hypoaldosteronism)
```

■ CORE 2 M

RTA at a glance

	Type 1 (distal)	Type 2 (proximal)	Type 4
Defect	H^+-ATPase secretion	HCO_3^- reabsorption threshold	Aldosterone deficiency/resis
Serum K^+	Low	Low	**High**
Urine pH	**>5.5 always**	<5.5 once below threshold	<5.5
Serum HCO_3^-	Can be <10	12–18 (plateau)	>17
Stones/nephrocalcinosis	**Yes**	No (citrate preserved)	No
Causes	Sjögren, SLE, amphotericin B, obstruction, sickle cell, **idiopathic (common in India)**	Myeloma, **tenofovir**, ifosfamide, Wilson, cystinosis, acetazolamide	Diabetes, CNIs, NSAIDs, ACEi/ARB, heparin, trimetho obstruction
Treatment	$NaHCO_3$ **1–2 mEq/kg/day** + **K^+ citrate**	Large alkali **5–15 mEq/kg/day** + K^+; thiazide (contraction)	Low-K^+ diet, **fludrocortiso 0.1 mg OD**, loop diuretic, K binder

■ ADDS 1 M

Emergency & CKD

MANAGEMENT

- **Treat the cause** — insulin + fluids in DKA, source control in sepsis, dialysis in poisoning.
- **Severe acidaemia (pH <7.1):** bicarbonate remains controversial. **BICAR-ICU (Lancet 2018)** showed no overall mortality benefit, but a **survival benefit in the AKIN stage 2–3 subgroup**. Give 1–2 mEq/kg slowly; watch for hypernatraemia, hypokalaemia, hypocalcaemia, volume overload and paradoxical CNS acidosis.
- **Chronic acidosis of CKD:** KDIGO recommends oral bicarbonate if serum HCO_3^- <22 mmol/L, targeting ≥22 (slows CKD progression, improves nutrition). Note the neutral **BiCARB trial (2020)** in older adults — individualise. **Veverimer** (HCl binder) is investigational.
- Dialysis for refractory acidosis with oliguria, uraemia, hyperkalaemia or poisoning.

■ INDIA 1 M

Indian relevance

One India line converts a good answer into a gold-medal answer.

INDIAN RELEVANCE

- **Normal-AG acidosis:** acute **diarrhoeal disease** is the commonest cause nationally. **Tenofovir** (NACO first-line ART) is the commonest drug cause of **proximal (type 2) RTA and Fanconi syndrome** — monitor creatinine, phosphate and urine dipstick; switch to TAF or abacavir. **Sjögren's-associated distal (type 1) RTA** is a common, treatable and frequently missed Indian cause of **hypokalaemic paralysis** presenting to medical casualty — check urine pH before labelling it periodic paralysis. Toluene (adhesive) inhalation in street youth gives a normal-AG acidosis with a **falsely positive urine anion gap** (hippurate) — use the urine osmolal gap.
- **High-AG acidosis:** the tropical quartet of **snake envenomation, falciparum malaria, leptospirosis and sepsis** dominates community-acquired AKI with acidosis in India.
- **Therapy:** oral **sodium bicarbonate 500 mg tablets (≈ 6 mEq each)** and **Shohl's solution / potassium citrate** are cheap and widely available — the practical mainstay. **Veverimer is not available in India.** Reliable nationally representative Indian data on RTA prevalence are limited.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

GFR is set by Starling forces across a high-Kf capillary, defended by myogenic and tubuloglomerular autoregulation. Each tubular segment carries a signature transporter, so each drug and each tubulopathy maps onto a segment. Metabolic acidosis is localised by the anion gap and then the **urine anion gap**: a positive urine anion gap means the kidney is at fault, and serum potassium then separates type 1, type 2 and type 4 RTA — which differ fundamentally in the dose of alkali they need.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

GFR = Kf[(P_GC − P_BS) − π_GC]; 45–10–25 → net **10–15 mmHg** · **AG = Na^+ − (Cl^- + HCO_3^-) = 8–12** · high AG = **GOLD MARK** · **UAG neGUTive = GI loss; positive = RTA** · **Type 1**: urine pH >5.5, K^+↓, stones, alkali **1–2 mEq/kg/day** · **Type 2**: FE-HCO_3^- >15%, alkali **5–15 mEq/kg/day** · **Type 4**: K^+↑, fludrocortisone **0.1 mg** · **BICAR-ICU (Lancet 2018)**: benefit only in AKIN 2–3 · KDIGO: oral bicarb if HCO_3^- <22 · veverimer investigational

Q8 Glomerular & PCT/loop/DCT disease

10 M | STD

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 10 M

Framing 0.5 M	Glomerular disease 2 M	Tubular disease by segment 2.5 M	Bedside discriminators 1 M	Stepwise Ix 1.5 M	Management principles 1.5 M	Recent 0.5 M	India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: whether you can organise renal disease **anatomically** — by the segment that has failed — rather than reproducing a memorised list of glomerulonephritides.
Earns the marks: one disease per segment tied to its transporter, plus the **bedside discriminators** that localise without a biopsy — **glycosuria with normal blood glucose = PCT**; hypokalaemic alkalosis with high urine Ca = TAL; with low urine Ca = DCT.
Loses the marks: answering only the glomerular half and ignoring the tubular half (which carries more marks here); offering a biopsy for a tubulopathy, where the answer is a **genetic panel**.

■ CORE 0.5 M

Framing

This is a 'localise the lesion' question. Say so in line 1.

Renal disease can be localised to a nephron segment because each segment has a unique transporter and a unique urinary signature. The examiner wants: glomerular disease → protein and blood; PCT disease → Fanconi; loop disease → Bartter/salt wasting; DCT disease → Gitelman/Gordon.

■ CORE 2 M

Glomerular disease

Nephritic vs nephrotic — must be in the answer.

DEFINITION / CRITERIA

Glomerular disease presents as one of five syndromes: asymptomatic urinary abnormality, **nephritic**, **nephrotic**, **rapidly progressive GN**, or chronic GN. The urinary hallmarks are dysmorphic RBCs (>5%, acanthocytes), RBC casts and albuminuria.

	Nephritic	Nephrotic
Proteinuria	<3.5 g/day (sub-nephrotic)	**>3.5 g/day/1.73 m²** (or ACR >3500 mg/g)
Sediment	**Active**: dysmorphic RBC, RBC casts	**Bland**: oval fat bodies, fatty casts, Maltese cross
Blood pressure / GFR	Hypertension, oliguria, GFR falls	Usually normal early
Oedema	Periorbital, from Na^+ retention	Generalised, from hypoalbuminaemia + Na^+ rete
Examples	IgA nephropathy (commonest globally), post-infectious GN, lupus, ANCA, anti-GBM	Minimal change, FSGS, membranous (PLA2R+ in 70–80%), diabetic nephropathy, **amyloidosis**

■ CORE 2.5 M

Tubular disease by segment

Learn this table. It answers PCT, loop and DCT in one block.

Segment	Transporter	Disease	Biochemical signature
PCT	NHE3, SGLT2, NaPi-IIa, URAT1, megalin/cubilin	**Fanconi syndrome**; type 2 (proximal) RTA	Normoglycaemic glycosuria + generalise aminoaciduria + hypophosphataemia + hypouricaemia + LMW proteinuria + norr acidosis; hypokalaemia
TAL	NKCC2, ROMK, ClC-Kb/barttin, claudin-16/19	**Bartter** (types 1–5); FHHNC (claudin-16/19); loop diuretics; hypercalcaemia (CaSR activation)	Hypokalaemic metabolic alkalosis + **hypercalciuria** ± nephrocalcinosis; **norr BP**; salt wasting
DCT	NCC, TRPV5, KCNJ10, WNK1/4-SPAK	**Gitelman** (SLC12A3); **Gordon/PHA2** (WNK1, WNK4, KLHL3, CUL3); EAST/SeSAME; thiazides; CNI toxicity	Gitelman: hypokalaemic alkalosis + **hypo** + **marked hypomagnesaemia**. Gordon **hyperkalaemia + hypertension + nor acidosis, thiazide-responsive**
CD	ENaC, ROMK, H^+-ATPase, AQP2, pendrin	**Liddle** (ENaC gain); PHA1; **distal (type 1) RTA**; nephrogenic DI (AVPR2/AQP2, **lithium**)	Liddle: hypertension + hypokalaemic alka **low renin and low aldosterone**, amiloride-responsive

■ CORE 1 M

Bedside discriminators

EXAMINER PEARL

- **Hypokalaemic alkalosis + normal BP** → Bartter / Gitelman / diuretics / vomiting. **+ Hypertension** → Liddle / primary aldosteronism / apparent mineralocorticoid excess / renovascular.
- **Urine calcium separates the tubulopathies:** Bartter = high, Gitelman = low.
- **Renin + aldosterone separate the hypertensive ones:** both low → Liddle or AME; renin low, aldosterone high → Conn's.
- **Glycosuria with a normal blood glucose** is **always** proximal tubular (or an SGLT2 inhibitor) — never diabetes.

■ ADDS 1.5 M

Stepwise Ix

Cheapest test first — the examiner is testing sequence, not exhaustiveness.

```
BEDSIDE   : BP, oedema, urine dipstick (blood/protein/GLUCOSE), fundus
ROUTINE   : urine microscopy (dysmorphic RBC? casts?), ACR / UPCR,
            creatinine + eGFR, electrolytes, ABG, Ca/PO4/Mg/urate, albumin
LOCALISE  : glycosuria + normal glucose      -> PCT
            urine anion gap / urine pH        -> RTA type
            spot urine Ca:Cr                  -> Bartter (high) vs Gitelman (
low)
            plasma RENIN + ALDOSTERONE + BP   -> Liddle vs Conn's vs PHA2
            LMW proteinuria (b2-M, RBP), albumin:total protein ratio
SPECIFIC  : ANA/dsDNA, C3/C4, ANCA, anti-GBM, anti-PLA2R, SPEP/FLC,
            HBsAg/anti-HCV/HIV, cryoglobulins, urine diuretic screen
IMAGING   : USG KUB (size, echogenicity, CMD), then Doppler if indicated
CONFIRM   : RENAL BIOPSY (glomerular) | GENETIC PANEL (tubulopathy)
```

■ ADDS 1.5 M

Management principles

Segment-specific, not generic.

Disease group	Treatment
Glomerular — all	**ACEi/ARB** titrated to maximum tolerated dose (antiproteinuric); BP <130/80; salt restriction <5 g/day; statin; **SGLT2 inhibitor** (dapagliflozin 10 mg OD / empagliflozin 10 mg OD) now indicate proteinuric CKD irrespective of diabetes (DAPA-CKD 2020, EMPA-KIDNEY 2023); anticoagulate if albumin <2.0–2.5 g/dL in membranous
Immune-mediated GN	Disease-specific immunosuppression — steroids (minimal change), rituximab (PLA2R+ membra MENTOR 2019), cyclophosphamide or rituximab + steroids (ANCA, lupus class III/IV), **plasma exchange + cyclophosphamide + steroids** (anti-GBM — start before biopsy if pulmonary haemorrhage)
Fanconi / type 2 RTA	**Withdraw the culprit (tenofovir → switch to TAF or abacavir under NACO)**; large alkali **5 mEq/kg/day** + K^+; phosphate and vitamin D replacement; treat myeloma if light-chain related
Bartter / Gitelman	KCl 1–3 mmol/kg/day; spironolactone 2–5 mg/kg/day or amiloride; **indomethacin 1–3 mg/kg/d** (Bartter); **magnesium** (essential in Gitelman); liberal salt
Liddle	**Amiloride 5–10 mg OD** or triamterene + low-salt diet. **Spironolactone does not work** — th receptor is normal, the channel is not
Gordon (PHA2)	**Low-dose thiazide** — dramatic response; low-salt diet
Type 4 RTA	Low-K^+ diet, loop diuretic, **fludrocortisone 0.1 mg OD**, K^+ binder to allow RAASi to continue

■ DIST 0.5 M

Recent advances

RECENT ADVANCE

- **SGLT2 inhibitors** — by restoring NaCl delivery to the macula densa they reactivate tubuloglomerular feedback, constrict the afferent arteriole and abolish hyperfiltration. Expect an **acute eGFR dip of up to ~30% — do not stop the drug**. Status: **standard of care** in proteinuric CKD (CREDENCE 2019, DAPA-CKD 2020, EMPA-KIDNEY 2023).
- **Finerenone** (non-steroidal MRA) 10–20 mg OD — reduces CKD progression and cardiovascular events in diabetic kidney disease (FIDELIO-DKD 2020, FIGARO-DKD 2021); less hyperkalaemia than spironolactone but still monitor K^+. Status: **standard**.
- **Anti-PLA2R antibody** titres now guide diagnosis, treatment intensity and relapse monitoring in membranous nephropathy — available in India and can spare a biopsy in the low-risk adult. Status: **standard**.
- **Targeted-release budesonide (NefIgArd 2023) and sparsentan (PROTECT 2023)** in IgA nephropathy; **NGS tubulopathy panels** now available in India (out-of-pocket). Status: **emerging**.

■ INDIA 0.5 M

India

INDIAN RELEVANCE

- **Acquired Fanconi syndrome is far commoner than genetic in India:** tenofovir disoproxil fumarate (NACO first-line ART — monitor creatinine, phosphate and urine dipstick for glycosuria), ifosfamide, multiple myeloma light chains, and **lead/cadmium in some Ayurvedic and herbal preparations**.
- **Distal RTA** is a common and treatable Indian cause of hypokalaemic paralysis and nephrocalcinosis — look for Sjögren's.
- IgA nephropathy and FSGS dominate Indian biopsy registries in adults; amyloidosis follows chronic infection (TB, bronchiectasis).

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

Localise before you list. Blood and protein in the urine mean **glomerulus**; normoglycaemic glycosuria with acidosis means **PCT**; hypokalaemic alkalosis with hypercalciuria and normal BP means **TAL (Bartter)**; the same picture with hypocalciuria and hypomagnesaemia means **DCT (Gitelman)**; and hypokalaemic alkalosis with hypertension and suppressed aldosterone means **collecting duct (Liddle)**. Three cheap tests — blood pressure, urinary calcium and plasma renin–aldosterone — localise almost every case.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

PCT → Fanconi, type 2 RTA (tenofovir, myeloma) · **TAL** → Bartter · **DCT** → Gitelman, Gordon · **CD** → Liddle, type 1 RTA, nephrogenic DI · **Glycosuria + normal blood glucose = PCT** · **Bartter urine Ca HIGH / Gitelman LOW** · **Liddle: renin AND aldosterone LOW → amiloride, not spironolactone** · **Gordon: thiazide** · **SGLT2i acute eGFR dip up to 30% — do NOT stop** (CREDENCE, DAPA-CKD, EMPA-KIDNEY) · **finerenone 10–20 mg** (FIDELIO/FIGARO) · anti-PLA2R 70–80% · tubulopathy → **genetic panel, not biopsy**

Q9 Potassium metabolism

10 M | STD

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 10 M

Open with numbers	Internal balance	Renal handling	Aldosterone paradox	Hypokalaemia	Hyperkalaemia	India & recent
1 M	1.5 M	2 M	1 M	1.5 M	2 M	1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: two separate things — **internal balance** (shift) vs **external balance** (renal excretion), and then whether you can run the **hyperkalaemia emergency drill** cold, with doses.
Earns the marks: the three determinants of K^+ secretion — **distal Na^+ delivery × aldosterone × flow**; **calcium first** to stabilise; and the exact **10 U insulin + 25 g dextrose**. Say **'treat the ECG, not the number'**.
Loses the marks: giving bicarbonate first-line (it is only for the acidotic); forgetting **magnesium** in refractory hypokalaemia; quoting **TTKG**, which is obsolete; prescribing **SPS with sorbitol**.

■ CORE 1 M
Open with numbers

Total body K^+ ≈ **50 mEq/kg (~3500 mEq)**, of which 98% is intracellular ($[K^+]_i$ ≈ 140 mEq/L) and only 2% (~70 mEq) extracellular ($[K^+]_e$ 3.5–5.0 mEq/L). This gradient, maintained by **Na^+/K^+-ATPase**, sets the resting membrane potential — hence every symptom of dyskalaemia is neuromuscular or cardiac. Daily intake 40–120 mEq; **90% is excreted renally**, 10% in stool.

BASIC SCIENCE

Two systems defend $[K^+]_e$: **internal balance** (minute-to-minute shift across cell membranes) and **external balance** (renal excretion over hours to days). An exam answer must separate them.

■ CORE 1.5 M
Internal balance

Shifts K^+ INTO cells (↓ serum K^+)	Shifts K^+ OUT of cells (↑ serum K^+)
Insulin (stimulates Na^+/K^+-ATPase)	Insulin deficiency; hyperglycaemia + hyperosmolality (solvent drag)
β_2-agonists (salbutamol), catecholamines	α-agonists; β-blockers (non-selective)
Alkalosis (H^+ leaves cell, K^+ enters)	**Mineral acidosis** (HCl, NH_4Cl) — *not* organic acidosis (keto)
Aldosterone; hypothermia; anabolic states (B_{12}/folate therapy)	Cell lysis: rhabdomyolysis, tumour lysis, haemolysis, bu massive transfusion
	Digoxin toxicity (Na^+/K^+-ATPase block); depolarising blockade (**suxamethonium**); exercise

■ CORE 2 M
Renal handling

Draw this — the secretion equation is the key.

```
K+ freely filtered (~750 mEq/day)
   PCT   : 65% reabsorbed (passive, solvent drag)
   TAL   : 25-30% reabsorbed via NKCC2 (K+ recycles through ROMK)
   DCT   : small reabsorption
   CNT/CD PRINCIPAL CELL = SITE OF REGULATION
        ENaC brings Na+ in -> lumen NEGATIVE -> K+ secreted via:
           ROMK (baseline secretion)  +  BK/maxi-K (FLOW-dependent)
   alpha-INTERCALATED CELL: H+/K+-ATPase reabsorbs K+ (in K+ depletion)
SECRETION depends on:  ALDOSTERONE  x  DISTAL Na+ DELIVERY & FLOW
                       x  non-reabsorbable anions (HCO3-, penicillin)
                       x  tubular fluid pH   x  plasma [K+]
```

■ DIST 1 M
Aldosterone paradox

One line — marks you out as a topper.

EXAMINER PEARL

Aldosterone rises both in **volume depletion** (must retain Na^+, must NOT lose K^+) and in **hyperkalaemia** (must excrete K^+). The **WNK–SPAK kinase switch** resolves this: with angiotensin II present (volume depletion), NCC is activated → less distal Na^+ delivery → Na^+ retained without kaliuresis; with hyperkalaemia alone, NCC is inhibited → more distal delivery → K^+ secreted. **Colonic BK channels** also upregulate in CKD, an important adaptive route (and why constipation precipitates hyperkalaemia).

■ CORE 1.5 M
Hypokalaemia

Approach = urine K^+ → acid–base → BP.

Step	Finding	Interpretation
Urine K^+	Spot K^+ <15 mEq/L or **K:Cr <13 mEq/g** (<1.5 mmol/mmol)	**Extrarenal**: GI loss, shift, poor intake
	K:Cr >13 mEq/g	**Renal** loss → go to acid–base
Acid-base	Acidosis	RTA type 1/2, DKA, ureteric diversion
	Alkalosis + **normal BP**	Vomiting, diuretics, Bartter, Gitelman
	Alkalosis + **hypertension**	Conn's, Liddle, AME (licorice), renovascular, Cushing

Clinical: weakness, ileus, cramps, rhabdomyolysis, arrhythmia; ECG — flat T, U waves, ST depression, long QU, VT/torsades. **Treat:** KCl 20–40 mEq oral; IV 10 mEq/h peripherally (max 20 mEq/h via central line with cardiac monitoring); **always correct magnesium** — hypomagnesaemia causes refractory hypokalaemia by disinhibiting ROMK. TTKG is **obsolete** — do not quote it.

■ CORE 2 M

Hyperkalaemia

The emergency — doses must be exact.

RED FLAG / EMERGENCY

ECG: peaked T → flat P, long PR → wide QRS → **sine wave** → VF/asystole. **ECG changes correlate poorly with the level — treat the ECG, not the number.**

DRUG DOSE

- **Stabilise:** calcium gluconate 10% 10 mL IV over 2–3 min (repeat at 5 min); onset 1–3 min, lasts 30–60 min. Give even in digoxin toxicity, but slowly over 20 min.
- **Shift: 10 U regular insulin + 25 g dextrose (50 mL of 50%) IV** — lowers K^+ by 0.5–1.2 mEq/L over 15 min (check glucose hourly × 6 h; use 5 U if eGFR <30 or non-diabetic). **Salbutamol 10–20 mg nebulised** (adds ~0.5–1.0 mEq/L; ~20% are non-responders). **$NaHCO_3$ only if metabolic acidosis is present**.
- **Remove:** furosemide 40–80 mg IV with volume; **sodium zirconium cyclosilicate 10 g TDS × 48 h then 5–10 g OD**; **patiromer 8.4 g OD**. **Dialysis** is definitive in oligo-anuric AKI/ESRD.
- ⚠ **Avoid sodium polystyrene sulfonate with sorbitol** — colonic necrosis; slow, weak evidence.

■ INDIA 1 M

India & recent

INDIAN RELEVANCE

- **Hypokalaemic periodic paralysis** is a common Indian emergency: think **thyrotoxic PP** (Asian males), and always test for **distal RTA and Sjögren's** — a treatable cause frequently missed. Barium and licorice ingestion are rarer causes.
- Hyperkalaemia drivers in India: RAAS blockers in diabetic CKD, NSAIDs, trimethoprim, **traditional 'low-sodium' salt substitutes (potassium chloride)** used by hypertensives, and coconut water/banana in CKD.
- **KDIGO 2024:** use K^+ binders (SZC, patiromer) to **enable continued RAASi therapy** rather than stopping it (DIAMOND trial, 2022). SZC is available in India; patiromer availability is limited and cost is a barrier.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

Potassium homeostasis is a two-tier system: **internal balance** (insulin, β_2, pH) buys minutes, and **renal secretion by the principal cell** — the product of **aldosterone × distal sodium delivery and flow** — provides definitive control. Hypokalaemia is worked up with urine K:Cr, acid–base status and blood pressure, and will not correct until magnesium is replaced. Hyperkalaemia is a five-step emergency: stabilise, shift, remove, stop the culprit, and dialyse.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Total body K^+ ~3500 mmol, **98% intracellular**; ICF 140 / ECF 4 mmol/L · **IN**: insulin, β_2-agonist, alkalosis, aldosterone · **OUT**: mineral acidosis, hyperosmolality, β-blocker, digoxin, **suxamethonium**, cell lysis · **K^+ secretion = distal Na^+ delivery × aldosterone × flow** · ECG: peaked T → PR long → P lost → QRS wide → sine wave · **Ca gluconate 10% 10 mL → insulin 10 U + 25 g dextrose → salbutamol 10–20 mg neb → SZC 10 g TDS → dialysis** · **Give Mg^{2+} in refractory hypokalaemia** · **TTKG obsolete** · **never SPS + sorbitol** · treat the ECG, not the number

Q10 Casts; telescoped sediment; AIN

10 M | STD

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 10 M

Cast formation 1 M	Types of casts 3 M	Telescoped sediment 2 M	AIN — definition 1 M	AIN — causes & clinics 2 M	AIN — treatment 1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: whether you can read a urine sediment **as a diagnosis**. The sediment is the renal biopsy you can do at the bedside — that is the sentence the examiner is waiting for.
Earns the marks: Tamm-Horsfall protein as the matrix of every cast; **RBC cast = glomerulonephritis**; **muddy-brown granular = ATN**; **waxy/broad = CKD**; and **telescoped sediment = lupus nephritis**, defined properly as all classes of cast coexisting.
Loses the marks: not **defining** telescoped sediment (it is named in the stem — it must be defined); still quoting **urine eosinophils** for AIN (sensitivity ~30% — abandoned); forgetting that AIN is now most often **drug-induced and non-oliguric**.

■ CORE 1 M

Cast formation

Start with uromodulin — examiners love it.

Casts are cylindrical moulds of the distal tubular lumen formed from Tamm–Horsfall protein (uromodulin), secreted exclusively by the **thick ascending limb**. Gelation is favoured by **low flow, acidic pH, high salt concentration and proteinuria**. Because casts form only in the tubule, their presence proves the abnormality is **renal, not urological**.

BEDSIDE PEARL

Examine a **fresh, first-morning, unspun-then-centrifuged** specimen within 2 h; casts lyse in alkaline, dilute urine. Low-light phase contrast is ideal. Dipstick 'blood positive but no RBC on microscopy' = haemoglobinuria or **myoglobinuria**, not a cast problem.

■ CORE 3 M

Types of casts

Table — do not write prose here.

Cast	Composition / appearance	Significance
Hyaline	Pure uromodulin, colourless, low refractile	**Normal**; dehydration, exercise, fever, diuretics
RBC cast	RBCs in a protein matrix, orange-red	**Pathognomonic of glomerular bleeding** — GN, vasculitis, RPGN (rarely AIN)
WBC cast	Neutrophils in matrix	**Acute interstitial nephritis**, acute pyelonephritis, proliferative GN
Muddy-brown granular	Degenerating tubular cell debris	**Acute tubular necrosis** — high specificity; drives th diagnosis
Renal tubular epithelial cell	Intact RTE cells	ATN, AIN, viral nephropathy
Fatty cast / oval fat body	Lipid; **'Maltese cross'** under polarised light	**Nephrotic syndrome** (lipiduria)
Waxy / broad cast	Highly refractile, sharp edges, wide	**Chronic kidney disease** — formed in dilated atrophi tubules ('renal failure casts')
Pigment casts	Haem-containing, red-brown	Rhabdomyolysis (myoglobin), haemolysis, **bile casts** cholemic nephropathy
Crystal / drug casts	Crystals in matrix	Acyclovir, sulfonamides, methotrexate, ethylene glyc (oxalate), **light-chain cast nephropathy**

■ CORE 2 M

Telescoped sediment

Define it, then give the answer they want: **lupus**.

DEFINITION / CRITERIA

Telescoped urinary sediment = the simultaneous presence of **all** classes of urinary element in one specimen — RBCs and RBC casts (nephritic), oval fat bodies and fatty casts (nephrotic), granular and epithelial casts (acute tubular injury), and waxy/broad casts (chronic damage). It reflects nephritic + nephrotic + acute + chronic injury occurring together.

Classic cause: lupus nephritis (especially ISN/RPS class IV). Also: membranoproliferative GN, post-infectious and endocarditis-associated GN, rapidly progressive GN of any cause, IgA nephropathy with crescents, Henoch–Schönlein purpura and cryoglobulinaemia. Finding it mandates urgent serology (ANA, dsDNA, C3/C4, ANCA, anti-GBM, cryoglobulins, hepatitis B/C, HIV) and an **urgent renal biopsy**.

■ CORE 1 M

AIN — definition

DEFINITION / CRITERIA

Acute interstitial nephritis = acute kidney injury due to an inflammatory infiltrate (lymphocytes, monocytes, eosinophils ± granulomas) with oedema in the **interstitium**, **sparing the glomeruli and vessels**. It causes 10–15% of biopsy-proven AKI and is **reversible if the drug is stopped early**.

■ ADDS 2 M

AIN — causes & clinics

Group	Examples
Drugs (70–75%)	**PPIs** (now the commonest in Western series), **NSAIDs**, β-lactams (methicillin classically), **rifam** (intermittent dosing), cotrimoxazole, fluoroquinolones, allopurinol, mesalamine, phenytoin, **imm checkpoint inhibitors** (the commonest cause of ICI-related AKI)
Infection	**Leptospirosis, scrub typhus, hantavirus**, **tuberculosis**, legionella, streptococci, CMV, EBV, BK virus
Autoimmune / systemic	**Sjögren's**, SLE, **sarcoidosis** (granulomatous), **IgG4-related disease**, **TINU syndrome** (tubulointerstitial nephritis with uveitis — young females)
Idiopathic	—

COMMON MISTAKE / TRAP

- The classic triad of **fever + rash + eosinophilia occurs in <10%** — its absence never excludes AIN.
- **Urine eosinophils are not useful** (Se ~30%, Sp ~68%; Muriithi, CJASN 2013) — KDIGO does not recommend them.
- Typical urine: **sterile pyuria, WBC casts, mild sub-nephrotic proteinuria** and a **bland** otherwise. **Exception: NSAID-induced AIN with concurrent minimal change disease presents with nephrotic-range proteinuria.**
- Latency: days to weeks for β-lactams, but **months** for PPIs and NSAIDs — take a long drug history including OTC drugs.
- **Renal biopsy is the gold standard.** Gallium scanning is obsolete. Urinary MCP-1, TNF-α and IL-9 are emerging but research-only.

■ INDIA 1 M

AIN — treatment

MANAGEMENT

- **Stop the offending drug** — the single most important step; supportive care, avoid further nephrotoxins, dialyse if needed.
- **Corticosteroids** if no improvement 3–7 days after withdrawal, or if biopsy shows florid interstitial inflammation without fibrosis: **prednisolone 1 mg/kg/day (max 60 mg) for 1–2 weeks, then taper over 4–6 weeks** (some use IV methylprednisolone 250–500 mg × 3 days first). **Early treatment (<7–10 days) predicts recovery** (González, *Kidney Int* 2008 — observational; no RCT exists, so this is a conditional, expert-opinion recommendation).
- ICI-associated AIN: steroids, and re-challenge only after multidisciplinary discussion.
- Prognosis: ~60–70% recover; interstitial fibrosis on biopsy, delayed withdrawal and NSAID aetiology predict CKD.

INDIAN RELEVANCE

- **Rifampicin-induced AIN/AKI** — classically with **intermittent or re-introduced** therapy, often with flu-like symptoms, haemolysis and thrombocytopenia. Much less frequent since NTEP moved to **daily fixed-dose combination regimens (2019)**.
- **Over-the-counter NSAIDs, analgesic combinations and PPIs** are freely available in India and are the commonest drug causes seen; always ask about pharmacy-bought medication and Ayurvedic/herbal use.
- **Tropical AIN:** leptospirosis (Odisha/coastal, post-monsoon), scrub typhus (with eschar), hantavirus — all cause AKI with sterile pyuria; empirical **doxycycline 100 mg BD** is reasonable in the endemic season while awaiting serology.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

Casts are uromodulin moulds that prove the lesion is intrarenal: **RBC casts mean glomerulonephritis, WBC casts and sterile pyuria mean interstitial nephritis, muddy-brown granular casts mean ATN, and broad waxy casts mean chronic disease**. A **telescoped sediment** — all of these together — is the classic sign of **lupus nephritis** and demands urgent serology and biopsy. AIN is a reversible, mostly drug-induced AKI in which the treatment is to **stop the drug early**, with steroids for those who do not recover — and in India, to remember rifampicin and the tropical infections.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Tamm-Horsfall protein (uromodulin) = the matrix of every cast, made in the TAL · hyaline = normal · **RBC cast = GN** · **WBC cast = AIN / pyelonephritis** · **muddy-brown granular = ATN** · **waxy / broad = CKD** · **fatty, Maltese cross = nephrotic** · **TELESCOPED = all classes together = LUPUS NEPHRITIS (class IV)** · **AIN: drugs ~70%** (PPI, NSAID, rifampicin, antibiotics) · classic triad <10% · **urine eosinophils obsolete** (Se ~30%, Muriithi CJASN 2013) · **steroids early** (González KI 2008)

Q11 Biomarkers of AKI

5 M | PYQ 2×

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

Why we need them 1 M	Classification 2 M	Where they fit 1 M	India 1 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: why **creatinine is a late, functional** marker, and what fills the diagnostic gap between injury and its rise.
Earns the marks: classifying rather than listing — functional vs damage vs **cell-cycle arrest**; the **[TIMP-2]×[IGFBP7] cut-offs (0.3 and 2.0)**; and saying honestly which are **actually available**, which is where the **furosemide stress test** earns its place in India.
Loses the marks: reciting an undifferentiated list of acronyms; not stating that NGAL is confounded by sepsis and CKD; presenting research assays as though they were routine.

■ CORE 1 M

Why we need them

The 'renal troponin' framing earns the opening mark.

DEFINITION / CRITERIA

Serum creatinine is a functional, not an injury, marker: it rises only after ~50% of GFR is lost, lags injury by 24–48 h, and is confounded by muscle mass, volume status, diet and drugs. An **AKI biomarker** aims to be the 'renal troponin' — detecting tubular injury before creatinine moves, and predicting severity, need for dialysis and recovery.

■ CORE 2 M

Classification

Classify by biology, not alphabetically — this is the mark-winner.

Class	Biomarker	Source / biology	Clinical use
Functional	Creatinine, **cystatin C**, urea; proenkephalin A (penKid)	Filtration markers	Estimate GFR; cystatin C rises ~12–24 h earlier than creatinine
Tubular injury / damage	**NGAL** (urine & plasma), **KIM-1**, L-FABP, IL-18, **NAG**	Released by injured proximal (KIM-1, L-FABP, NAG) or distal (NGAL) tubule	Early detection 2–6 h post-insul NGAL is also raised in sepsis an (↓ specificity)
Cell-cycle arrest ('stress')	**[TIMP-2] × [IGFBP7]** — NephroCheck®	G1 cell-cycle arrest in stressed tubular cells	**FDA-approved (2014)**; predic **moderate-severe AKI within** Cut-offs: **>0.3** = risk, **>2.0** = h risk
Persistence / repair	**CCL14** (urine), DKK3 (urine)	Macrophage chemokine; Wnt antagonist	CCL14 predicts **persistent sev AKI** (RUBY study); DKK3 predict post-operative AKI and CKD

■ DIST 1 M

Where they fit

RECENT ADVANCE

ADQI consensus (23rd, 2020): combining a damage biomarker with creatinine reclassifies patients into four groups — and identifies 'subclinical AKI' (biomarker-positive, creatinine-negative), which independently predicts dialysis, CKD and death. This is the conceptual advance the examiner is testing.
Status: [TIMP-2]×[IGFBP7] and NGAL are **optional/adjunctive**, not standard of care; none replaces creatinine or the KDIGO 2012 definition. Evidence for biomarker-guided care bundles improving hard outcomes remains **limited** (PrevAKI was small and single-centre).

■ INDIA 1 M

India

This is where you win the gold medal.

INDIAN RELEVANCE

- Novel biomarker assays are **not routinely available or affordable** in India outside research and a few tertiary centres; cost per test far exceeds a creatinine.
- The Indian AKI phenotype is largely **community-acquired and tropical** — diarrhoeal disease, **snake envenomation**, **falciparum malaria**, **leptospirosis and scrub typhus**, sepsis, and **obstetric AKI** (a persistent and largely preventable burden). The ISN **0by25** initiative piloted low-cost AKI detection in India.
- **The affordable Indian 'biomarker' is the furosemide stress test**: furosemide 1.0 mg/kg (1.5 mg/kg if previously exposed) IV after volume repletion; urine output <200 mL over 2 h predicts progression to KDIGO stage 3 (Chawla, 2013) — cheap, bedside and validated.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

AKI biomarkers convert a delayed **functional** diagnosis into an early **structural** one. Classify them as functional, damage, cell-cycle-arrest and repair markers; [TIMP-2]×[IGFBP7] is the only FDA-approved risk-stratification test and CCL14 best predicts persistence. In Indian practice they remain adjunctive and unaffordable — careful serial creatinine, urine output, urine microscopy and the **furosemide stress test** remain the pragmatic tools.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Creatinine = late, functional · cystatin C rises **12–24 h earlier** · **Damage**: NGAL, KIM-1, L-FABP, IL-18, NAG — **2–6 h**; NGAL confounded by sepsis and CKD · **Cell-cycle arrest: [TIMP-2]×[IGFBP7] — >0.3 = risk, >2.0 = high risk** (NephroCheck, FDA 2014) · CCL14 = persistence (RUBY) · **Furosemide stress test 1.0–1.5 mg/kg → UO <200 mL over 2 h = progression to stage 3** (Chawla 2013) · ADQI 23 (2020) · KDIGO AKI: ↑Cr ≥0.3 in 48 h / ≥1.5× in 7 d / UO <0.5 mL/kg/h × 6 h

Q12 Metabolic & hormonal functions

5 M | PYQ 2×

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

Framing 0.5 M	Hormones secreted 2 M	Kidney as target 1 M	Metabolic functions 1 M	Recent & India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: the kidney as an **endocrine and metabolic organ** — and, in every viva, **what fails when it fails**.
Earns the marks: hormones (**EPO, calcitriol, renin**) and metabolic roles (**gluconeogenesis, ammoniagenesis, catabolism of insulin/PTH/β₂-microglobulin**) — each paired with its **CKD consequence**: anaemia, CKD–MBD, hypertension, hypoglycaemia, acidosis, β₂-M amyloid.
Loses the marks: listing hormones with no CKD correlate — **the correlate is the mark**; forgetting the kidney is also a **target** organ (PTH, ADH, aldosterone, FGF23) and a site of drug clearance.

■ CORE 0.5 M

Framing

Split into 'secretes', 'responds to', 'metabolises'. This structure is the answer.

Besides excretion, the kidney is a **metabolic and endocrine organ**. Answer under three heads: hormones it **secretes**, hormones it is a **target** for, and its **metabolic** functions — then correlate each with a feature of CKD.

■ CORE 2 M

Hormones secreted

Hormone	Site	Stimulus	Action / CKD correlate
Erythropoietin	Peritubular interstitial fibroblasts (cortex/outer medulla)	Hypoxia via **HIF-2α** (PHD/VHL oxygen sensing)	Erythropoiesis → **normocytic anaemi CKD**
Calcitriol (1,25-(OH)₂D)	PCT — **1α-hydroxylase**	↑PTH, ↓PO_4; **inhibited by FGF23**	Ca^{2+}/PO_4 absorption → **CKD-MBD**, sec hyperparathyroidism, osteomalacia
Renin	JG granular cells	↓Afferent stretch, ↓NaCl at macula densa, β₁-sympathetic	RAAS → BP and volume; renovascular hypertension
Prostaglandins (PGE_2, PGI_2)	Medullary interstitial cells, macula densa	Ischaemia, Ang II	Afferent vasodilatation → **NSAIDs abo this → AKI in volume depletion**
Klotho	DCT	—	FGF23 co-receptor; **the earliest abnormality in CKD-MBD**
Dopamine, kallikrein-kinin, urodilatin	PCT / distal nephron	Salt load	Natriuresis, local vasodilatation

■ ADDS 1 M

Kidney as target

BASIC SCIENCE

PTH → ↑Ca^{2+} reabsorption (DCT, TRPV5), ↓PO_4 reabsorption (NaPi-IIa), ↑ 1α-hydroxylase. **ADH** → V2 → AQP2 → water. **Aldosterone** → ENaC/ROMK → Na^+ in, K^+ and H^+ out. **ANP/BNP** → natriuresis, afferent dilatation. **FGF23** (bone) → phosphaturia + **suppresses calcitriol** — the first biochemical change in CKD–MBD, before PTH or phosphate. **Insulin** → Na^+ retention, K^+ shift.

■ CORE 1 M

Metabolic functions

Function	Detail	Clinical correlate
Gluconeogenesis	Renal cortex from glutamine, lactate, glycerol; up to **~40% of total in prolonged fasting**	**Hypoglycaemia in advanced CKD** (with re insulin clearance)
Ammoniagenesis	From glutamine in the PCT; the main route of **net acid excretion** (NH_4^+)	Failure → **normal-anion-gap acidosis of CK** then high-AG uraemic acidosis
Peptide catabolism	Degrades **insulin (~30–40%)**, PTH, β₂-microglobulin, glucagon, calcitonin	Falling insulin requirement in diabetic CKD; **β₂-microglobulin (dialysis) amyloidosis** – carpal tunnel
Amino-acid handling	Arginine synthesis from citrulline; serine, tyrosine; glutathione and carnitine metabolism	Carnitine deficiency and muscle weakness on maintenance haemodialysis
Vitamin D activation; drug met abolism/excretion	1α-hydroxylation; renal excretion of most water-soluble drugs	Dose adjustment mandatory; nutritional vitam alone will not work in advanced CKD

■ INDIA 0.5 M

Recent & India

INDIAN RELEVANCE

HIF prolyl-hydroxylase inhibitors (roxadustat, daprodustat) mimic hypoxia → stabilise HIF-2α → raise endogenous EPO *and* improve iron mobilisation (↓hepcidin). **Roxadustat is approved in India (CDSCO, 2021)** for anaemia of CKD including non-dialysis patients — oral, no cold chain, attractive for rural India; the FDA declined approval over cardiovascular safety, so counsel about thrombosis and MACE risk. Evidence: **emerging**.
In India, ESA biosimilars are inexpensive and widely available, but the dominant treatable contributor to anaemia in CKD remains **iron deficiency and nutritional anaemia** — correct iron first (KDIGO 2012: initiate ESA at Hb <10, target 10–11.5 g/dL, never >13 — CHOIR, CREATE, TREAT).

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

The kidney **secretes** erythropoietin, calcitriol, renin, prostaglandins and klotho; **responds** to PTH, ADH, aldosterone, ANP and FGF23; and **performs** gluconeogenesis, ammoniagenesis and peptide catabolism. This single slide explains why CKD produces **anaemia, renal bone disease, hypertension, acidosis and hypoglycaemia** — the non-excretory face of renal failure.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

EPO — peritubular interstitial fibroblasts, HIF-2α → **anaemia** · **Calcitriol** — PCT 1α-hydroxylase, inhibited by FGF23 → **CKD-MBD** · **Renin** — JG cells → hypertension · **Prostaglandins** — medullary interstitial cells → **NSAID AKI** · **Klotho** — DCT, **earliest CKD-MBD change** with ↑FGF23 · **Gluconeogenesis ~40% in fasting** → hypoglycaemia · **ammoniagenesis = net acid excretion** → acidosis · catabolises **insulin 30–40%**, PTH, **β₂-microglobulin** → dialysis amyloid, carpal tunnel

B1 Histology of the kidney

5 M | SN

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

Overview 1 M	Segment histology 2 M	Vasculature 1 M	Stains & biopsy 0.5 M	India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: whether you could **identify a segment down a microscope** — this is a histology note, not a gross anatomy note.
Earns the marks: the three identifiers — **brush border = PCT**; **squamous with no RBCs in the lumen = thin limb**; **sharply defined cell borders = collecting duct**; plus the **LM / IF / EM** triad and **IFTA as the strongest predictor of progression**.
Loses the marks: describing cortex and medulla grossly and never reaching the epithelium; omitting the stains; forgetting that EPO comes from **interstitial fibroblasts**, not tubular cells.

■ CORE 1 M

Overview

Each kidney weighs 125–170 g and contains an outer **cortex** (glomeruli, PCT, DCT, cortical CD, cortical labyrinth + medullary rays) and an inner **medulla** of 8–18 pyramids (loops of Henle, vasa recta, collecting ducts) whose papillae drain into minor calyces. ~1 million nephrons per kidney; nephrogenesis ceases at 34–36 weeks, so nephron number is fixed at birth.

■ CORE 2 M

Segment histology

Brush border and cell height are the discriminators under the microscope.

Structure	Epithelium	Identifying feature
Glomerulus	Fenestrated endothelium, GBM, visceral podocytes; mesangium	Capillary tuft in Bowman's space; PAS-positive GBM
PCT	Tall cuboidal, eosinophilic	**Prominent brush border** (PAS+), abundant mitochondria, indistinct lumen, few nuclei per section
Thin limbs	Simple **squamous**	Resemble capillaries but have no RBCs in the lumen
TAL	Low cuboidal, no brush border	Distinct lumen, more nuclei per section; contains **macula d** at the hilum
DCT	Cuboidal, pale	No brush border, wide clear lumen, basal infoldings
Collecting duct	**Principal** (pale, distinct borders) + **intercalated** (dark, eosinophilic)	'Cobblestone' with sharply defined cell margins — the class identifier
Interstitium	Fibroblast-like cells, dendritic cells	Cortical peritubular fibroblasts secrete **erythropoietin**

■ CORE 1 M

Vasculature

```
Renal a. -> segmental -> interlobar -> ARCUATE (corticomedullary jn)
  -> interlobular -> AFFERENT arteriole -> GLOMERULUS -> EFFERENT arteriole
        |                                                      |
  cortical nephron                                    juxtamedullary nephron
        v                                                      v
  PERITUBULAR CAPILLARIES                          VASA RECTA (countercurrent exc
hanger)
  ** A PORTAL system: two capillary beds in series **
```

BASIC SCIENCE

The medulla receives only ~10% of renal blood flow and works at a PO_2 of 10–20 mmHg — the outer medullary S3/TAL is the most hypoxia-vulnerable zone, explaining why ATN strikes there first.

■ ADDS 0.5 M

Stains & biopsy

Say 'light, IF and EM' — the triad is expected.

INVESTIGATION

Light microscopy: H&E; **PAS** (GBM, brush border, mesangial matrix); **silver methenamine** (GBM spikes in membranous, double contours in MPGN); **Masson trichrome** (fibrosis); **Congo red** with apple-green birefringence (amyloid).
Immunofluorescence: IgG, IgA, IgM, C3, C1q, κ, λ, fibrinogen — linear (anti-GBM), granular (immune complex), pauci-immune (ANCA).
Electron microscopy: deposit location, GBM thickness, podocyte foot-process effacement. An adequate biopsy needs ≥10 glomeruli (≥8 for LM). **Interstitial fibrosis and tubular atrophy (IFTA) is the strongest histological predictor of progression**, irrespective of the primary diagnosis.

■ INDIA 0.5 M

India

INDIAN RELEVANCE

Percutaneous real-time USG-guided biopsy is now standard in Indian nephrology units. IF requires fresh unfixed tissue and a cold chain; **EM is available only at a few centres**, so **IF on paraffin (pronase-digested)** is a validated Indian workaround. Autopsy series suggest lower nephron endowment in Indians consistent with the high prevalence of low birth weight (NFHS-5: ~18%) — a plausible contributor to India's CKD burden.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

Cortex = glomeruli and convoluted tubules; medulla = loops, vasa recta and collecting ducts. The **brush border marks the PCT**, the **squamous thin limb has no RBCs**, and **distinct cell borders mark the collecting duct**. The renal circulation is a portal system, the medulla is chronically hypoxic, and every biopsy must be read by light microscopy, immunofluorescence and electron microscopy.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

125–170 g · **~1 million nephrons, fixed at 34–36 wk** · cortex + **8–18 medullary pyramids** · **Brush border = PCT** · **squamous with no RBCs = thin limb** · **distinct cell borders = collecting duct** · macula densa sits in the **TAL** · **EPO from cortical peritubular fibroblasts** · **medulla: 10% of RBF, PO_2 10–20 mmHg → S3/TAL most hypoxia-vulnerable** · PAS, silver methenamine, trichrome, Congo red · **≥10 glomeruli** · **IFTA = strongest predictor of progression** · renal circulation = **portal system**

B2 Bowman's capsule & the filtration barrier

5 M | SN

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

Bowman's capsule 1 M	The filtration barrier 2 M	Selectivity 1 M	Starling forces 0.5 M	Clinical & India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: three layers, each with **a named protein and a named disease**. That pairing is the entire answer.
Earns the marks: nephrin-podocin slit diaphragm as the principal size barrier; **collagen IV α3α4α5** → Alport and anti-GBM; the **anionic glycocalyx** → charge barrier (hence albumin, at 69 kDa, is filtered <1%); and the Starling equation with numbers.
Loses the marks: naming the three layers with no proteins and no diseases; claiming the GBM is the main size barrier (it is the podocyte); forgetting that parietal epithelial cells form **crescents**.

■ CORE 1 M

Bowman's capsule

DEFINITION / CRITERIA

Bowman's capsule is the double-walled, blind, cup-shaped beginning of the nephron. The **parietal layer** is simple squamous epithelium on its own basement membrane; the **visceral layer** is made of **podocytes** applied to the glomerular capillaries; between them lies **Bowman's (urinary) space**, continuous with the PCT.

Parietal epithelial cells (PECs) are not inert: they proliferate to form cellular crescents in RPGN and are a progenitor reserve for podocytes; parietal cells reflect onto the visceral layer at the vascular pole and become the tubular epithelium at the urinary pole.

■ CORE 2 M

The filtration barrier

Three layers — name a protein for each or lose the mark.

Layer	Structure	Key molecules	Disease when it fails
1. Fenestrated endothelium	Pores 70–100 nm, **no diaphragms**; coated by anionic glycocalyx	VEGF-dependent; heparan sulfate glycocalyx	**Pre-eclampsia** (sFlt-1 sequesters VEGF), TMA/HUS anti-VEGF drugs (bevacizun
2. Glomerular basement membrane	300–350 nm; lamina rara interna – densa – rara externa; fused endothelial + podocyte BM	**Collagen IV α3α4α5**, laminin-521, nidogen, agrin/perlecan (heparan sulfate → **charge barrier**)	**Alport** (COL4A3/4/5 — X-lin 85%), thin basement memb nephropathy, **anti-GBM di** (α3 NC1 domain), Pierson (LAMB2)
3. Podocyte slit diaphragm	Foot processes interdigitate; **~40 nm zipper-like** slit — the **main size barrier**	**Nephrin (NPHS1)**, **podocin (NPHS2)**, CD2AP, TRPC6, α-actinin-4, ZO-1	Congenital nephrotic syndro of the Finnish type (NPHS1) steroid-resistant NS (NPHS2 FSGS (TRPC6, ACTN4); **MCD/FSGS = foot-proces effacement**

■ CORE 1 M

Selectivity

BASIC SCIENCE

Size: free filtration <~4 nm radius (<20 kDa); restricted 4–8 nm; essentially none >8 nm (>70 kDa). **Charge:** the anionic glycocalyx and heparan sulfate repel anions — hence albumin (69 kDa, anionic) is filtered <1% despite being near the size cut-off. **Shape/deformability** also matters. Loss of charge selectivity → **selective** albuminuria (minimal change); loss of size selectivity → **non-selective** proteinuria.

■ ADDS 0.5 M

Starling forces

Write the equation and the numbers.

```
GFR = Kf x [ (P-GC - P-BS) - (pi-GC - pi-BS) ]
   P-GC   = 45-50 mmHg     (glomerular capillary hydrostatic)
   P-BS   = 10-15 mmHg     (Bowman's space hydrostatic)
   pi-GC  = 25-30 mmHg     (rises along the capillary - protein concentrates)
   pi-BS  = 0              (filtrate is protein-free)
   NET ultrafiltration pressure ~ 10-15 mmHg;  Kf is very HIGH
   -> 'FILTRATION EQUILIBRIUM' may be reached before the efferent end
```

■ INDIA 0.5 M

Clinical & India

INDIAN RELEVANCE

Membranous nephropathy is a podocyte antigen disease: **anti-PLA2R in 70–80%** (also THSD7A, NELL-1, semaphorin-3B, EXT1/2). Anti-PLA2R testing is available in India and can **avoid biopsy** in a low-risk adult with nephrotic syndrome and normal GFR. In Indian biopsy registries, **secondary membranous** (hepatitis B, lupus, drugs) is proportionally commoner than in the West — always screen for HBsAg, anti-HCV, HIV, ANA and malignancy.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

Bowman's capsule collects the ultrafiltrate; its parietal cells form crescents. The barrier is a three-layer sieve — **fenestrated endothelium + glycocalyx (charge), GBM of collagen IV α3α4α5 (charge + support), slit diaphragm of nephrin-podocin (size)**. Each layer has its own disease: pre-eclampsia, Alport and anti-GBM, and minimal change/FSGS respectively. Filtration itself is Starling physics across a very high-Kf capillary with a net pressure of only ~10–15 mmHg.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Fenestrae 70–100 nm, no diaphragms + anionic glycocalyx · **GBM 300–350 nm, collagen IV α3α4α5**, laminin-521, agrin/perlecan · **Slit diaphragm ~40 nm — nephrin (NPHS1) + podocin (NPHS2) = the MAIN SIZE BARRIER** · free <4 nm / <20 kDa; none >8 nm / >70 kDa · **albumin 69 kDa filtered <1% — charge** · **Alport: X-linked 85%** · **anti-GBM = α3 NC1** · pre-eclampsia = sFlt-1 vs VEGF · **MCD/FSGS = foot-process effacement** · **anti-PLA2R 70–80%** · net UF pressure 10–15 mmHg, Kf high · **PECs → crescents**

B3 Collecting system

5 M | SN

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

What it is 1 M	Two cell types 2 M	Urea & water 1 M	Pelvicalyceal system 0.5 M	Drugs & India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: the collecting duct as the kidney's **final regulator** — principal vs α- vs β-intercalated cells.
Earns the marks: three cell types × transporter × hormone × disease in one table; **ureteric bud** origin; and the point that although it reabsorbs only ~3% of Na^+, **almost all regulation and drug action happens here**.
Loses the marks: writing pelvicalyceal anatomy and stopping — the cell biology carries the marks; confusing α (secretes acid) with β (secretes bicarbonate).

■ CORE 1 M
What it is

DEFINITION / CRITERIA

The **collecting system** = connecting tubule → **cortical collecting duct** → outer medullary CD → inner medullary CD → **papillary duct of Bellini** → minor calyx → major calyx → renal pelvis → ureter. Embryologically it derives from the **ureteric bud**, whereas the nephron proper derives from metanephric mesenchyme — hence the two cell types found only here.

It handles only the final **~3% of filtered Na^+**, yet it is where almost all regulation and almost all drug action occurs, because it is the last chance to alter the urine.

■ CORE 2 M
Two cell types

This table is the whole answer.

Cell	Proportion	Transporters	Function / hormone	Disease
Principal cell	~65%	**ENaC** (apical), **ROMK** + BK, **AQP2** (apical), AQP3/4 (basolateral), Na^+/K^+-ATPase	**Aldosterone** → Na^+ in, K^+ out. **ADH → V2 → cAMP → PKA → AQP2 (Ser256-P) inserted**	**Liddle** (ENaC gain), PHA 1 (ENaC/MR loss), **nephrogenic DI** (AVPR2 AQP2, **lithium** via ENaC
α-intercalated cell	~30%	Apical **H^+-ATPase** + H^+/K^+-ATPase; basolateral **AE1 (band 3)** Cl^-/HCO_3^- exchanger	**Secretes acid**, reabsorbs HCO_3^- and K^+; titrates NH_3 → NH_4^+	**Distal (type 1) RTA** — amphotericin B, Sjögren's *SLC4A1*; hereditary spherocytosis overlap
β-intercalated cell	~5%	Apical **pendrin** (Cl^-/HCO_3^-); basolateral H^+-ATPase	**Secretes HCO_3^-**, reabsorbs Cl^- — the mirror image; active in alkalosis	Pendrin upregulation contributes to thiazide-resistant and mineralocorticoid hyperte

■ CORE 1 M
Urea & water

```
ADH  -> V2 (Gs, cAMP, PKA) -> AQP2 to apical membrane   [WATER]
     -> UT-A1 / UT-A3 in the INNER medullary CD          [UREA]
                    |
                    v  urea recycles into the interstitium
        maintains ~50% of the medullary osmotic gradient
NOTE: cortical & outer medullary CD are UREA-IMPERMEABLE
      -> urea stays in tubule until IMCD -> concentrates -> then exits
```

■ ADDS 0.5 M
Pelvicalyceal system

BASIC SCIENCE

Lined by **urothelium (transitional epithelium)** with umbrella cells and uroplakin plaques — an impermeable barrier that makes the urine 'final'. Pacemaker cells in the minor calyces generate **peristalsis** (2–6/min). The **oblique vesico-ureteric junction** is a flap-valve preventing reflux — a short intramural tunnel causes **primary VUR** and reflux nephropathy. Obstruction here → hydronephrosis, then **type 4 RTA and nephrogenic DI** (the collecting system fails first).

■ INDIA 0.5 M
Drugs & India

DRUG DOSE

Amiloride/triamterene block ENaC → K^+-sparing (and the specific treatment of Liddle syndrome and of **lithium-induced nephrogenic DI**, since lithium enters through ENaC). **Spironolactone/eplerenone** block the mineralocorticoid receptor. **Tolvaptan** is a V2 antagonist — aquaresis in SIADH and slows ADPKD progression (TEMPO 3:4, REPRISE); hepatotoxicity requires monitoring and cost limits Indian use. **Acetazolamide, thiazides and loops act upstream** — their kaliuresis is *caused* by increased distal Na^+ delivery to this segment.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

The collecting system is the kidney's **final regulator**: principal cells handle sodium, potassium and water under aldosterone and ADH; α-intercalated cells secrete acid and β-intercalated cells secrete bicarbonate. It is derived from the ureteric bud, drains through a urothelium-lined pelvicalyceal system with an anti-reflux VUJ, and is the site of action of amiloride, spironolactone and tolvaptan — and of Liddle syndrome, distal RTA and nephrogenic diabetes insipidus.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Ureteric bud origin (nephron = metanephric mesenchyme) · **Principal ~65%**: ENaC, ROMK/BK, AQP2 — **aldosterone + ADH** → Liddle, PHA1, nephrogenic DI · **α-intercalated ~30%**: H^+-ATPase + **AE1** — **secretes acid** → **type 1 RTA** · **β-intercalated ~5%**: **pendrin** — secretes HCO_3^- · **UT-A1/A3 in the IMCD**; cortical/outer medullary CD are urea-impermeable · **only ~3% of Na^+ but nearly all regulation and drug action** · amiloride (Liddle, **lithium DI — Li^+ enters via ENaC**), spironolactone, **tolvaptan** (TEMPO 3:4, REPRISE) · urothelium + uroplakin · oblique VUJ flap-valve → VUR

B4 Juxtaglomerular apparatus

5 M | SN

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

Definition 1 M	Components 2 M	Renin control 1 M	TGF & SGLT2i 0.5 M	Pathology & India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: four components and **two outputs** — tubuloglomerular feedback and renin. The examiner wants the apparatus, not the cascade.
Earns the marks: all four components named; **macula densa → NKCC2 → ATP/adenosine → A1 → afferent constriction**; and the modern hook — **SGLT2 inhibitors restore NaCl delivery, reactivate TGF, and cause the benign acute eGFR dip**.
Loses the marks: writing out the whole RAAS and never describing the JGA itself; omitting the **extraglomerular mesangial (lacis) cells**, which almost everyone forgets; not knowing why NSAIDs reduce renin.

■ CORE 1 M

Definition

DEFINITION / CRITERIA

The **juxtaglomerular apparatus (JGA)** is a specialised structure at the **vascular pole** of each glomerulus where the **thick ascending limb of that same nephron** returns to touch its own afferent and efferent arterioles. It is the anatomical basis of tubuloglomerular feedback and of renin release — i.e. it couples what the tubule senses to what the glomerulus filters.

■ CORE 2 M

Components

Four — name all four.

Component	Origin	Function
1. Macula densa	Specialised, tall, closely packed TAL cells at the vascular pole	**Senses luminal NaCl via NKCC2**; high NaCl → ATP/**adenosine** release → **A1 receptor** → afferent constriction (↓GFR) and **inhibition of renin**. Low NaC **PGE_2/NOS1** → renin release
2. Juxtaglomerular (granular) cells	Modified smooth-muscle cells of the **afferent arteriole**	Contain **renin** granules; act as an intrarenal **barorece** — reduced wall stretch → renin release
3. Extraglomerular mesangial (lacis / Goormaghtigh) cells	Between the two arterioles and the macula densa	Gap-junction relay transmitting the macula densa signa the granular cells and to the afferent arteriole
4. Sympathetic nerve endings	Renal sympathetic nerves on the afferent arteriole	**β_1-adrenergic → direct renin release** (the basis of β-blockers lowering renin, and of renal denervation)

■ CORE 1 M

Renin control

↑ Renin release	↓ Renin release
↓ Afferent arteriolar stretch (hypotension, haemorrhage, RAS)	↑ Perfusion pressure / volume expansion
↓ NaCl at the macula densa (salt depletion, loop diuretics)	↑ NaCl at the macula densa; **adenosine (A1)**
β_1-sympathetic activity; PGI_2/PGE_2	**Angiotensin II (short-loop negative feedback)**; ADH; A
Upright posture; β-agonists; hypokalaemia	β-blockers; **NSAIDs** (block PG); direct renin inhibitors

```
Renin -> Angiotensinogen (liver) -> ANGIOTENSIN I
      -ACE (lung endothelium)->    ANGIOTENSIN II
   |-- EFFERENT arteriolar constriction  -> maintains GFR
   |-- Aldosterone (zona glomerulosa)    -> Na+ retention, K+/H+ loss
   |-- ADH + thirst; PCT Na+/H+ exchange; sympathetic facilitation
   |-- Growth/fibrosis (AT1)  -> the target of ACEi / ARB / MRA
```

■ DIST 0.5 M

TGF & SGLT2i

This is the modern high-yield twist — include it.

RECENT ADVANCE

In diabetes, **SGLT2-mediated proximal Na^+ reabsorption is increased**, so less NaCl reaches the macula densa → TGF is deactivated → afferent dilatation → glomerular hyperfiltration. **SGLT2 inhibitors restore NaCl delivery → reactivate TGF → afferent constriction** → the characteristic, benign **acute 'dip' in eGFR** followed by long-term nephroprotection (EMPA-KIDNEY 2023, DAPA-CKD 2020, CREDENCE 2019). **Do not stop the drug for the initial dip of up to ~30%.**

■ INDIA 0.5 M

Pathology & India

INDIAN RELEVANCE

JG hyperplasia: Bartter and Gitelman syndromes, renal artery stenosis, chronic diuretic use. **Reninoma (JG cell tumour):** rare; severe hypertension with hypokalaemia and very high renin in a young patient — curable by resection. **Renovascular hypertension:** in India, **Takayasu arteritis is the leading cause in the young** (unlike fibromuscular dysplasia in the West), with atherosclerotic disease in the elderly — look for absent pulses, bruits and a blood-pressure differential.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

The JGA is where a nephron's own tubule reports back to its own glomerulus. Its four components — **macula densa, granular cells, extraglomerular mesangial cells and sympathetic nerves** — deliver two outputs: **tubuloglomerular feedback** (adenosine → afferent constriction) for minute-to-minute GFR autoregulation, and **renin** for systemic volume and pressure control. It is the target of ACE inhibitors, ARBs, β-blockers, NSAIDs and, most topically, of SGLT2 inhibitors.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

4 components: macula densa · JG granular cells · extraglomerular mesangial (lacis / Goormaghtigh) · sympathetic nerves · MD senses NaCl via NKCC2 → ATP/adenosine → A1 → afferent constriction + renin OFF; low NaCl → PGE_2/NOS1 → renin ON · **β_1 → renin ON**; Ang II → renin OFF (short loop); **NSAIDs → renin OFF** · ACE in lung → Ang II → **efferent constriction**, aldosterone, ADH, fibrosis · **SGLT2i restore NaCl → TGF ON → afferent constriction → eGFR dip ≤30%, do NOT stop** · JG hyperplasia: Bartter, Gitelman, RAS · **reninoma** · **Takayasu = renovascular HTN in young Indians**

B5 Water balance & ADH

5 M | SN

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

The set point 1 M	ADH physiology 1.5 M	Disorders 1.5 M	Treatment 0.5 M	Recent & India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: that **water is defended by osmolality and volume by sodium** — and the **correction limits**, which are a patient-safety issue, not a fact.
Earns the marks: ADH threshold **280–285** vs thirst **290–295**; the **>7–10% volume fall overrides osmolality** (the whole explanation for hyponatraemia in heart failure and cirrhosis); **V2 → cAMP → AQP2**; and **≤8 mmol/L in 24 h** with 3% saline 100–150 mL boluses.
Loses the marks: confusing water balance with sodium balance — the commonest conceptual error in the paper; getting the correction limit wrong; not knowing the **2022 renaming** to AVP-deficiency / AVP-resistance.

■ CORE 1 M

The set point

DEFINITION / CRITERIA

Water balance defends **plasma osmolality at 275–295 mOsm/kg** (tonicity, essentially [Na^+]) — **not** volume, which is defended by sodium and the RAAS. Hyponatraemia is a water problem; hypovolaemia is a sodium problem. Two effectors: **ADH** (excretes/retains water) and **thirst** (takes water in). Thirst is the more powerful — hypernatraemia essentially requires no access to water.

■ CORE 1.5 M

ADH physiology

Element	Detail
Synthesis	Supraoptic and paraventricular nuclei → axonal transport → stored/released from the **posterior pituitary**; co-se with **copeptin** (a stable surrogate) and neurophysin II
Osmotic trigger	**Osmoreceptors in the OVLT**; **threshold 280–285 mOsm/kg** (a 1% change alters ADH); **thirst threshold is higher, 290–295**
Non-osmotic triggers	**Baroreceptor: >7–10% fall in effective circulating volume overrides osmolality** (the reason for hyponat in heart failure and cirrhosis); nausea (very potent), pain, stress, hypoxia, surgery, morphine, nicotine, carbama SSRIs
Receptors	**V1a** — vascular smooth muscle (vasoconstriction, platelets); **V1b** — pituitary (ACTH); **V2** — basolateral principa (water), and endothelium (releases **vWF/factor VIII** — why DDAVP treats mild haemophilia A and uraemic blee
V2 signalling	V2 → Gs → adenylate cyclase → **cAMP → PKA → phosphorylates AQP2 at Ser256** → vesicles fuse with the ap membrane; water exits basolaterally via **AQP3/AQP4**. Long-term: increased AQP2 transcription and UT-A1 urea transport

■ CORE 1.5 M

Disorders

	SIAD(H)	AVP-deficiency (central DI)	AVP-resistance (nephrogenic
Problem	Too much ADH	Too little ADH	Kidney will not respond
Serum Na^+	**Low**	High-normal / high	High-normal / high
Urine osm	**>100** (inappropriately concentrated)	<300 (dilute)	<300 (dilute)
Urine Na^+	**>30 mmol/L** (euvolaemic)	Variable	Variable
Causes	SCLC, CNS/pulmonary disease, drugs (SSRI, carbamazepine, cyclophosphamide), pain/nausea, **TB meningitis**	Trauma, surgery, tumour, granuloma, **TB/sarcoid hypophysitis**, autoimmune	**Lithium**, hypercalcaemia, hypokalaemia, obstruction, AVPR2/AQP2 mutation
Response to DDAVP	—	**Urine osm rises >50%**	**No response**

■ ADDS 0.5 M

Treatment

Correction limits are the most examined numbers in nephrology.

DRUG DOSE

- **Severe symptomatic hyponatraemia** (seizures, coma): **3% NaCl 100–150 mL IV over 20 min, repeat up to 3 times** until symptoms resolve or Na^+ rises 4–6 mmol/L.
- **Correction limit: ≤8 mmol/L in any 24 h** (absolute maximum 10; ≤8 if high-risk — chronic hyponatraemia, alcohol use, malnutrition, hypokalaemia, liver disease). Exceeding it → osmotic demyelination syndrome (locked-in syndrome, 2–6 days later). If over-corrected → **relower** with 5% dextrose ± DDAVP 2 µg IV.
- SIAD: fluid restriction <800–1000 mL/day; **oral urea 15–30 g/day** (cheap, effective, under-used); **tolvaptan 15–60 mg OD** (start in hospital, no fluid restriction, hepatotoxicity, expensive); salt tablets ± furosemide.
- AVP-D: **desmopressin** intranasal 10–20 µg BD or oral 100–400 µg BD/TDS. AVP-R: treat the cause; **amiloride** for lithium; thiazide + low-salt, low-protein diet ± NSAID (paradoxical antidiuresis).

■ INDIA 0.5 M

Recent & India

INDIAN RELEVANCE

2022 nomenclature change: central DI → **AVP-deficiency**, nephrogenic DI → **AVP-resistance** (to prevent fatal confusion with diabetes mellitus and missed desmopressin doses). **Arginine-stimulated copeptin** outperforms the water deprivation test (Fenske, *NEJM* 2018) but is **not available in most Indian laboratories**. In India, always think **tuberculous meningitis** (SIAD *and* cerebral salt wasting) and **tuberculous hypophysitis**; tolvaptan cost restricts use, making **fluid restriction and oral urea** the practical mainstays.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

ADH is released from the posterior pituitary when osmolality exceeds ~283 mOsm/kg, or when volume falls by >7–10% (which overrides osmolality), and acts through **V2 → cAMP → AQP2**. Too much ADH is SIAD, too little is AVP-deficiency, and renal resistance is AVP-resistance — separated by urine osmolality and the response to desmopressin. Whatever the cause, **never correct sodium by more than 8 mmol/L in 24 hours**.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

Osmolality **275–295** · **ADH threshold 280–285** · **thirst 290–295** · **volume fall >7–10% OVERRIDES osmolality** · SON/PVN → posterior pituitary; **copeptin** · **V1a** vessels · **V1b** ACTH · **V2** water + **vWF** · **V2 → Gs → cAMP → PKA → AQP2 Ser256**; AQP3/4 basolateral · **SIAD: U-osm >100, U-Na >30, euvolaemic** · **CORRECT ≤8 mmol/L per 24 h — else osmotic demyelination** · **3% NaCl 100–150 mL over 20 min × up to 3** · over-corrected → **5% dextrose + DDAVP 2 µg** · **2022: AVP-deficiency / AVP-resistance**

B6 Erythropoietin

5 M | SN

MARK DISTRIBUTION · segment width = marks · colour = Pareto tier — TOTAL 5 M

The molecule 1 M	Oxygen sensing 1 M	Clinical states 1.5 M	Therapy 1 M	Recent & India 0.5 M

WHAT THE EXAMINER WANTS TO KNOW

Tests: where EPO is made, **how** oxygen is sensed, and **what** the treatment targets are. All three are asked.
Earns the marks: peritubular interstitial fibroblasts (not tubular cells); the **PHD–VHL–HIF-2α** pathway (Nobel Prize 2019); **iron first**; **Hb target 10–11.5, never deliberately above 13** (NORMAL HAEMATOCRIT, CHOIR, CREATE, TREAT); and **roxadustat, CDSCO-approved in India** though FDA-declined.
Loses the marks: siting EPO in tubular cells; giving an ESA without correcting iron — in India also B_{12}/folate and hookworm; targeting a normal haemoglobin; forgetting **pure red cell aplasia**.

■ CORE 1 M

The molecule

DEFINITION / CRITERIA

Erythropoietin (EPO) is a 30.4 kDa, 165-amino-acid, heavily glycosylated glycoprotein hormone encoded on **chromosome 7q22**. ~90% is produced by the kidney — by **peritubular interstitial fibroblast-like (REP) cells** in the **cortex and outer medulla** — and ~10% by the liver (the main fetal source, which is why anephric patients are not completely anaemic). Normal level 4–26 mU/mL; half-life 6–9 h.

■ CORE 1 M

Oxygen sensing

The 2019 Nobel — always worth a line.

```
NORMAL O2 :  PHD (prolyl hydroxylase) hydroxylates HIF-2 alpha
             -> VHL binds -> ubiquitination -> proteasome -> NO EPO
HYPOXIA   :  PHD needs O2 (+Fe2+, 2-oxoglutarate) -> INACTIVE
             -> HIF-2 alpha stabilised -> binds HIF-1 beta (ARNT)
             -> hypoxia response element -> EPO GENE TRANSCRIBED
                          |
                          v
  EPO -> EPO-R on BFU-E / CFU-E -> JAK2 -> STAT5 -> Bcl-xL
       -> ANTI-APOPTOSIS of erythroid progenitors -> RBC mass rises
  [Kaelin, Ratcliffe, Semenza - Nobel Prize 2019]
```

■ CORE 1.5 M

Clinical states

EPO level	Setting	Example
Low (inappropriately normal for the Hb)	**Anaemia of CKD** — loss of REP cells + uraemic inhibitors + **hepcidin-driven functional iron deficiency**	Normocytic normochromic anaemia from eGFR <60; universal 30
High — appropriate	Tissue hypoxia	High altitude, COPD, cyanotic heart disease, high-affinity Hb, s
High — inappropriate (paraneoplastic)	Autonomous production	**Renal cell carcinoma**, hepatocellular carcinoma, **cerebellar haemangioblastoma**, uterine leiomyoma, phaeochromocyto ADPKD
High — iatrogenic	ESA therapy; **doping**	Detectable by isoelectric focusing
High — post-transplant	**Post-transplant erythrocytosis** in 10–15%, 8–24 months on	Treat with an ACE inhibitor or ARB

■ ADDS 1 M

Therapy

DRUG DOSE

- **Correct iron first**: target TSAT >20–30% and ferritin >100 (ND-CKD) / >200 ng/mL (HD) before or with any ESA.
- **Epoetin alfa/beta** 50–100 U/kg SC three times weekly; **darbepoetin alfa** every 1–2 weeks; **CERA** monthly.
- **KDIGO 2012 targets:** initiate when **Hb <10 g/dL**; maintain **10–11.5 g/dL**; **never deliberately exceed 13 g/dL** — excess mortality, stroke and vascular access thrombosis (**NORMAL HAEMATOCRIT, CHOIR, CREATE, TREAT**).
- **Hyporesponsiveness:** iron deficiency (commonest), infection/inflammation, hyperparathyroidism, aluminium, B_{12}/folate deficiency, haemolysis, blood loss, malignancy, inadequate dialysis.
- ⚠ **Pure red cell aplasia** from anti-EPO neutralising antibodies — classically with subcutaneous epoetin; sudden reticulocytopenic transfusion-dependent anaemia. Stop all ESAs.

■ INDIA 0.5 M

Recent & India

INDIAN RELEVANCE

HIF-PHI (roxadustat, daprodustat, vadadustat) — oral PHD inhibitors that stabilise HIF-2α → endogenous EPO **plus** reduced hepcidin and better iron mobilisation. **Roxadustat is approved in India (CDSCO, 2021)** for anaemia of CKD in both dialysis and non-dialysis patients; the FDA declined approval over cardiovascular safety, so counsel about thrombosis/MACE. Oral route and no cold chain are genuine advantages in rural India. Status: **emerging**.
Indian practice: ESA **biosimilars are widely available and inexpensive**, but anaemia in Indian CKD is usually **multifactorial** — iron deficiency, nutritional (B_{12}/folate), hookworm, chronic infection and haemoglobinopathy coexist with EPO deficiency. Treating with an ESA alone without iron and deworming is a common and expensive error. Dialysis and ESA costs are covered for eligible patients under **PM-JAY** and the **Pradhan Mantri National Dialysis Programme**.

CORNELL SUMMARY · WRITE THIS VERBATIM AS YOUR CONCLUSION

EPO is made by renal peritubular interstitial fibroblasts under the control of the **PHD–VHL–HIF-2α** oxygen-sensing pathway and acts via JAK2/STAT5 to rescue erythroid progenitors from apoptosis. Its loss explains the normocytic anaemia of CKD; its excess explains the erythrocytosis of hypoxia and of renal cell carcinoma. Treat with **iron first, then an ESA to a target of 10–11.5 g/dL and never above 13** — with oral HIF-PHIs as an emerging, now India-approved, alternative.

CRAM BOX · 60-SECOND RECALL · NIGHT BEFORE THE PAPER

30.4 kDa, 165 aa, chr 7q22 · peritubular interstitial fibroblasts, cortex + outer medulla; 90% kidney / 10% liver · **Normoxia: PHD + O_2 → VHL → proteasome. Hypoxia: HIF-2α stabilised → EPO gene · EPO-R → JAK2 → STAT5 → Bcl-xL = anti-apoptosis of BFU-E/CFU-E · Nobel 2019 · Iron FIRST: TSAT >20–30%, ferritin >100 (ND) / >200 (HD) · Start Hb <10, maintain 10–11.5, NEVER >13** (NORMAL HAEMATOCRIT, CHOIR, CREATE, TREAT) · **PRCA = anti-EPO antibodies · roxadustat CDSCO-approved 2021; FDA declined**

1 · THE NEPHRON MAP — segment → transporter → drug → disease

Segment	% Na^+	Transporter	Also does	Drug	Disease
PCT	65%	NHE3, SGLT2/1, NaPi-IIa, URAT1, megalin	Glucose, AA, HCO_3^- 80–90%, PO_4, urate; organic anion/cation secretion	Acetazolamide, SGLT2i, mannitol	Fanconi, type 2 RTA
Thin desc. limb	0	AQP1	Water only	—	—
TAL	25%	NKCC2, ROMK, ClC-Kb/barttin, claudin-16/19	Diluting segment; paracellular Ca^{2+}/Mg^{2+}; macula densa	Furosemide, torsemide	Bartter 1–5, FHHNC
DCT	5–10%	NCC, TRPV5, KCNJ10, WNK-SPAK	Ca^{2+} reabsorption; Mg^{2+} (TRPM6)	Thiazides	Gitelman, Gordon, EAST
CNT/CD principal	3%	ENaC, ROMK/BK, AQP2	K^+ secretion; water	Amiloride, spironolactone, tolvaptan	Liddle, PHA, nephrogenic DI
CD α-intercalated	—	H^+-ATPase, H^+/K^+-ATPase, AE1	Acid secretion, NH_4^+ trapping	Amphotericin B (toxin)	Distal (type 1) RTA
CD β-intercalated	—	Pendrin	HCO_3^- secretion, Cl^- reabsorption	—	Thiazide-resistant HTN

2 · TUBULOPATHIES — the five-column discriminator

Disorder	Gene / defect	BP	K^+	Acid-base	Urine Ca^{2+}	Clue
Bartter	NKCC2/ROMK/ClC-Kb/barttin (TAL)	N ↓	↓	Alkalosis	↑	Antenatal, nephrocalcinosis, deafness (type 4)
Gitelman	SLC12A3 — NCC (DCT)	N ↓	↓	Alkalosis	↓	Adult, **Mg^{2+} very low**, tetany, chondrocalcinosis
Liddle	ENaC gain of function	↑	↓	Alkalosis	N	Renin AND aldosterone **low**; amiloride works
Conn's	Aldosterone excess	↑	↓	Alkalosis	N	Renin low, **aldosterone high**; ARR screening
AME / licorice	11β-HSD2 loss	↑	↓	Alkalosis	N	Both low; cortisol acts on MR
Gordon (PHA2)	WNK1/4, KLHL3, CUL3	↑	↑	**Normal-AG acidosis**	↓	**Thiazide-responsive**; mirror image of Gitelman
PHA1	MR or ENaC loss	↓	↑	Acidosis	N	Salt wasting infant; high renin + aldosterone
Vomiting	Acquired	↓	↓	Alkalosis	N	**Urine Cl^- <25 mEq/L**
Diuretic abuse	Acquired	↓ N	↓	Alkalosis	Variable	Urine diuretic screen; variable urine Cl^-

3 · GFR — equations, caveats, cut-offs

Item	Detail
Gold standard	**Inulin clearance**; practical measured GFR = iohexol, ^{99m}Tc-DTPA, ^{51}Cr-EDTA, iothalamate
Current equation	**CKD-EPI 2021 (race-free) creatinine**; confirm with **cystatin C** when accuracy changes management (KDIGO 2024)
Cockcroft–Gault	[(140−age)×wt]/(72×Scr) × 0.85 if female — gives **CrCl, not indexed**; still used on many drug labels
CrCl vs GFR	24-h CrCl **overestimates GFR by 10–20%** (tubular secretion)
Falsely HIGH eGFR	Low muscle: elderly, cirrhosis, amputee, malnutrition, **vegetarian/low-protein Indian diet**
Falsely LOW eGFR	High muscle mass, creatine supplements, cooked-meat meal
Creatinine ↑ without GFR fall	**Trimethoprim, cimetidine, dolutegravir, cobicistat, ritonavir** — block tubular secretion
KDIGO staging	**G1** ≥90 · **G2** 60–89 · **G3a** 45–59 · **G3b** 30–44 · **G4** 15–29 · **G5** <15. Albuminuria **A1** <30 · **A2** 30–300 · **A3** >300 mg/g. **Always report G × A**; CKD needs ≥90 days
AKI (KDIGO 2012)	↑Scr ≥0.3 mg/dL in 48 h, **or** ≥1.5× baseline in 7 days, **or** UO <0.5 mL/kg/h for 6 h

4 · RENAL TUBULAR ACIDOSIS — the four-line table

	Type 1 (distal)	Type 2 (proximal)	Type 4
Defect	H^+-ATPase (α-intercalated cell)	HCO_3^- reabsorption threshold (PCT)	Aldosterone deficiency / resistance
Serum K^+	↓	↓	↑
Urine pH	**>5.5 always**	<5.5 (once below threshold)	<5.5
Serum HCO_3^-	May fall <10	Plateaus 12–18	>17
Stones / nephrocalcinosis	**Yes** (hypocitraturia + alkaline urine)	No	No
Confirm	Urine pH on acidaemia; furosemide–fludrocortisone test	**FE-HCO_3^- >15%** on alkali load	Hyperkalaemia + low renin/aldosterone
Alkali dose	**1–2 mEq/kg/day** + K^+ citrate	**5–15 mEq/kg/day** + K^+ ± thiazide	Usually low dose; fludrocortisone 0.1 mg
Indian causes	Idiopathic, **Sjögren's**, amphotericin B, obstruction, sickle cell	**Tenofovir**, myeloma, ifosfamide, Wilson, cystinosis	Diabetes, CNI, NSAID, ACEi/ARB, trimethoprim, obstruction

EXAMINER PEARL

Urine anion gap = $Na^+ + K^+ - Cl^-$ → neGUTive = GI loss (NH_4^+ present); **positive = renal (RTA)**. Invalid with ketones, hippurate (toluene) or other unmeasured anions — use the **urine osmolal gap** ($NH_4^+ \approx ½ \times$ gap; <150 mOsm/kg = renal defect).

5 · POTASSIUM — shifts, causes, and the emergency drill

K^+ INTO cells (↓ serum)	K^+ OUT of cells (↑ serum)	Hypokalaemia — renal loss	Hyperkalaemia — causes
Insulin; β_2-agonist; alkalosis; aldosterone; hypothermia; B_{12}/folate therapy; hypokalaemic PP	Mineral acidosis; insulin deficiency + hyperosmolality; α-agonist; β-blocker; digoxin toxicity; **suxamethonium**; cell lysis; exercise	Diuretics; RTA 1 & 2; Bartter/Gitelman; Conn's, Liddle, AME; **hypomagnesaemia**; amphotericin B; osmotic diuresis	**AKI/CKD (oliguria)**; RAASi, NSAIDs, trimethoprim, heparin, digoxin, β-blockers; type 4 RTA; Addison's; rhabdomyolysis, tumour lysis; **K^+ salt substitutes**; pseudohyperkalaemia (haemolysis, ↑↑platelets/WBC, tight tourniquet)

DRUG DOSE

HYPERKALAEMIA — 5 steps. 1 Stabilise: calcium gluconate 10% 10 mL IV over 2–3 min (repeat at 5 min); onset 1–3 min, lasts 30–60 min. **2 Shift: 10 U regular insulin + 25 g dextrose** IV (↓ 0.5–1.2 mEq/L; use 5 U if eGFR <30; glucose hourly × 6 h) ± **salbutamol 10–20 mg nebulised** ± $NaHCO_3$ **only if acidotic**. **3 Remove:** furosemide 40–80 mg IV + volume; **SZC 10 g TDS × 48 h → 5–10 g OD**; patiromer 8.4 g OD; **dialysis** if oligo-anuric. **4 Stop the culprit. 5 Prevent:** diet, review RAASi (KDIGO 2024 — use a binder to *keep* the RAASi). ⚠ **Never SPS + sorbitol** (colonic necrosis). **Treat the ECG, not the number.**
HYPOKALAEMIA: oral KCl 20–40 mEq; IV 10 mEq/h peripheral, max 20 mEq/h central with monitoring. **Always give magnesium** — hypomagnesaemia disinhibits ROMK and makes hypokalaemia refractory. Work-up: spot **urine K:Cr** (<13 mEq/g = extrarenal) → acid–base → BP. **TTKG is obsolete.**

6 · URINARY CASTS — instant diagnosis

Cast	Means	Cast	Means
Hyaline	**Normal**; dehydration, exercise, diuretics	Fatty / oval fat body (**Maltese cross**)	**Nephrotic syndrome**
RBC cast	**Glomerulonephritis / vasculitis** (pathognomonic)	Waxy / **broad**	**Chronic kidney disease** ('renal failure cast')
WBC cast	**AIN**, pyelonephritis, proliferative GN	Pigment (red-brown)	Rhabdomyolysis, haemolysis, **bile casts**
Muddy-brown granular	**Acute tubular necrosis**	Crystal / drug	Acyclovir, sulfa, methotrexate, oxalate, **light-chain cast nephropathy**
RTE cell cast	ATN, AIN, viral nephropathy	**TELESCOPED (all of them)**	**LUPUS NEPHRITIS** (esp. class IV); also MPGN, RPGN, endocarditis GN, HSP

7 · AKI BIOMARKERS

Class	Marker	Window / cut-off	Status
Functional	Creatinine, cystatin C, penKid	Cystatin C rises 12–24 h earlier	Standard / optional
Damage	NGAL, KIM-1, L-FABP, IL-18, NAG	2–6 h post-insult; NGAL confounded by sepsis & CKD	Optional
Cell-cycle arrest	**[TIMP-2]×[IGFBP7]** (NephroCheck®)	**>0.3 = risk; >2.0 = high risk** of KDIGO 2–3 within 12 h	**FDA-approved 2014**
Persistence / repair	CCL14; DKK3	CCL14 → persistent severe AKI (RUBY)	Emerging
□□□□ **Furosemide stress test**	**1.0–1.5 mg/kg IV** after volume repletion	**Urine output <200 mL over 2 h → progression to stage 3** (Chawla 2013)	**Cheap, bedside, India-appropriate**

8 · THE KIDNEY AS AN ENDOCRINE ORGAN

Secretes	Site	Trigger	Fails in CKD →
Erythropoietin	Peritubular interstitial fibroblasts (cortex/outer medulla)	Hypoxia → **HIF-2α** (PHD/VHL)	**Normocytic anaemia**
Calcitriol	PCT 1α-hydroxylase	↑PTH, ↓PO_4; **inhibited by FGF23**	**CKD-MBD**, 2° hyperparathyroidism
Renin	JG granular cells	↓Stretch, ↓NaCl at macula densa, β_1	Hypertension
Prostaglandins	Medullary interstitial cells	Ischaemia, Ang II	**NSAID → AKI** when volume-depleted
Klotho	DCT	—	**Earliest CKD-MBD change** (with ↑FGF23)
Metabolic: gluconeogenesis (~40% in fasting) · ammoniagenesis (net acid excretion) · catabolism of insulin (30–40%), PTH, β_2-microglobulin			**Hypoglycaemia · acidosis · β_2-M amyloid (carpal tunnel)**

9 · WATER, ADH AND SODIUM — numbers you must not get wrong

Parameter	Value / rule
Plasma osmolality	275–295 mOsm/kg; calculated = 2×Na^+ + glucose/18 + urea/2.8 (mg/dL)
ADH osmotic threshold / thirst	**280–285** / **290–295** mOsm/kg
Non-osmotic override	Fall in effective circulating volume of **>7–10%** overrides osmolality
Urine osmolality range	50 → 1200 mOsm/kg; medullary gradient ≈ **50% NaCl + 50% urea**
V2 pathway	V2 → Gs → cAMP → PKA → **AQP2 Ser256-P** → apical insertion (AQP3/4 basolateral)
Na^+ correction limit	**≤8 mmol/L per 24 h** (absolute max 10; ≤8 if high-risk) — else **osmotic demyelination**
Symptomatic hyponatraemia	**3% NaCl 100–150 mL over 20 min × up to 3**, or until Na^+ ↑ 4–6 mmol/L
Over-correction rescue	5% dextrose ± **DDAVP 2 µg IV** to re-lower
SIAD diagnosis	Hypotonic hyponatraemia + **U_{osm} >100** + **U_{na} >30 mmol/L** + clinical euvolaemia + normal thyroid/adrenal/renal function, no diuretic
2022 nomenclature	Central DI → **AVP-deficiency**; nephrogenic DI → **AVP-resistance**

10 · □□□□ INDIAN ONE-LINERS — drop one into every answer

INDIAN RELEVANCE

- **CKDu — Uddanam belt (coastal Andhra / south Odisha):** chronic interstitial nephritis in farming communities; bland sediment, small kidneys, early loss of concentrating ability; heat stress ± agrochemical/silica hypotheses; ICMR studies ongoing.
- **Tenofovir (NACO first-line ART)** → proximal tubular injury, Fanconi syndrome, type 2 RTA — monitor creatinine, phosphate, urine dipstick.
- **Rifampicin (intermittent/re-introduced)** → AIN + AKI ± haemolysis; far less common since NTEP moved to **daily FDC regimens (2019)**.
- **OTC NSAIDs, analgesic combinations, PPIs and herbal/Ayurvedic preparations (lead, cadmium)** — the commonest drug causes of TIN in India.
- **Tropical community-acquired AKI:** snake envenomation, falciparum malaria, leptospirosis, scrub typhus, diarrhoeal disease, **obstetric AKI** — the ISN **0by25** initiative piloted low-cost detection in India.
- **Distal RTA ± Sjögren's** is a common, treatable and frequently missed Indian cause of hypokalaemic paralysis and nephrocalcinosis.
- **Takayasu arteritis** is the leading cause of renovascular hypertension in young Indians (not fibromuscular dysplasia).
- **Pott's spine / tubercular myelitis** is the leading non-traumatic cause of neurogenic bladder; reusable clean catheters for CIC are standard practice.
- **Roxadustat approved by CDSCO (2021)** for anaemia of CKD (FDA declined) — oral, no cold chain; ESA biosimilars are cheap and widely available, but correct **iron, B_{12}/folate and hookworm** first. Dialysis is covered by **PM-JAY** and the **Pradhan Mantri National Dialysis Programme**.
- **Low birth weight (NFHS-5 ≈ 18%)** → low nephron endowment → hyperfiltration → CKD and hypertension (Brenner hypothesis).
- Where nationally representative data do not exist, say so: *"Reliable contemporary nationally representative Indian data are limited."*

11 · DIAGRAMS TO DRAW IN THE EXAM (2 minutes each, high marks)

Diagram	Essential labels	Best used in
Nephron with transporters	PCT (NHE3, SGLT2), TDL (AQP1), TAL (NKCC2, ROMK, ClC-Kb), DCT (NCC), CD (ENaC, AQP2, H^+-ATPase)	Q1, Q7, Q8 — **draw this in almost any renal answer**
Countercurrent multiplier	300 → 1200 mOsm; single effect 200; urea recycling UT-A1/A3; vasa recta as exchanger	Q2, Q3, B5
Filtration barrier	Fenestrated endothelium · GBM (collagen IV α3α4α5) · slit diaphragm (nephrin–podocin)	B2
JGA	Macula densa · granular cells · lacis cells · afferent/efferent arterioles · adenosine A1 arrow	B4, Q7
Micturition reflex	S2–S4 pelvic (M3) · T10–L2 hypogastric (α_1, β_3) · pudendal (Onuf) · PMC · PAG · cortex	Q4, Q5
Acidosis algorithm	AG → GOLD MARK / normal AG → urine AG → serum K^+ → RTA type	Q7
K^+ secretion in principal cell	ENaC → lumen negative → ROMK + BK; aldosterone × distal Na^+ delivery × flow	Q9
HIF/PHD/VHL oxygen sensing	PHD + O_2 → VHL → proteasome; hypoxia → HIF-2α → EPO gene	B6, Q12

12 · MARK DISTRIBUTION AT A GLANCE — where the marks actually sit

■ **CORE** ■ **ADDS** ■ **DIST** ■ **INDIA** *CORE = the vital few you cannot pass without · ADDS = separates good from average · DIST = gold-medal differentiator · INDIA = Indian relevance*

#	Topic	M	Mark split — bold = Pareto core · orange = Indian relevance · gold = distinction only
Q1	Nephron segments; RFTs for TIN	10M	**Open with this 1** · **Segments & function 3** · **What is TIN? 1** · **RFTs for TIN 3** · Traps 1 · **Indian relevance 1**
Q2	Loop of Henle; Bartter's syndrome	10M	**Anatomy first 1** · **Countercurrent multiplier 3** · **TAL transport 2** · **Bartter syndrome 2** · Clinical & DDx 1 · **Management 1**
Q3	Urinary concentrating mechanism	5M	**Definition 1** · **Three requirements 1.5** · **Key numbers 1** · When it fails 1 · **Test & India 0.5**
Q4	Bladder innervation; dysfunction	10M	**Open with this 1** · **Innervation 3** · **Reflex arc 2** · **Classification 2** · Red flags 0.5 · Evaluation 0.5 · **Management 1**
Q5	Bladder nerve supply; automatic bladder	10M	**Definition 1** · **Nerve supply 3** · **Evolution after SCI 2** · **Automatic vs autonomous 2** · Complications 1 · **Management 1**

#	Topic	M	Mark split — bold = Pareto core · orange = Indian relevance · gold = distinction only
Q6	Estimation of GFR	5M	**Definition 1** · **Methods 2** · Caveats 1 · **Guideline & India 1**
Q7	GFR; tubular transport; acidosis mgmt	10M	**Part 1 — GFR 2** · **Part 2 — Tubular transport 2** · **Part 3 — Acidosis 2** · **RTA at a glance 2** · Emergency & CKD 1 · **Indian relevance 1**
Q8	Glomerular & PCT/loop/DCT disease	10M	**Framing 0.5** · **Glomerular disease 2** · **Tubular disease by segment 2.5** · **Bedside discriminators 1** · Stepwise Ix 1.5 · Management principles 1.5 · Recent advances 0.5 · **India 0.5**
Q9	Potassium metabolism	10M	**Open with numbers 1** · **Internal balance 1.5** · **Renal handling 2** · Aldosterone paradox 1 · **Hypokalaemia 1.5** · **Hyperkalaemia 2** · **India & recent 1**
Q10	Casts; telescoped sediment; AIN	10M	**Cast formation 1** · **Types of casts 3** · **Telescoped sediment 2** · **AIN — definition 1** · AIN — causes & clinics 2 · **AIN — treatment 1**
Q11	Biomarkers of AKI	5M	**Why we need them 1** · **Classification 2** · Where they fit 1 · **India 1**
Q12	Metabolic & hormonal functions	5M	**Framing 0.5** · **Hormones secreted 2** · Kidney as target 1 · **Metabolic functions 1** · **Recent & India 0.5**
B1	Histology of the kidney	5M	**Overview 1** · **Segment histology 2** · **Vasculature 1** · Stains & biopsy 0.5 · **India 0.5**
B2	Bowman's capsule & the filtration barrier	5M	**Bowman's capsule 1** · **The filtration barrier 2** · **Selectivity 1** · Starling forces 0.5 · **Clinical & India 0.5**
B3	Collecting system	5M	**What it is 1** · **Two cell types 2** · **Urea & water 1** · Pelvicalyceal system 0.5 · **Drugs & India 0.5**
B4	Juxtaglomerular apparatus	5M	**Definition 1** · **Components 2** · **Renin control 1** · TGF & SGLT2i 0.5 · **Pathology & India 0.5**
B5	Water balance & ADH	5M	**The set point 1** · **ADH physiology 1.5** · **Disorders 1.5** · Treatment 0.5 · **Recent & India 0.5**
B6	Erythropoietin	5M	**The molecule 1** · **Oxygen sensing 1** · **Clinical states 1.5** · Therapy 1 · **Recent & India 0.5**

EXAMINER PEARL

Read the orange down the right-hand column: **every single answer in this chapter carries 5–20% of its marks in Indian relevance**, and it is the one component almost no candidate writes. It is the cheapest mark on the paper.
Read the bold: **60–80% of every answer sits in three or four blocks** — the definition, the classification table and the mechanism. If you are short of time, write those and the conclusion, and abandon the rest. That is the whole Pareto principle applied to this paper.

13 · GOLD-MEDAL ANSWER-WRITING STRATEGY

Marks	Time	Page budget	Structure that scores
5 M (short note)	8–10 min	**1 page**	Definition box (2 lines) → **one** classification table **or** flowchart → clinical features/investigations in bullets → management with **one exact dose** → **one** □□□□ or recent-advance line → two-line conclusion. **Do not write prose paragraphs.**
10 M (LAQ)	18–22 min	**2 pages**	Definition + epidemiology (3 lines) → classification table → **pathogenesis flowchart (draw it)** → clinical features → differential diagnosis table → stepwise investigations → diagnostic criteria with source + year → **management algorithm with doses** → complications → □□□□ Indian relevance → recent advance (state whether standard / emerging) → crisp conclusion.

EXAMINER PEARL

The four marks most candidates leave on the table: (1) an **exact drug dose**; (2) a **named guideline with its year**; (3) an **Indian data point or Indian-practice line**; (4) a **drawn diagram**. Each costs under a minute. **Underline keywords**, box the definition, and never start an answer without defining the term.

14 · REFERENCES USED IN THIS CHAPTER

Category	Source
Core texts	Harrison's Principles of Internal Medicine, 22e · Brenner & Rector's The Kidney · Guyton & Hall Textbook of Medical Physiology · Ganong's Review of Medical Physiology · Davidson's Principles and Practice of Medicine, 24e · Kumar & Clark's Clinical Medicine, 10e · Goldman-Cecil Medicine · CMDT 2026 · API Textbook of Medicine · Comprehensive Clinical Nephrology (Feehally) · Wein's Campbell-Walsh-Wein Urology
International guidelines	KDIGO 2012 AKI · KDIGO 2012 Anaemia in CKD · **KDIGO 2024 CKD Evaluation and Management** · ADQI 23 consensus on AKI biomarkers (2020) · European/US hyponatraemia guidance · 2022 international consensus on AVP-D / AVP-R nomenclature
Indian sources	ICMR (CKDu / Uddanam studies) · MoHFW · **NTEP** daily FDC regimen (2019) · **NACO** ART guidelines (tenofovir) · NFHS-5 (low birth weight) · Indian Society of Nephrology · CDSCO approval of roxadustat (2021) · PM-JAY / Pradhan Mantri National Dialysis Programme · ISN 0by25 initiative
Trials / key papers cited	BICAR-ICU (*Lancet* 2018) · BiCARB (2020) · CREDENCE (2019) · DAPA-CKD (2020) · EMPA-KIDNEY (2023) · DIAMOND (2022) · TEMPO 3:4 and REPRISE (tolvaptan in ADPKD) · NORMAL HAEMATOCRIT, CHOIR, CREATE, TREAT (ESA targets) · Muriithi et al., *CJASN* 2013 (urine eosinophils) · González et al., *Kidney Int* 2008 (steroids in AIN) · Chawla et al., 2013 (furosemide stress test) · Fenske et al., *NEJM* 2018 (arginine-stimulated copeptin) · RUBY (CCL14)
Note on evidence	Guideline positions and trial findings are stated as **standard / strong / conditional / emerging / investigational** in the text. No image is reproduced from any copyrighted source; all flowcharts and diagrams in this chapter are original schematics.