

Topic 10

University Medicine

What this course is, and how to use it

This is the tenth course in University Medicine: **pathology** – the study of disease at the level of cells, tissues and organs. MED04 gave the normal histology and MED05 the physiology; this course explains what goes wrong, from reversible injury to the structured report that carries the answer.

Scope limit, stated once: a study course, not a medical degree; every case below is fictional, diagrams are schematic (no surgical photographs) and nothing here licenses or guides treatment.

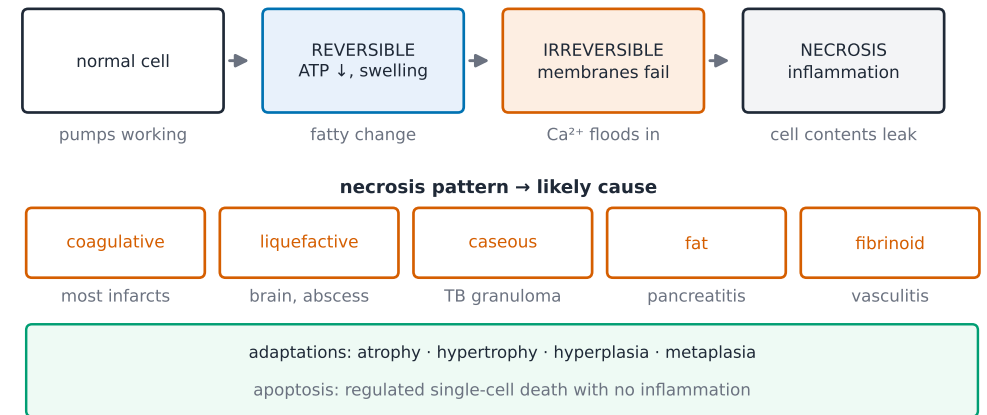
- Units 10.1–10.4 are general pathology: injury, inflammation, haemodynamics, **neoplasia**.
- Units 10.5–10.7 are the systems and the laboratory: cardiorespiratory and gut/liver/kidney disease, then the report itself.

The pathology habit: **mechanism predicts finding** – every lesion below is traced from its mechanism to the finding it produces, and every number is something you recompute.

Cell injury, adaptation and death

Why it matters. All disease begins as cell stress: whether a cell recovers or dies decides everything downstream – and the **PATTERN** of death names the cause.

The idea, with a picture. Reversible injury: hypoxia/ischaemia → ATP falls → Na^+/K^+ pump fails → cell and organelle swelling, fatty change ✓. Irreversible: membrane damage (phospholipase activation), Ca^{2+} influx, mitochondrial damage – the point of no return ✓.



ATP depletion swells the cell; membrane damage kills it – and the death pattern names the cause

The derivation (why necrosis patterns name causes). Dead cells keep their outlines when **PROTEOLYSIS** is slow – coagulative necrosis in solid organs after ischaemia ✓; the brain's lysosome-rich tissue liquefies – liquefactive; TB debris with granulomas gives cheese-like caseous; lipase on fat cells gives fatty necrosis (pancreas); immune deposits damage vessel walls – fibrinoid ✓. **Apoptosis** is regulated deletion: no inflammation, single cells, caspases.

Worked example 1 – the adaptation quartet. (Fictional teaching set) disuse → atrophy (smaller cells); hypertension → hypertrophy (bigger cells, no new fibres in cardiac muscle); hormones/liver → hyperplasia (more cells); smoking → bronchial **metaplasia** (squamous replaces columnar – one differentiation traded for another) ✓.

Worked example 2 – clinical link: the reversible window. (Fictional) ischaemic kidney tubule cells at 20 minutes: swollen, ATP low, Na^+ in – restore perfusion and they recover. At hours: membranes leak cytosolic enzymes such as LDH into the blood, where a laboratory detects them, and Ca^{2+} has entered – beyond the point of no return ✓. The enzyme curve is the cell's biography, readable from the blood.

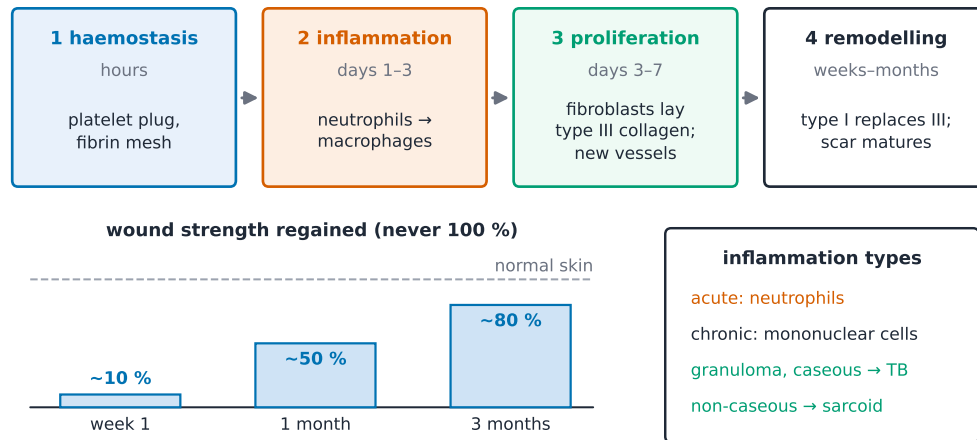
Common mistakes. Calling apoptosis a kind of necrosis (opposite mechanisms: regulated deletion vs enzymatic dissolution with inflammation). Reading **caseous necrosis** as specific to TB (it is granuloma-associated, classically TB). Forgetting fatty change is reversible (an early sign of injury, not of death).

Summary. Low ATP → swelling (reversible); membrane failure + Ca^{2+} → death (irreversible); necrosis patterns: coagulative (ischaemia, solid organs), liquefactive (brain, abscess), caseous (TB), fat (pancreas), fibrinoid (vessels); adaptations: atrophy, hypertrophy, hyperplasia, metaplasia.

Inflammation and repair

Why it matters. Inflammation is the body's response to injury – mediated by the same cells MED07 introduced. Its duration and cell type decide whether you heal, scar, or wall off a pathogen.

The idea, with a picture. Acute: minutes–hours, **neutrophils**, exudate, the cardinal signs (rubor, calor, tumor, dolor, functio laesa) ✓. Chronic: days–onward, mononuclear cells (macrophages, lymphocytes), scarring – and **granulomas**: aggregated macrophages, caseous (TB) or non-caseous (sarcoid) ✓.



Haemostasis → inflammation → proliferation → remodelling: each phase has its cells and its clock

The derivation (why wounds gain strength on a schedule). Repair runs a fixed programme: haemostasis (platelet plug, hours) → inflammation (neutrophils then macrophages, days 1–3) → proliferation: **granulation tissue** (fibroblasts, type III collagen, new vessels, days 3–7) → remodelling (type I replaces III, months – wound strength ~10 % at 1 week, rising fast over the next month and levelling at ~70–80 % from about 3 months, never 100 %) ✓. This schedule is why dehiscence risk peaks early and why sutures hold what collagen cannot yet.

Worked example 1 – dating a wound. (Fictional post-mortem teaching case) neutrophils dominate day 1–3; granulation tissue and type III collagen appear by day 3–7; by week 2 macrophages recede and collagen bridges – each histological field carries a date ✓.

Worked example 2 – clinical link: the granuloma fork. (Fictional biopsy) lung nodule with caseating granulomas → think mycobacteria (TB); non-caseating with no organism → sarcoid pattern ✓. The presence of necrosis inside the granuloma is the fork – one finding, two investigative worlds.

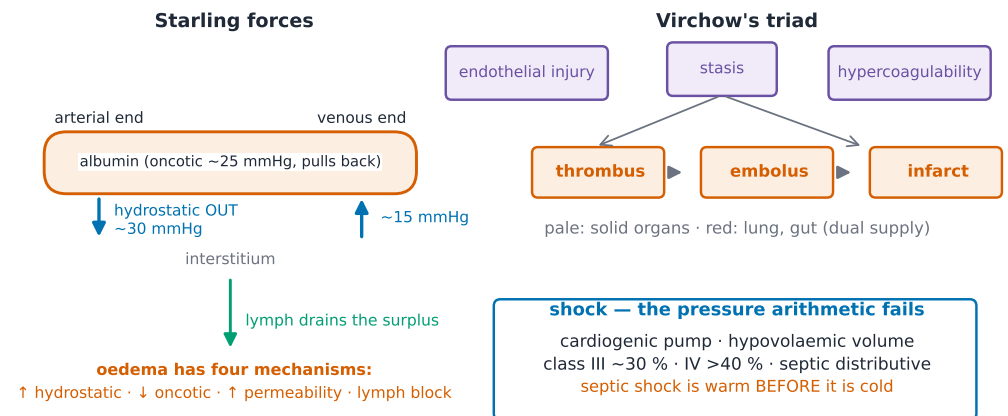
Common mistakes. Defining chronic inflammation by time alone (it is defined by its cells – macrophages, lymphocytes, plasma cells – with tissue destruction and repair going on together). Calling granulation tissue “granuloma” (granulation = repair vessels + collagen; granuloma = aggregated macrophages). Forgetting first-intention (clean approximated wound) heals faster than second-intention (open, granulating).

Summary. Acute: neutrophils, exudate, cardinal signs; chronic: mononuclear + scarring; granulomas caseous (TB) vs non-caseous (sarcoid); healing: clot (h) → inflammation (d 1–3) → granulation tissue (d 3–7) → remodelling to type I (~70–80 % strength from 3 months).

Haemodynamic disorders

Why it matters. Fluids and clots: **oedema**, thrombosis, **embolism**, **infarction** and shock are the final common paths of half of internal medicine – and all are arithmetic on pressures.

The idea, with a picture. **Starling forces:** capillary hydrostatic pressure pushes out (~30 mmHg arterial end, ~15 venous); plasma **oncotic pressure** (albumin, ~25 mmHg) pulls back; the small net surplus returns as lymph ✓. **Virchow's triad**: endothelial injury, stasis, hypercoagulability → thrombosis → embolism → infarction ✓.



Push out, pull back, drain the surplus – and the three forces that turn blood to clot

The derivation (why oedema has four main mechanisms). Net filtration = (capillary – tissue hydrostatic) – (plasma – tissue oncotic), and oedema collects when filtration outruns lymph drainage. So it arises when hydrostatic pressure rises (heart failure, with the kidney's sodium and water retention adding volume), oncotic pressure falls (liver, kidney, malnutrition), permeability rises (inflammation, exudate) or lymph is blocked (after surgery, filarial) ✓ – almost every clinical oedema is one of these four, and the mechanism names the treatment logic. Shock follows the same

arithmetic: cardiogenic (pump), hypovolaemic (volume; class III 30–40 % blood loss, class IV >40 %), distributive (septic: vasodilated capacity).

Worked example 1 – reading the pressure pair. (Fictional) right heart failure: venous hydrostatic rises → dependent pitting oedema; **nephrotic syndrome** : albumin lost (≥ 3.5 g/day) → oncotic falls → periorbital oedema ✓. Same finding, opposite mechanism – the distribution and the blood albumin separate them.

Worked example 2 – clinical link: triad to infarct. (Fictional) long flight (stasis) + post-op state (hypercoagulability) → calf thrombus → embolises → pulmonary artery occlusion → infarct or sudden death ✓. Each step of the chain has its own test: D-dimer, ultrasound, CT.

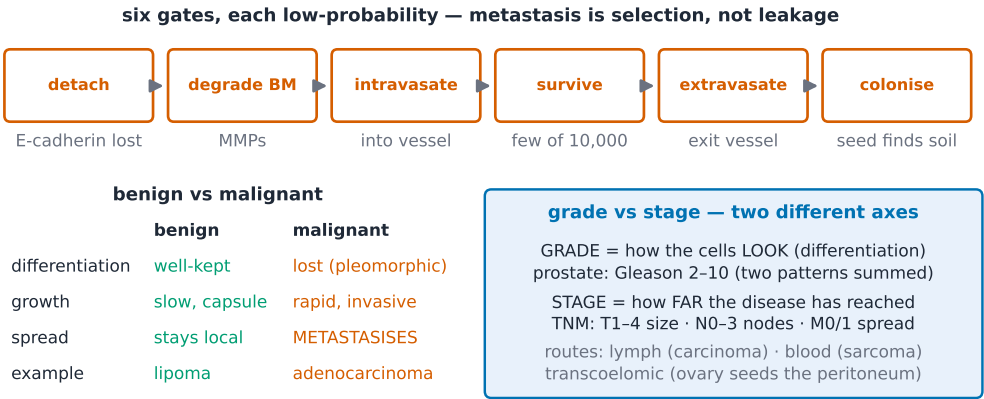
Common mistakes. Calling all oedema the same disease (four mechanisms, four arithmetic causes). Forgetting infarcts are usually pale (solid organs) but red in lung, gut and testis (loose tissue, dual supply) – and septic infarcts become abscesses. Equating shock with low pressure alone (septic shock is warm and vasodilated before it is cold).

Summary. Starling: out (~30/15) – back (~25) = lymph; oedema = ↑ hydrostatic, ↓ oncotic, ↑ permeability, lymph block; Virchow: injury + stasis + hypercoagulability → thrombus → embolus → infarct; shock: cardiogenic, hypovolaemic (class III 30–40 %), distributive.

Neoplasia

Why it matters. Neoplasia is regulated growth lost – and the vocabulary (benign, malignant, grade, stage) decides every prognosis conversation. The steps of spread explain every metastasis.

The idea, with a picture. Benign: well-differentiated, slow, encapsulated, local ✓. Malignant: pleomorphism, rapid, invasive, **metastasis** – the defining property ✓. Invasion in steps: growth → detach (E-cadherin lost) → degrade basement membrane (MMPs) → intravasate → survive the bloodstream (fewer than 1 in 10,000 cells do) → arrest → extravasate → colonise a hospitable soil ✓.



Detach, degrade, enter, survive, exit, colonise – six gates, and the last one is the soil

The derivation (why grade and stage are different axes). Grade = how abnormal the cells LOOK (well/moderate/poorly differentiated; prostate’s Gleason score sums the two commonest patterns, 6–10 in modern practice, reported as Grade Groups 1–5) – a tissue property ✓. Stage = how FAR the disease has reached (TNM: T1–T4 size/invasion, N0–N3 nodes, M0/M1 metastasis) – an anatomy property ✓. Prognosis follows stage first, grade second; treatment follows both.

Worked example 1 – the arithmetic of spread. (Fictional teaching set) a 1 cm tumour (about 10^9 cells) can shed $\sim 10^6$ cells a day into the blood, yet fewer than 1 in 10,000 survive to colonise – metastasis is a cascade of low-probability gates, not leakage ✓. That is why “positive circulation cells” alone do not equal metastases.

Worked example 2 – clinical link: routes predict addresses. (Fictional) carcinomas travel lymphatic-first (breast → axillary nodes); sarcomas go haematogenous, and so do renal cell carcinoma (into the renal vein) and hepatocellular carcinoma (into the hepatic and portal veins), with the lung a common target; prostate cancer reaches the vertebrae through the valveless vertebral veins; ovarian carcinoma seeds the peritoneum (transcoelomic) ✓. The route explains the destination – and the first scan is chosen accordingly.

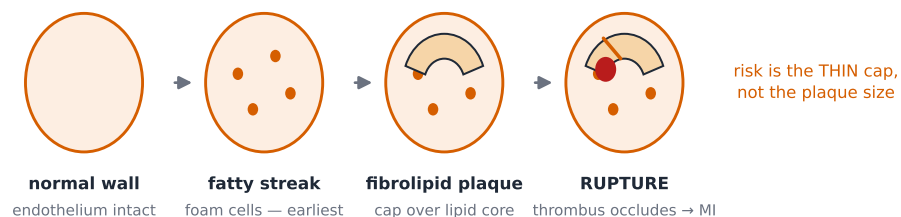
Common mistakes. Using “metastasis” loosely (it defines malignancy – benign tumours do not metastasise). Mixing grade with stage (look vs reach). Assuming larger always means worse (stage T is size/invasion, but N and M outrank it).

Summary. Benign: differentiated, slow, local; malignant: atypia, invasion, metastasis; cascade: detach (E-cadherin) → MMPs → intravasation → survival (under 1 in 10,000) → colonisation (seed and soil); grade = appearance (Gleason 6–10, Grade Groups 1–5), stage = extent (TNM); routes: lymphatic (carcinoma), blood (sarcoma, kidney, liver), transcoelomic (ovary).

Cardiovascular and respiratory pathology

Why it matters. Atherosclerosis and its rupture are the world's leading cause of death; airflow limitation is its respiratory mirror. Both are read off timelines and ratios.

The idea, with a picture. The plaque sequence: endothelial injury (LDL entry) → **fatty streak** (foam cells, the earliest lesion) → fibrolipid plaque (fibrous cap over lipid core) → **complicated plaque**: rupture → thrombosis → occlusion → infarction ✓.



the troponin clock

troponin: 3–4 h, stays ~7–10 days
CK-MB: 1–3 days (second-event clock)
necrosis 4–12 h → neutrophils 1–3 d

one ratio, two diseases

obstructive: $FEV1/FVC < 0.70$ (trapped)
restrictive: both low, ratio ≥ 0.8
 $1.6/4.0 = 0.40 \cdot 1.8/2.0 = 0.90$

Foam cells to fibrous cap to rupture – and the troponin clock that dates the event

The derivation (why troponin is the clock). Myocardial cells dying release **troponin**: blood rises 3–4 h after injury, stays elevated ~7–10 days ✓; CK-MB rises and falls faster (~1–3 days), flagging a SECOND event troponin cannot separate. The infarct itself runs a histological timeline: coagulative necrosis from 4–12 h, neutrophils 1–3 days, macrophages 3–7 days, granulation tissue from about 7–10 days, a firm scar by about 2 months – coagulative necrosis again, from 10.1's rulebook.

Worked example 1 – reading the spirometry pair. (Fictional lab) FEV1 1.6 L, FVC 4.0 L: ratio $0.40 < 0.70$ → obstructive (asthma/COPD pattern) ✓. FEV1 1.8, FVC 2.0: ratio 0.90 with both volumes low → restrictive (fibrosis) ✓. Obstruction traps air (FEV1 falls more); restriction shrinks both (ratio preserved or raised).

Worked example 2 – clinical link: the ratio as mechanism. (Fictional) emphysema destroys alveolar walls: elastic recoil falls, airways collapse on expiration – FEV1 collapses with them, FVC less so, ratio falls ✓. Fibrosis stiffens the lung: both volumes shrink but flow per volume is preserved, ratio ≥ 0.8 . One ratio, two disease families, two mechanism chains.

Common mistakes. Reading plaque size as risk (vulnerable thin-cap plaques rupture; heavily calcified stable ones often do not). Using troponin as an old-event marker

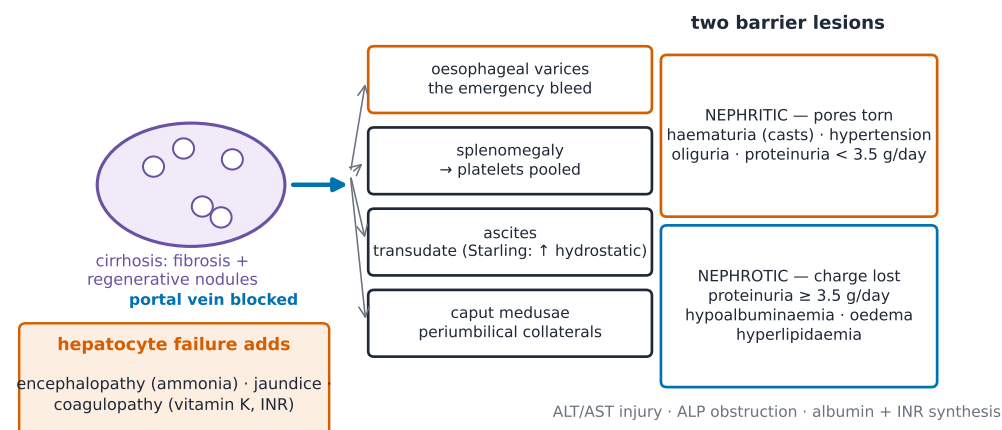
beyond its window (use it to diagnose the acute; troponin persists ~7–10 days). Equating COPD with chronic bronchitis (one umbrella, several phenotypes).

Summary. Injury → LDL → foam-cell fatty streak → fibrolipid plaque → rupture → thrombosis → infarct; troponin 3–4 h, ~7–10 d; CK-MB 1–3 d (second-event clock); FEV1/FVC < 0.70 = obstruction, both low with preserved ratio = restriction.

Gastrointestinal, liver and renal pathology

Why it matters. Cirrhosis, nephritis and nephrosis are pattern diseases: one organ's structure fails, and the consequences cascade through pressures and pores. Reading their blood tests is applied pathophysiology.

The idea, with a picture. Cirrhosis: bridging fibrosis + regenerative nodules → **portal hypertension** → oesophageal varices, splenomegaly (→ thrombocytopenia), ascites, caput medusae; hepatocyte failure adds encephalopathy (ammonia), jaundice, coagulopathy (vitamin K, INR) ✓.



One blocked vein, five collateral consequences – each with its own emergency

The derivation (why nephritic and nephrotic are different holes). Nephritic: inflammation RIPS pores → red cells and protein leak modestly: haematuria, hypertension, oliguria, proteinuria < 3.5 g/day ✓. Nephrotic: the podocytes and their slit diaphragms are damaged (in minimal change disease the foot processes flatten), so the barrier's size and charge selectivity fail → albumin floods through: proteinuria ≥ 3.5 g/day, hypoalbuminaemia, oedema, hyperlipidaemia ✓. Two patterns, two barrier lesions, two workups.

Worked example 1 – the liver panel decoded. (Fictional) ALT/AST high with ALP normal = hepatocellular (injury pattern); ALP high with transaminases low-normal = cholestatic (obstruction pattern); albumin + INR = synthetic function – a failing liver makes less of everything ✓. Three questions, one panel.

Worked example 2 – clinical link: the urine that grades the barrier. (Fictional) frothy urine + periorbital oedema + albumin <3 g/dL + protein 4.2 g/day: nephrotic ✓. Coca-Cola urine with blood pressure up and red-cell casts: nephritic ✓. The dipstick and the microscope separate the two barrier lesions before any biopsy.

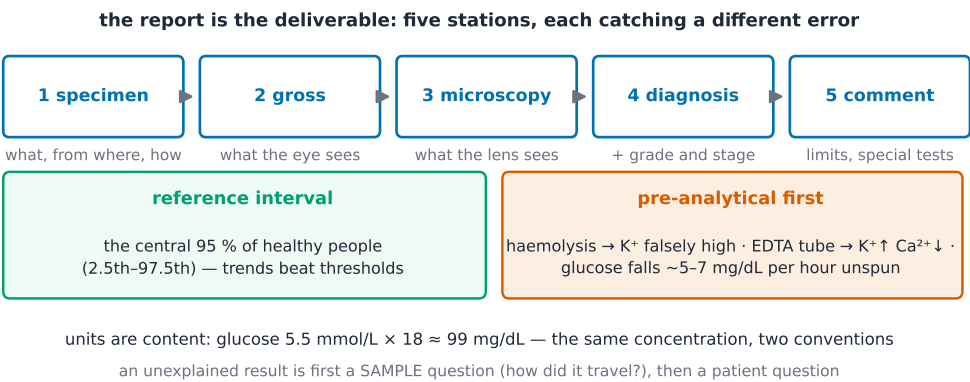
Common mistakes. Attributing varices to gastritis (they are portal pressure’s escape valves). Forgetting cirrhosis’s thrombocytopenia is splenic sequestration (a haemodynamic cause, not marrow failure). Reading “proteinuria” without quantity (3.5 g/day is the nephrotic line).

Summary. Cirrhosis = fibrosis + nodules → portal HTN: varices, splenomegaly, ascites, caput medusae; failure adds encephalopathy (NH₃), jaundice, coagulopathy. ALT/AST = injury, ALP = obstruction, albumin/INR = synthesis. Nephritic: torn pores (blood, HTN, <3.5 g); nephrotic: injured podocytes (≥3.5 g/day, hypoalbuminaemia, oedema, lipids).

Laboratory medicine and the pathology report

Why it matters. The laboratory is where mechanism becomes number – and where numbers are made wrong by tubes, time and temperature. The report is the deliverable of this whole course.

The idea, with a picture. A reference interval holds ~95 % of healthy people (2.5th–97.5th percentile); a structured report runs: specimen → gross description → microscopy → diagnosis (+ grade/stage) – plus comment ✓.



Specimen, gross, microscopy, diagnosis, comment – five stations, each catching a different error

The derivation (why pre-analytical errors dominate). The test measures the SAMPLE, not the patient: **haemolysis** bursts red cells (K⁺ falsely high); EDTA tube wrong for chemistry (K⁺ high, Ca²⁺ low); glucose falls ~5–7 % per hour in an

unseparated tube (cells keep eating); delay and heat denature ✓. An unexplained result is first a sample question, then a patient question.

Worked example 1 – the unit trap. (Fictional) glucose 5.5 mmol/L vs 99 mg/dL – the same concentration, two conventions; multiply mmol/L by 18 for mg/dL ✓. A “high” result in the wrong units is a phone call, not a diagnosis.

Worked example 2 – clinical link: three impossible results. (Fictional) K⁺ 8.2 with a calm ECG and a recently shaken tube: haemolysis until proven otherwise. Glucose “2.8” drawn after a delayed transport: pre-analytical consumption. Calcium “1.9” in an EDTA tube: tube error, redraw ✓. Each is caught by asking HOW the sample travelled before WHY the patient is ill.

Common mistakes. Treating the interval as normal/abnormal (5 % of healthy people, 2.5 % on each side, sit outside by definition; trends and prior probability decide). Skipping the specimen description in the report (it anchors the diagnosis). Believing the analyser cannot lie (it measures the tube’s contents faithfully).

Summary. Interval = central 95 % of healthy; report stations: specimen, gross, microscopy, diagnosis, comment; pre-analytical first: haemolysis (K⁺), wrong tube (EDTA: K⁺ ↑ Ca²⁺ ↓), glucose –5–7 % per hour unspun; units: glucose mmol/L × 18 = mg/dL.