



Notes by PharmacoLearn

Human Anatomy, Physiology and Pathophysiology I

BP104T — B.Pharm Semester I

Concept Mastery Notes

Deep concepts for GPAT & competitive exams — nothing missed

As per PCI B.Pharm (NEP 2020) syllabus

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Unit I — Introduction to human body; cell & tissue organization; cell injury; integumentary system

Anatomy, physiology, pathophysiology — what each one gives you

- Anatomy describes structure: what is where, and how parts connect. Its branches include gross anatomy (what you can see), histology (tissues under the microscope), developmental anatomy, and surface anatomy.
- Physiology describes function: how those structures actually work — the chemistry and physics that keep you alive minute to minute.
- Pathophysiology describes what breaks: how normal function derails in disease. This is your bridge subject. In pharmacology you will learn that a drug "lowers blood pressure" — pathophysiology tells you which broken mechanism it is fixing, so the drug's action makes sense instead of being a fact to memorise.

Why a pharmacy student needs all three: structure tells you where a drug acts, physiology tells you what it changes, and pathophysiology tells you what is wrong in the patient in front of you. Skip any one of them and pharmacology becomes rote learning.

Levels of organization, body systems, life processes

From smallest to largest: chemical (atoms, molecules — water, proteins, DNA) → cellular (the cell, smallest living unit) → tissue (similar cells doing one job) → organ (two or more tissues, e.g., the heart) → organ-system (organs working together) → organismal (you).

The 11 organ systems: integumentary, skeletal, muscular, nervous, endocrine, cardiovascular, lymphatic/immune, respiratory, digestive, urinary, and reproductive. You will study each one across this subject's two papers — this paper covers the first five in the syllabus order: integumentary (Unit I), skeletal + muscular (Unit II), cardiovascular/lymphatic (Units III and V), nervous (Unit IV).

Life processes — organisation, metabolism (catabolism breaks down, anabolism builds up), responsiveness, movement, growth, differentiation, reproduction. Examiners love this as a 2-mark list, so keep it ready.

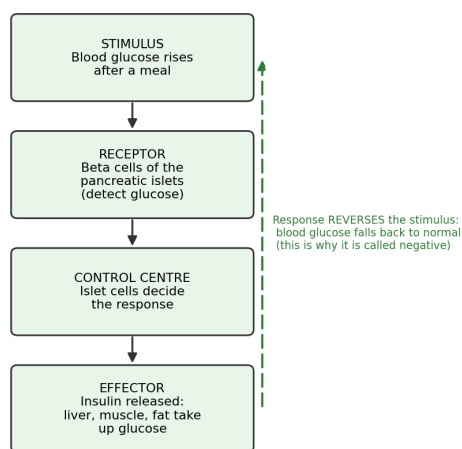
Homeostasis and feedback systems

Homeostasis is the body's refusal to let its internal conditions swing wildly: temperature near 37 °C, blood pH 7.35–7.45, fasting glucose roughly 70–110 mg/dL, no matter what is happening outside. Every feedback loop has the same three parts:

- 1 Receptor — detects the change (a sensor).

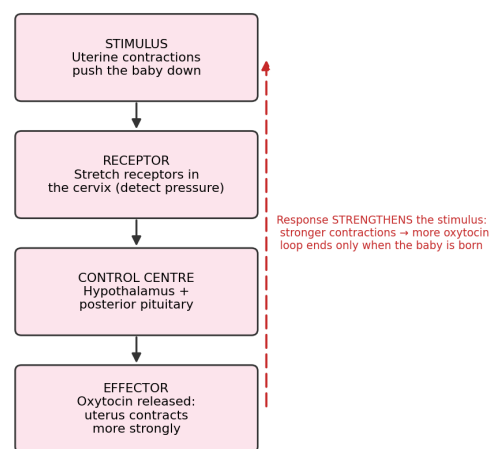
- 2 Control centre — usually the brain or an endocrine gland; decides what to do.
 - 3 Effector — muscle or gland that carries out the order.
- Negative feedback reverses the change — the response shuts the stimulus off. This runs almost everything: high blood glucose → insulin release → glucose falls. Body temperature, blood pressure, blood calcium — all negative feedback.
 - Positive feedback strengthens the change — rare, used when the body wants a rapid, all-or-nothing event. Oxytocin in childbirth: contractions push the baby down → more oxytocin → stronger contractions, until delivery ends the loop. Blood clotting is the other classic: activated platelets recruit more platelets.

NEGATIVE FEEDBACK — blood glucose control



Pharmacy link: diabetes drugs hijack this loop — metformin cuts liver glucose output; insulin analogues replace the signal.

POSITIVE FEEDBACK — childbirth (oxytocin)



Pharmacy link: synthetic oxytocin induces labour — the same positive loop, switched on deliberately.

Negative vs positive feedback loops — glucose control and childbirth

Trap alert: students write "positive feedback is good, negative feedback is bad". Wrong. The words describe direction, not desirability. Negative feedback is the normal, healthy mode for nearly every regulated variable. Also: clotting looks like pure positive feedback, but it is bounded — clotting factors get used up and inhibitors (like antithrombin) stop the spread, otherwise one cut would clot your whole circulation.

Anatomical terminology — the language of the subject

All directions assume the anatomical position: standing upright, feet together, face and palms forward.

- Planes: sagittal (left/right halves), frontal or coronal (front/back halves), transverse or horizontal (upper/lower halves).

- Directional terms: superior/inferior (toward head/feet), anterior or ventral/posterior or dorsal (front/back), medial/lateral (toward/away from the midline), proximal/distal (nearer/farther from the trunk or attachment point), superficial/deep (near the surface/far from it).
- Body cavities: dorsal cavity (cranial cavity for the brain + vertebral/spinal cavity for the cord) and ventral cavity (thoracic cavity — pleural cavities for lungs, pericardial cavity for the heart — plus the abdominopelvic cavity below the diaphragm).
- Abdominopelvic regions: nine — right and left hypochondriac, epigastric, right and left lumbar, umbilical, right and left iliac (inguinal), hypogastric. Clinicians also use four quadrants (RUQ, LUQ, RLQ, LLQ); pain in the RLQ is the classic pointer toward appendicitis.

GPAT angle: "proximal vs distal" trips people in limb questions — proximal always means nearer the point where the limb joins the trunk. The elbow is proximal to the wrist; the wrist is distal to the elbow. In drug questions the same logic appears with "proximal convoluted tubule" vs "distal convoluted tubule" of the nephron.

The cell — structure with a purpose

The cell is the structural and functional unit of life. Each organelle exists because the cell needs that job done:

- Plasma membrane — phospholipid bilayer with embedded proteins, cholesterol (keeps it fluid, not stiff), and a carbohydrate coat (glycocalyx, for recognition). The fluid-mosaic model: proteins drift in a fluid lipid sea. It is a selective barrier, a transport hub, and the cell's ID card.
- Nucleus — DNA in chromosomes; the control room. Nuclear pores let messages (mRNA) out. The nucleolus builds ribosomes.
- Mitochondria — aerobic respiration, ATP production. They carry their own small DNA — a leftover from when they were free-living bacteria.
- Ribosomes — protein synthesis. Free ribosomes make proteins for use inside the cell; ribosomes on rough ER make proteins for export.
- Endoplasmic reticulum — rough ER folds and ships proteins; smooth ER makes lipids, detoxifies drugs (the liver's smooth ER is rich in cytochrome P450 enzymes — the same enzymes that metabolise most medicines), and stores calcium (in muscle it is the sarcoplasmic reticulum).
- Golgi apparatus — modifies, labels, and packages proteins into vesicles for delivery.
- Lysosomes — bags of digestive enzymes; recycle worn-out organelles and digest engulfed microbes.
- Cytoskeleton — microtubules, actin microfilaments, intermediate filaments; shape, internal transport, cell division.
- Centrosome/centrioles — organise the spindle during cell division.

Pharmacy link: drug-metabolising enzymes live in the smooth ER of liver cells, drug receptors sit in the plasma membrane, and many antibiotics (aminoglycosides, macrolides) kill bacteria by attacking their ribosomes while sparing ours — the small structural difference between bacterial and human ribosomes is the whole basis of selective toxicity.

Transport across the cell membrane

Everything the cell needs must cross the membrane, and the route depends on size and solubility.

Passive transport — no ATP, movement down the concentration gradient:

- Simple diffusion — small lipid-soluble molecules slip through (O_2 , CO_2 , steroid hormones).
- Facilitated diffusion — via channel proteins (aquaporins for water) or carrier proteins (glucose via GLUT transporters). No energy, but the carriers can be saturated — there is a maximum speed.
- Osmosis — water moving across a semipermeable membrane toward the higher solute concentration. This is why IV fluids must be isotonic: hypotonic fluid makes RBCs swell and burst (haemolysis), hypertonic fluid shrivels them (crenation).
- Filtration — hydrostatic pressure pushes water and solutes through (glomerular filtration in the kidney).

Active transport — needs ATP, moves against the gradient:

- Primary active transport — the sodium-potassium pump (Na^+/K^+ ATPase): 3 Na^+ out, 2 K^+ in, every cycle. It maintains the resting membrane potential, cell volume, and the Na^+ gradient that powers everything below.
- Secondary active transport — rides on the Na^+ gradient the pump built. Symport moves two things the same way (Na^+ /glucose in the intestine — this coupling is exactly how oral rehydration salts pull water into the body); antiport moves them opposite ways (Na^+/Ca^{2+} exchanger).

Vesicular transport — for large cargo: endocytosis (phagocytosis — "cell eating" by neutrophils; pinocytosis — "cell drinking"; receptor-mediated endocytosis — e.g., LDL uptake), exocytosis (vesicles fuse and dump contents — neurotransmitters, insulin), transcytosis (across the cell, e.g., IgA across gut epithelium).

GPAT angle: the Na^+/K^+ ATPase is the most examined transport protein in this paper. Digoxin (cardiac glycoside) inhibits it: intracellular Na^+ rises → the Na^+/Ca^{2+} exchanger slows → intracellular Ca^{2+} rises → stronger heart contraction. One pump, one drug, one clear mechanism chain — that is how competitive exams ask it.

Cell division

- Interphase (G₁ growth, S DNA replication, G₂ preparation) is where the cell spends most of its life — division is the brief finale.
- Mitosis — one cell → two identical diploid cells, for growth and repair. Prophase (chromosomes condense, spindle forms), metaphase (chromosomes line up at the equator), anaphase (sister chromatids pulled apart), telophase (nuclei reform), then cytokinesis (cytoplasm splits). Mnemonic: "People Meet And Talk".
- Meiosis — one cell → four haploid gametes (23 chromosomes), only in the gonads; creates genetic variation.

Pharmacy link: anticancer drugs are cell-cycle poisons aimed at dividing cells. Antimetabolites (methotrexate, 5-fluorouracil) strike in S phase by faking DNA building blocks; vinca alkaloids (vincristine) wreck the mitotic spindle in M phase. Their side effects — hair loss, gut damage, low blood counts — hit the body's other rapidly dividing tissues for the same reason.

Cell junctions — how cells hold together and talk

Junction	What it does	Where it matters
Tight junction	Seals neighbours; nothing leaks between cells	Gut lining, blood-brain barrier
Adherens junction	Anchors cells via actin filaments	Epithelial sheets under tension
Desmosome	Strong "spot weld" via intermediate filaments	Skin, cardiac muscle — tissues under mechanical stress
Gap junction	Channels (connexons) pass ions/small molecules directly	Cardiac and smooth muscle — lets them contract as one unit
Hemidesmosome	Anchors the cell to the basement membrane	Epithelium sitting on connective tissue

Trap alert: tight junction = seal (between cells, nothing passes); gap junction = connect (between cells, signals pass). Students swap them constantly. Think: "tight shuts, gap chats".

Cell communication — four named forms

The syllabus names four, and each is defined by how far the signal travels:

- Contact-dependent (juxtacrine) — cells physically touch; the signal never leaves the surface (immune cells checking each other's identity).
- Paracrine — signal acts on nearby cells (histamine released by mast cells in inflammation; growth factors in wound healing).

- Synaptic — signal crosses a synapse to one specific target (neurotransmission — the NMJ in Unit II is the model example).
- Endocrine — hormone travels in blood to distant targets (insulin, thyroid hormone). Slower, longer-lasting.

(Autocrine — a cell signalling itself — is sometimes added as a fifth; cancer cells use it to drive their own growth.)

Pharmacy link: drug design copies these routes. Inhaled salbutamol is a local (paracrine-like) delivery to the airways; oral tablets rely on the endocrine-style route — absorption into blood, distribution everywhere. Understanding the route explains why the same drug can be an inhaler, a tablet, or an injection with very different effects.

Tissues — the four families

Epithelial tissue covers surfaces, lines cavities, and forms glands. Named by layers × cell shape:

Type	Structure	Location	Job
Simple squamous	Single flat layer	Alveoli, endothelium, Bowman's capsule	Filtration, diffusion
Simple cuboidal	Single cube layer	Kidney tubules, gland ducts	Secretion, absorption
Simple columnar	Single tall layer, often with goblet cells	Stomach to rectum	Absorption, mucus secretion
Stratified squamous (keratinised)	Many layers, dead surface	Skin	Protection against abrasion
Stratified squamous (non-keratinised)	Many living layers	Mouth, oesophagus, vagina	Protection, stays moist
Pseudostratified columnar	Looks layered, isn't; ciliated	Trachea	Sweeps mucus upward
Transitional	Stretchable layers	Urinary bladder	Stretches as bladder fills

Connective tissue — most abundant; few cells scattered in matrix: loose areolar (under skin), dense (tendons, ligaments); cartilage — hyaline (nose, trachea, joint surfaces), elastic (ear pinna, epiglottis), fibrocartilage (intervertebral discs, menisci); bone (mineralised); blood (fluid matrix).

Muscular tissue — skeletal (striated, voluntary, multinucleated), cardiac (striated, branched, intercalated discs, involuntary), smooth (spindle-shaped, involuntary; gut and vessel walls). Full comparison table in Unit II.

Nervous tissue — neurons (conduct impulses) plus neuroglia (support, insulation, defence).

GPAT angle: transitional epithelium appears in exactly one exam-relevant place — the urinary bladder (and ureters). If a question asks "which epithelium lines the bladder", the answer is never stratified squamous.

Cell injury and adaptation — the logic of damage

Causes of injury: hypoxia/ischaemia (the commonest — e.g., myocardial infarction), physical agents (trauma, heat, radiation), chemicals and drugs, infections, immunologic reactions (autoimmunity, hypersensitivity), nutritional imbalance, genetic defects.

Pathogenesis — what breaks inside the cell, step by step:

- ATP depletion — the Na^+/K^+ pump fails → Na^+ and water flood in → cell swelling; protein synthesis stalls.
- Cell membrane damage — lipid peroxidation by free radicals chews up the phospholipid bilayer → the membrane leaks.
- Mitochondrial damage — the permeability transition pore opens, cytochrome c escapes → triggers apoptosis; ATP production collapses.
- Ribosomal damage — ribosomes detach from the rough ER → protein synthesis falls, so the cell cannot make the enzymes and membrane proteins it needs to repair itself.
- Cytosolic calcium overload — free Ca^{2+} activates destructive enzymes (phospholipases, proteases, endonucleases) that digest the cell from inside.
- Nuclear damage — DNA injury; if severe and irreparable, the cell dies.

Notice the chain: ATP loss → pump failure → swelling and calcium rise → enzyme activation → membrane and DNA damage. One domino line, not six separate facts.

Morphology — what the damage looks like:

- Reversible injury: cell swelling (hydropic change — the first visible change, from Na^+ /water entry) and fatty change (steatosis — lipid droplets inside liver cells, as in chronic alcohol use). Remove the cause and the cell recovers.
- Irreversible injury → death by two routes:
- Necrosis — messy, unplanned death; membrane ruptures, contents spill, inflammation follows. Types: coagulative (commonest — heart, kidney; tissue outline preserved), liquefactive (brain, abscesses — tissue turns liquid), caseous (tuberculosis — cheese-like), fat necrosis (pancreatitis), fibrinoid (vessel walls in severe hypertension/vasculitis), gangrenous (limb ischaemia plus infection).
- Apoptosis — programmed, tidy death: cell shrinks, chromatin condenses, membrane blebs, fragments are eaten by neighbours — no inflammation. Driven by caspases, often triggered by cytochrome c release. The body uses it daily to delete old or damaged cells.

Adaptive changes — the cell adjusts without dying:

Change	What happens	Examples
Atrophy	Cell size decreases	Muscle wasting in a plaster cast; disuse atrophy
Hypertrophy	Cell size increases	Left ventricular hypertrophy in hypertension; muscle with exercise
Hyperplasia	Cell number increases	Benign prostatic hyperplasia; endometrial hyperplasia
Metaplasia	One adult cell type replaced by another	Smoker's bronchial epithelium: columnar → squamous; Barrett's oesophagus
Dysplasia	Disordered, abnormal growth	Cervical dysplasia — premalignant, not a benign adaptation

Trap alert: atrophy vs dystrophy — atrophy is shrinkage from disuse or lost stimulation (reversible-ish, acquired); dystrophy is defective development/nutrition of tissue (e.g., muscular dystrophy — genetic, progressive). Examiners pair them precisely because they sound alike. And never call dysplasia an adaptation — it is disordered growth on the road toward cancer, while metaplasia is an orderly, reversible substitution.

Intracellular accumulations — things piling up inside cells: lipids (fatty liver), proteins, glycogen, pigments — lipofuscin (the brown "wear-and-tear" pigment of ageing), melanin, haemosiderin (iron overload, as in repeated transfusions).

Medical terminologies — decode, don't memorise

Learn roots and you can decode hundreds of terms:

- Prefixes: hyper- (excess), hypo- (deficient), a-/an- (without), dys- (abnormal/painful), brady- (slow), tachy- (fast), endo- (inside), exo-/ecto- (outside), peri- (around), sub- (below).
- Suffixes: -itis (inflammation — arthritis, dermatitis), -oma (tumour — carcinoma), -pathy (disease — neuropathy), -emia (blood condition — anaemia), -lysis (breakdown — haemolysis), -plasia (growth — hyperplasia), -rrhage (bursting forth — haemorrhage), -stasis (standing still — haemostasis).
- Test yourself: hypertension (high pressure), bradycardia (slow heart), dyspnoea (difficult breathing), gastritis (stomach inflammation), nephritis (kidney inflammation).

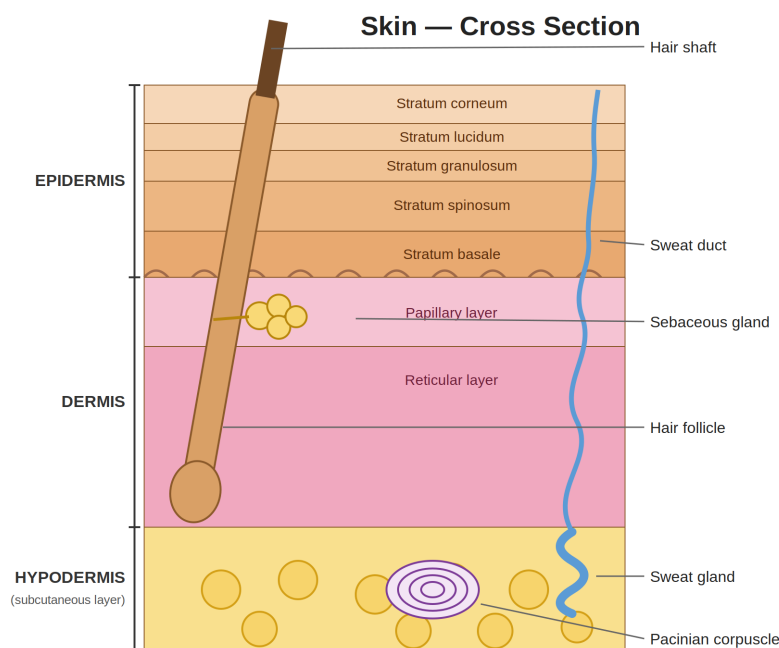
Integumentary system — the skin

The skin is the largest organ — about 2 m², roughly 16% of body weight. Three layers:

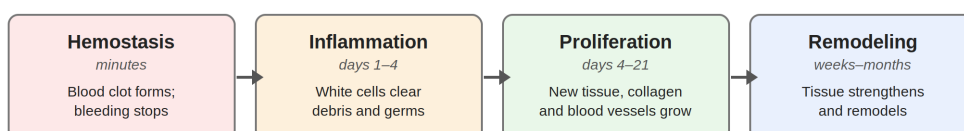
- **Epidermis** — stratified squamous keratinised epithelium, no blood vessels (it is fed by diffusion from below). Strata, deep to surface: basale (stem cells divide here — the only dividing layer), spinosum, granulosum, lucidum (thick skin only — palms, soles), corneum (dead keratinised cells, constantly shed). Mnemonic: "Beauty Salons Give Lovely Colour". Cell types: keratinocytes (make keratin), melanocytes (melanin — UV protection; differences in melanin, not cell number, explain skin colour variation), Langerhans cells (immune sentinels), Merkel cells (touch).
- **Dermis** — connective tissue with vessels, nerves, hair follicles, glands. Papillary layer (dermal papillae shape the ridges of fingerprints) and reticular layer (collagen and elastic fibres — strength and stretch).
- **Hypodermis (subcutaneous layer)** — fat and loose connective tissue; insulation, energy store, shock absorber.

Appendages: hair, nails, sebaceous glands (sebum oils skin and hair), sweat glands — eccrine (all over the body; temperature control) and apocrine (axilla, groin; scent glands, active after puberty).

Functions — protection (microbes, UV, chemicals, water loss), temperature regulation (sweating, vasodilation/vasoconstriction), sensation (touch, pressure, pain, temperature), vitamin D synthesis (UV converts 7-dehydrocholesterol — the reason sunlight matters for bones), excretion (sweat), absorption (the entire basis of transdermal drug delivery — nicotine, fentanyl, nitroglycerin patches), and immune defence.



Wound Healing — Timeline



Skin in cross-section — layers, strata, and appendages

Pharmacy link: every transdermal patch is applied physiology — the drug must cross the stratum corneum, the skin's main barrier. That is why transdermal drugs are small, lipid-soluble molecules, and why damaged skin absorbs drugs unpredictably (never apply a fentanyl patch to broken skin).

Skin disorders — psoriasis, dermatitis, leprosy

- Psoriasis — chronic autoimmune disorder: T-cells drive keratinocyte hyperproliferation, so skin cells pile up faster than they shed. Thick red plaques with silvery scales, typically on extensor surfaces (elbows, knees) and scalp. Auspitz sign (pinpoint bleeding when a scale is lifted), Koebner phenomenon (new lesions at sites of skin trauma), nail pitting. Treated with topical corticosteroids, vitamin D analogues (calcipotriol), and biologics that block the immune cytokines.
- Dermatitis — inflammation of the skin: redness, itching, swelling. Atopic dermatitis (eczema — allergic, common in children), contact dermatitis (irritant or allergic — nickel, cosmetics, detergents), seborrheic dermatitis (oily areas — scalp dandruff).
- Leprosy (Hansen's disease) — caused by *Mycobacterium leprae*; it invades skin and peripheral nerves (painless injuries and deformities follow the nerve damage). Two poles: tuberculoid (paucibacillary) — few lesions, strong cell-mediated immunity; lepromatous (multibacillary) — many lesions, weak immunity, leonine facies. Treated with multidrug therapy: dapsone + rifampicin + clofazimine. Still asked in Indian exams — know the causative organism and the drug trio.

GPAT angle: psoriasis = autoimmune hyperproliferation (silvery scales, Auspitz sign); dermatitis = inflammation (itchy, red); leprosy = *M. leprae* with nerve involvement. The nerve damage is what separates leprosy from every other skin disease in a question stem.

Wound healing — principles

Four overlapping phases:

- 1 Haemostasis (minutes) — vasoconstriction, platelet plug, clot; bleeding stops.
 - 2 Inflammatory (1–3 days) — neutrophils then macrophages clear debris and bacteria.
 - 3 Proliferative (day 3 to ~3 weeks) — fibroblasts lay collagen (type III first), angiogenesis builds new vessels, granulation tissue fills the gap, epithelium resurfaces.
 - 4 Remodelling/maturation (weeks to months) — type III collagen is replaced by stronger type I; the scar contracts and strengthens but never regains full original strength.
- Primary intention — clean surgical wound with edges closed; fast healing, thin scar.

- Secondary intention — open wound healing by granulation (pressure ulcers); slower, larger scar.
- What helps: protein, vitamin C (collagen synthesis), zinc, good blood supply. What delays: infection, diabetes, old age, smoking, poor circulation — and drugs: corticosteroids and NSAIDs slow healing.

Pharmacy link: this is why diabetic foot care is a pharmacy counselling topic, and why surgeons ask about steroid or NSAID use before operations. You will also meet this in pharmacology: corticosteroids suppress the fibroblast activity that the proliferative phase depends on.

Very short questions (2 marks)

- 1 Define anatomy, physiology and pathophysiology in one line each.
- 2 Name the three components of a feedback system.
- 3 Give one example each of negative and positive feedback.
- 4 State the mnemonic order of mitosis phases.
- 5 Name the five strata of the epidermis from deep to superficial.

Short questions (5 marks)

- 1 Explain homeostasis with the components of a feedback loop, giving one negative and one positive feedback example.
- 2 Compare passive and active transport across the cell membrane with two examples each.
- 3 Describe the pathogenesis of cell injury (ATP depletion → membrane, mitochondrial, ribosomal and nuclear damage) as a connected sequence.

Long questions (10 marks)

- 1 Describe the structure and functions of the skin with a labelled diagram. Add the pathophysiology of psoriasis and leprosy.
- 2 Define cell injury. Discuss its causes, the morphology of reversible and irreversible injury (necrosis vs apoptosis), and the five adaptive changes with examples.

How to approach these answers

- Very-short Q1: three one-line definitions; no extra explanation.
- Very-short Q2: list receptor, control centre, effector — one line each.
- Very-short Q3: glucose-insulin loop and oxytocin/childbirth (or clotting) — one line each.
- Very-short Q4: PMAT with one identifying event per phase.
- Very-short Q5: basale → spinosum → granulosum → lucidum → corneum; mention lucidum is thick-skin only.

- Short Q1: define homeostasis, draw the loop with three labelled parts, then one negative and one positive example with the mechanism.
- Short Q2: open with the energy/gradient distinction, then a two-column table of types with examples; close with the Na^+/K^+ pump and digoxin link.
- Short Q3: present it as a domino chain, not a list — ATP loss first, then pump failure, swelling, calcium overload, membrane and DNA damage.
- Long Q1: structure — three layers and five strata with the diagram, then functions as points, then psoriasis and leprosy as two short pathophysiology paragraphs with drug trios.
- Long Q2: structure — intro with definition, causes as points, reversible vs irreversible with the necrosis/apoptosis table, adaptive changes in a table with examples, one-line conclusion.

Unit II — Skeletal system, joints, bones and joint diseases

Divisions of the skeleton — and why bones are more than scaffolding

The adult skeleton has 206 bones: 80 axial (skull, vertebral column, ribs, sternum) + 126 appendicular (pectoral girdle, upper limbs, pelvic girdle, lower limbs). Children have more — many fuse with age (the sacrum's five vertebrae become one bone, for instance).

Functions examiners expect as a list: support (body framework), protection (skull → brain, rib cage → heart and lungs, vertebrae → spinal cord), movement (bones are levers that muscles pull), mineral storage (calcium, phosphorus — the skeleton is the body's mineral bank), blood cell formation (red bone marrow), and fat storage (yellow marrow). The storage function is the pharmacy-relevant one: calcium homeostasis drugs, bisphosphonates, and vitamin D all act on this mineral bank.

Types of bones

Type	Shape	Examples
Long	Longer than wide; shaft (diaphysis) + ends (epiphyses)	Femur, humerus — femur is the longest and strongest bone
Short	Cube-shaped	Carpals (wrist), tarsals (ankle) — gliding movements
Flat	Thin, curved plates	Skull bones, ribs, sternum, scapula — protection; sternum and pelvis house marrow

Type	Shape	Examples
Irregular	Complex shapes	Vertebrae, facial bones
Sesamoid	Embedded in tendons	Patella (kneecap) — the largest sesamoid; protects the tendon and improves leverage

Axial skeleton — salient features

- Skull: cranium (frontal, 2 parietal, 2 temporal, occipital, sphenoid, ethmoid = 8) protects the brain; 14 facial bones form the orbits, nasal cavity, and jaws; plus 6 auditory ossicles and 1 hyoid. The foramen magnum in the occipital bone passes the spinal cord. Skull bones meet at sutures — fibrous joints that fuse with age.
- Vertebral column: 7 cervical (C1 atlas and C2 axis — the dens of the axis lets the head rotate), 12 thoracic (anchor the ribs), 5 lumbar (large bodies — they carry the most weight), 5 fused sacral, 4 fused coccygeal. Normal curves: cervical and lumbar lordosis (inward), thoracic and sacral kyphosis (outward). Intervertebral discs — fibrocartilage with a soft nucleus pulposus — cushion the vertebrae; a "slipped disc" is herniation of this nucleus pressing on a nerve.
- Rib cage: 12 pairs — 7 true ribs (direct cartilage to sternum), 3 false ribs (join via cartilage above), 2 floating ribs (no anterior attachment). Protects heart and lungs and moves during breathing.
- Sternum: manubrium, body, xiphoid process. Its marrow is sampled in bone marrow aspiration in adults.

Appendicular skeleton — salient features

- Pectoral girdle: clavicle (collarbone — the most commonly fractured bone, it breaks protecting the shoulder) and scapula (acromion and coracoid processes, glenoid cavity receiving the humerus).
- Upper limb: humerus (head into the glenoid cavity); radius (thumb side) and ulna (forearm); 8 carpals (scaphoid fractures most often — classically after a fall on an outstretched hand); 5 metacarpals; 14 phalanges.
- Pelvic girdle: each hip bone = ilium + ischium + pubis fused at the acetabulum (hip socket). The female pelvis is wider with a broader sciatic notch — shaped for childbirth.
- Lower limb: femur (head into the acetabulum); patella; tibia (medial, weight-bearing shinbone) and fibula (lateral, slender); 7 tarsals (calcaneus — heel bone, largest tarsal); 5 metatarsals; 14 phalanges.

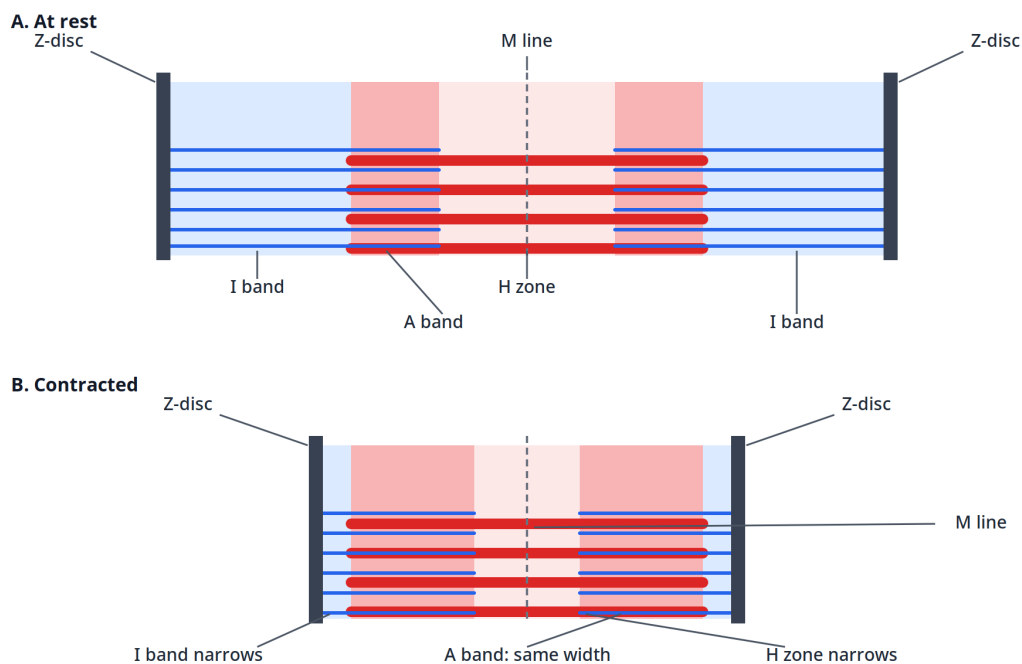
Trap alert: radius is on the thumb (lateral) side, ulna on the little-finger side; tibia is the thick medial weight-bearer, fibula the thin lateral one. In X-ray questions students routinely flip these pairs. Thumb side = radius is the anchor memory.

Organisation of skeletal muscle — down to the sarcomere

From outside in: whole muscle wrapped in epimysium → bundles of fibres (fascicles) in perimysium → each muscle fibre (one long cell) in endomysium. Tendons (dense collagen) attach muscle to bone; aponeuroses are flat tendons.

Inside a fibre: myofibrils, built of repeating sarcomeres — the contractile unit, measured Z-disc to Z-disc. Within a sarcomere: thin filaments (actin, with troponin and tropomyosin) and thick filaments (myosin). Bands: A band (thick filaments — dark), I band (thin only — light), H zone (pale centre of the A band), M line (midline anchor).

Sarcomere: Rest vs Contracted (Sliding Filament Theory)



Key point: A band width is unchanged — filaments slide past each other; they do not shorten.

Legend: — Actin — thin filament — Myosin — thick filament

Sarcomere structure — bands, filaments, and Z-discs

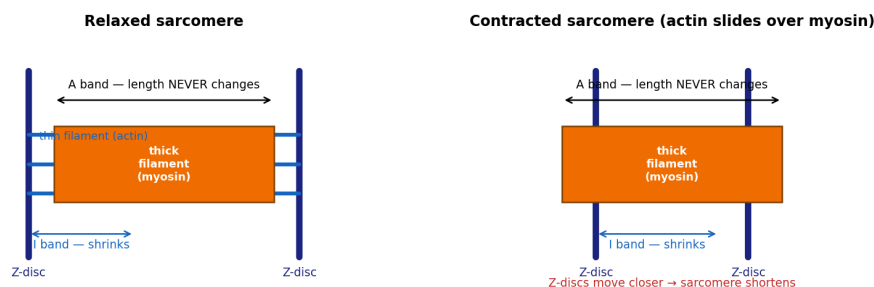
Physiology of muscle contraction — the sliding filament theory

The filaments do not shorten; the thin filaments slide over the thick ones, pulling the Z-discs together. Sequence:

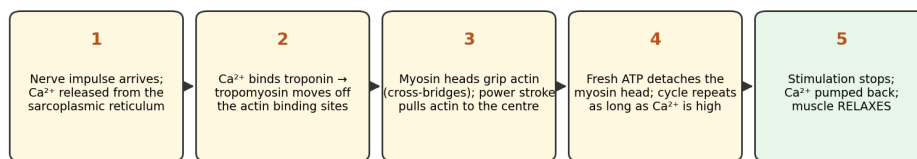
- 1 A nerve impulse reaches the fibre; Ca^{2+} floods out of the sarcoplasmic reticulum.
- 2 Ca^{2+} binds troponin → tropomyosin rolls off the actin binding sites (at rest, tropomyosin physically blocks myosin from touching actin).

- 3 Myosin heads grip actin (cross-bridges); powered by ATP, each head pivots — the power stroke — dragging actin toward the centre.
- 4 Fresh ATP binds the myosin head and detaches it; the cycle repeats while Ca^{2+} stays high. Each cycle shortens the sarcomere a fraction; thousands of cycles = visible contraction.
- 5 Stimulation stops → Ca^{2+} is pumped back into the reticulum → tropomyosin re-covers the sites → relaxation.

What changes: I bands and H zone shrink, Z-discs approach each other — but the A band never changes length (thick filaments stay the same size). That single fact answers most diagram-based questions.



Sliding-filament sequence — what happens in order



ATP is needed TWICE: for the power stroke AND for detachment (no ATP after death → myosin stays locked → rigor mortis).

Pharmacy links: botulinum toxin blocks ACh release (flaccid paralysis); neostigmine (AChE inhibitor) strengthens contraction in myasthenia gravis; tubocurarine blocks nicotinic receptors (surgical muscle relaxation).

Sarcomere at rest vs contracted, and the contraction sequence step by step

Key consequences students miss: ATP is needed twice — for the power stroke and for detachment. When ATP runs out after death, myosin stays locked to actin: rigor mortis. And a single stimulus gives a twitch; repeated stimuli summate; fast enough stimulation gives tetanus (sustained contraction — how normal posture and movement actually work). Isotonic contraction shortens the muscle (lifting a bag); isometric contraction builds tension without shortening (pushing a wall).

The neuromuscular junction — receptor-level detail

The NMJ is the synapse between a motor neuron and a muscle fibre, and it is one of the most drug-targeted synapses in the body:

- 1 The action potential reaches the axon terminal → voltage-gated Ca^{2+} channels open.
- 2 Ca^{2+} entry triggers acetylcholine (ACh) vesicles to fuse and dump ACh into the synaptic cleft.

- 3 ACh binds nicotinic (Nm) receptors on the motor end plate → Na⁺ rushes in → end-plate potential → muscle action potential → Ca²⁺ release → contraction (the sequence above).
- 4 Acetylcholinesterase (AChE) in the cleft destroys ACh within milliseconds, ending the signal — without this step, one nerve impulse would lock the muscle in spasm.

GPAT angle: the NMJ is a drug-target map. Myasthenia gravis (autoimmune destruction of nicotinic receptors) is treated with AChE inhibitors (neostigmine, pyridostigmine) that keep ACh around longer. Tubocurarine and its modern cousins (vecuronium, atracurium) block nicotinic receptors — non-depolarising muscle relaxants for surgery. Succinylcholine overstimulates then desensitises the same receptor — a depolarising blocker. Botulinum toxin blocks ACh release (flaccid paralysis — and, in tiny doses, a cosmetic/therapeutic drug). One synapse, five drug classes: that is why examiners keep returning to it.

Muscle tissue — the three types compared

Feature	Skeletal	Cardiac	Smooth
Appearance	Striated	Striated	Non-striated
Control	Voluntary	Involuntary	Involuntary
Cells	Long, multinucleated, unbranched	Branched, one or two nuclei	Spindle-shaped, single nucleus
Junctions	None special	Intercalated discs + gap junctions	Gap junctions
Contraction	Fast, powerful, fatigues	Rhythmic, never fatigues	Slow, sustained
Location	Attached to bones	Heart wall only	Gut, vessels, airways, uterus

The gap junctions in cardiac and smooth muscle are the point: they let the tissue contract as a single unit (Unit I junctions table applied).

Joints — structural and functional classification

Structural (what binds the bones):

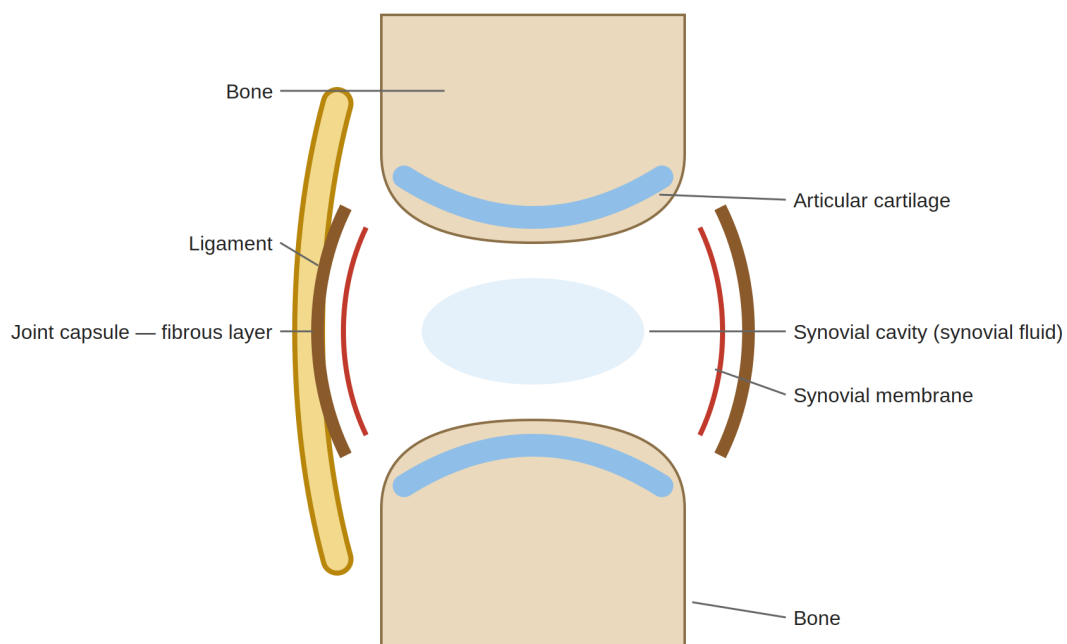
- Fibrous — dense connective tissue; immovable. Skull sutures, gomphosis (tooth in socket).
- Cartilaginous — cartilage; slightly movable. Intervertebral discs, pubic symphysis.
- Synovial — fluid-filled cavity between the bones; freely movable. Components: articular cartilage (friction-free surface), synovial cavity with synovial fluid (lubrication + nourishment), articular capsule, reinforcing ligaments. This is the joint that arthritis attacks.

Functional: synarthrosis (immovable), amphiarthrosis (slightly movable), diarthrosis (freely movable) — these map onto fibrous, cartilaginous, and synovial respectively.

Synovial joint shapes (memorise one example each — a favourite exam list):

Type	Movement	Example
Ball-and-socket	All planes	Shoulder, hip
Hinge	Flexion/extension only	Elbow, knee, ankle
Pivot	Rotation	Atlas–axis (head rotation)
Saddle	Two planes	Thumb carpometacarpal
Condylloid/ellipsoid	Two planes, no rotation	Wrist
Gliding/plane	Sliding	Between carpals, between tarsals

Synovial Joint — Cross Section



Most mobile joint type — e.g. knee, shoulder

Synovial joint in section — cartilage, cavity, capsule, ligaments

Rheumatoid arthritis — pathophysiology chain

- What it is: chronic autoimmune inflammation of the synovial membrane — small joints of hands and feet first, symmetrically (both sides together).

- Chain: unknown trigger (infection, smoking, genetics in a susceptible person) → immune attack on the synovium → synovitis (the membrane swells and fills with inflammatory cells) → formation of pannus (aggressive granulation tissue that creeps over the cartilage) → pannus destroys cartilage and erodes bone → tendons rupture, joints sublux → classic deformities: swan-neck, boutonnière fingers, ulnar deviation.
- Markers: rheumatoid factor (RF) and anti-CCP antibodies (anti-CCP is more specific — it can be positive years before symptoms).
- Clinical: morning stiffness > 30-60 minutes (the signature — it eases with movement), symmetric polyarthritis, fatigue, rheumatoid nodules, anaemia of chronic disease.

Contrast with osteoarthritis (examiners love the pair): OA is degenerative "wear and tear" of weight-bearing joints (knees, hips) in the elderly, asymmetric, stiffness < 30 min, worse with activity; RA is autoimmune, symmetric, small joints, worse with rest (morning stiffness).

Pharmacy link: NSAIDs ease symptoms; DMARDs modify the disease — methotrexate is first-line; biologics (TNF- α inhibitors like etanercept, adalimumab) target the cytokines driving the pannus. Long-term steroids are avoided because of the osteoporosis link below.

Osteoporosis — pathophysiology

- What it is: reduced bone mineral density plus deteriorated microarchitecture → bones fracture under trivial trauma.
- Chain: bone is constantly remodelled — osteoblasts build, osteoclasts resorb. When resorption outruns formation, density falls. The main driver is oestrogen deficiency after menopause (oestrogen normally restrains osteoclasts); other drivers: ageing, low calcium/vitamin D, smoking, alcohol, immobility, and long-term corticosteroids.
- Clinical: silent until a fracture. Classic sites: hip (neck of femur), vertebrae (compression → height loss, kyphosis, back pain), distal radius (Colles' fracture).
- Diagnosis: DEXA scan; T-score ≤ -2.5 = osteoporosis (-1 to -2.5 is osteopenia).

Pharmacy link: calcium + vitamin D supplementation, weight-bearing exercise — and bisphosphonates (alendronate): they poison osteoclasts. Counselling point: take on an empty stomach with a full glass of water, stay upright 30 minutes (oesophageal irritation/ulceration if it refluxes). Also: any patient on long-term steroids should be screened for bone loss — this connects straight back to RA treatment above.

Gout — pathophysiology

- What it is: crystal-induced arthritis from hyperuricaemia → monosodium urate crystals deposit in joints and tissues.
- Chain: uric acid overproduction (high-purine diet — red meat, seafood, alcohol; rapid cell turnover) or underexcretion (kidney disease, thiazide diuretics) → blood urate exceeds

solubility → needle-shaped crystals deposit in the joint → neutrophils try to eat them, fail, and burst → sudden violent inflammation.

- Clinical: classic podagra — abrupt agonising pain, redness, swelling of the first metatarsophalangeal joint (big toe), often starting at night. Chronic disease: tophi (chalky urate lumps in ears, elbows, joints) and urate kidney stones.

Pharmacy link: acute attack — NSAIDs or colchicine (colchicine blocks neutrophil migration; warn about GI toxicity — diarrhoea is the dose-limiting signal). Long-term control — allopurinol, a xanthine oxidase inhibitor that cuts uric acid production (never start it during an acute attack — shifting urate levels can worsen the flare). And note the loop: thiazides prescribed for hypertension can precipitate gout — a drug causing the disease in the next chapter.

Very short questions (2 marks)

- 1 How many bones are in the axial and appendicular skeleton?
- 2 Name the two components of a synovial joint's binding structures (any two).
- 3 Which band of the sarcomere does not change length during contraction?
- 4 Name the neurotransmitter and the enzyme that terminates it at the NMJ.
- 5 Which joint is classically affected first in gout?

Short questions (5 marks)

- 1 Describe the sliding filament theory of muscle contraction with the role of calcium, troponin and ATP.
- 2 Classify joints structurally and functionally, giving one example of each synovial joint type.
- 3 Differentiate rheumatoid arthritis from osteoarthritis across any five parameters.

Long questions (10 marks)

- 1 Describe the neuromuscular junction step by step. Explain how myasthenia gravis, neostigmine and tubocurarine each relate to it.
- 2 Discuss the pathophysiology of osteoporosis and gout, including causes, clinical features and the drug classes used in each.

How to approach these answers

- Very-short Q1: 80 axial + 126 appendicular = 206; one line.
- Very-short Q2: any two of articular cartilage, synovial cavity/fluid, capsule, ligaments.
- Very-short Q3: A band — with the one-line reason (thick filaments don't shorten).
- Very-short Q4: acetylcholine; acetylcholinesterase.
- Very-short Q5: first metatarsophalangeal joint of the big toe (podagra).

- Short Q1: five steps in order, then the band-length changes; close with rigor mortis as proof ATP matters twice.
- Short Q2: structural three with the functional terms mapped, then the six synovial types in a table with examples.
- Short Q3: table — pathology (autoimmune vs degenerative), symmetry, joint size, morning stiffness duration, effect of rest vs activity.
- Long Q1: structure — four NMJ steps with a diagram, then one paragraph each on myasthenia gravis (receptor loss), neostigmine (AChE inhibition), tubocurarine (receptor blockade); conclusion contrasting the three.
- Long Q2: structure — two halves; each half: definition, pathogenesis chain, clinical features, then drug classes mapped to the mechanism; close with the steroid-osteoporosis and thiazide-gout links.

Unit III — Body fluids, blood, lymphatic system, inflammation, haematological diseases

Body fluids — where the water lives

Water is about 60% of body weight (less in females and the elderly, who carry more fat; more in infants). It sits in two compartments:

- Intracellular fluid (ICF) — inside cells; ~40% of body weight (two-thirds of total water). Cation king: K^+ (with Mg^{2+} and phosphate).
- Extracellular fluid (ECF) — outside cells; ~20% of body weight (one-third of total water). Cation king: Na^+ (with Cl^- and HCO_3^-). Subdivided into plasma (~4–5% of body weight — the fluid part of blood) and interstitial fluid (~15% — the fluid bathing cells), plus small special volumes: lymph, cerebrospinal fluid, synovial fluid.

Fluid shifts between compartments by osmosis and by filtration/reabsorption at capillaries (Starling forces). Oedema is excess interstitial fluid, and it has only three possible mechanisms — learn them as a trio because examiners ask "give the mechanisms of oedema": increased capillary permeability (inflammation), decreased plasma osmotic pressure (low albumin — liver failure, malnutrition, nephrotic loss), and blocked lymphatic drainage (filariasis, mastectomy). Each one also explains a disease you will meet: inflammation, liver disease, elephantiasis.

Blood — composition and functions

About 5 litres in an adult (~7–8% of body weight):

- Plasma (~55%) — 90% water, plus: albumin (holds water in vessels by osmotic pressure; carries many drugs — hypoalbuminaemia raises the free fraction of highly bound drugs

like phenytoin and warfarin, a classic pharmacy trap), globulins (antibodies, transport proteins), fibrinogen (clotting), nutrients, hormones, gases, waste, electrolytes.

- Formed elements (~45%):

Cell	Count	Key facts
RBCs (erythrocytes)	4.5–5.5 million/ μL	Biconcave discs, no nucleus, packed with haemoglobin; ~120-day lifespan; cleared in the spleen
WBCs (leukocytes)	4,000–11,000/ μL	Neutrophils (phagocytose bacteria), eosinophils (parasites, allergy), basophils (histamine/heparin); lymphocytes (B cells make antibodies, T cells kill infected cells), monocytes (become macrophages)
Platelets (thrombocytes)	1.5–4 lakh/ μL (150,000–400,000)	Cell fragments from megakaryocytes; form the platelet plug

Functions: transport (O_2 , CO_2 , nutrients, hormones, waste — and drugs), regulation (pH, temperature, fluid balance), protection (clotting, immunity).

Haematocrit (PCV) — % of blood volume taken by RBCs: ~40–54% men, ~36–46% women. Rises in dehydration and polycythaemia; falls in anaemia and bleeding.

Trap alert: plasma vs serum. Plasma = fluid of unclotted blood (contains fibrinogen and clotting factors). Serum = fluid left after blood clots (plasma minus fibrinogen and clotting factors). Lab tests specify which one they need — mixing them up is a standard 2-mark trap.

Haemopoiesis and haemoglobin formation

Haemopoiesis — blood cell formation — happens in red bone marrow (adults: pelvis, vertebrae, sternum, ribs, skull). All blood cells descend from haematopoietic stem cells, splitting into myeloid (RBCs, platelets, granulocytes, monocytes) and lymphoid (lymphocytes) lines.

- Erythropoiesis (RBC production): driven by erythropoietin (EPO), made by the kidney when it senses low oxygen. This is why chronic kidney disease causes anaemia — the EPO factory fails — and why recombinant EPO (epoetin) treats it. Needs iron, vitamin B₁₂, and folic acid — the three nutrients every anaemia question revolves around. Maturation runs erythroblast → reticulocyte → mature RBC, losing the nucleus along the way.
- Haemoglobin: 4 haem groups (each holding one Fe^{2+}) + 4 globin chains (2 alpha + 2 beta in adult HbA). Iron is absorbed in the duodenum (vitamin C helps by keeping it reduced), transported by transferrin, stored as ferritin and haemosiderin. Old RBCs die in spleen and liver; haem → bilirubin (excreted in bile — excess = jaundice); iron is recycled.

Coagulation — the mechanism examiners build questions on

Haemostasis (stopping bleeding) has three stages: vascular spasm (the cut vessel constricts) → platelet plug (platelets stick to exposed collagen via von Willebrand factor, then aggregate — ADP and thromboxane A₂ recruit more) → coagulation (the fibrin mesh cements the plug).

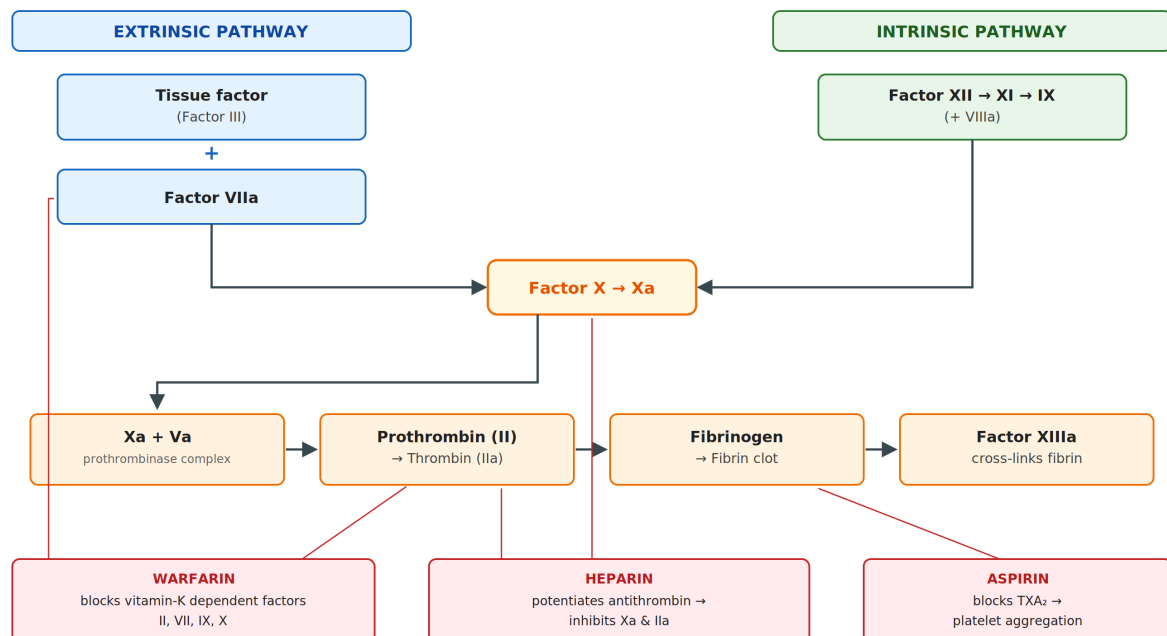
The clotting cascade — learn it as two roads joining one highway:

- Extrinsic pathway — tissue injury releases tissue factor (factor III); fast; monitored by PT/INR.
- Intrinsic pathway — blood touching exposed collagen (the "inside" trigger); slower; monitored by aPTT.
- Common pathway — both converge: factor X → Xa → converts prothrombin (II) → thrombin (IIa) → thrombin converts fibrinogen (I) → fibrin → fibrin mesh, cross-linked by factor XIII = stable clot.

Factors to name cold: I fibrinogen, II prothrombin, III tissue factor, IV calcium, VIII (missing in haemophilia A), IX (missing in haemophilia B), X the convergence point. Vitamin K is needed to synthesise factors II, VII, IX, X (mnemonic: "1977, 2, 9 10" — factors 2, 7, 9, 10) — which is exactly why warfarin, a vitamin K antagonist, is an anticoagulant.

Fibrinolysis — the cleanup: plasmin dissolves the clot once healing is done. Streptokinase and alteplase work by activating plasminogen → used in MI and stroke.

Blood Clotting Cascade & Drug Action Sites



Red callouts mark drug action sites — a favourite exam focus.

Clotting cascade — extrinsic, intrinsic and common pathways with drug targets

GPAT angle: this one cascade answers: heparin → prolongs aPTT (intrinsic pathway); warfarin → prolongs PT/INR (extrinsic, vitamin K-dependent factors); aspirin/clopidogrel → antiplatelet (they block the platelet-plug stage — ADP and thromboxane — not the cascade itself, so PT/aPTT stay normal). If a question gives a prolonged aPTT with normal PT, think heparin or haemophilia; prolonged PT/INR with normal aPTT, think warfarin.

Blood grouping, Rh factor, transfusion

- ABO system (Landsteiner): RBCs carry A and/or B antigens; plasma carries antibodies against whichever antigens you lack. Group A → anti-B; group B → anti-A; group AB → neither antibody (universal recipient — accepts anyone's RBCs); group O → both antibodies (universal donor for RBCs — no antigens for anyone to attack).
- Rh factor: Rh-positive RBCs carry the D antigen. Rh-negative people have no anti-D naturally but make it after exposure (transfusion or an Rh-positive pregnancy) — then a later Rh-positive baby's RBCs are attacked: haemolytic disease of the newborn. Prevented with anti-D immunoglobulin (RhoGAM) given to the Rh-negative mother.
- Transfusion rules: always cross-match. ABO mismatch → acute haemolytic reaction: donor RBCs agglutinate and burst — fever, chills, haemolysis, renal failure, shock.

Trap alert: "universal donor" applies to red cells (group O). For plasma transfusion it reverses — group AB plasma (no antibodies) is the universal donor. Questions exploit this flip regularly.

Lymphatic system

- Organs/tissues: lymph nodes (filter lymph — they swell in infection, which is why doctors palpate them), spleen (filters blood, destroys old RBCs, mounts immune responses), thymus (T-cell maturation — largest in childhood, shrinks after puberty), tonsils and Peyer's patches (MALT — guarding the entry points).
- Vessels: begin as blind capillaries → drain through nodes → return lymph to blood at the subclavian veins (thoracic duct on the left, right lymphatic duct on the right). One-way valves prevent backflow.
- Lymph formation: plasma filters out of capillaries → interstitial fluid → the ~3 L/day not reabsorbed enters lymph capillaries as lymph.
- Functions: return tissue fluid to blood, absorb dietary fats (lacteals in the intestine — which is why very fatty meals make lymph milky), immune surveillance (lymphocytes in nodes trap pathogens).

Inflammation — mechanism and repair

Inflammation is the vascular + cellular response to injury or infection. The five cardinal signs: rubor (redness), tumor (swelling), calor (heat), dolor (pain), functio laesa (loss of function).

Classification: acute (seconds to days; neutrophils lead; a cut, bacterial infection) vs chronic (weeks to years; macrophages and lymphocytes lead; granulomas — TB, rheumatoid arthritis).

Pathophysiology — vascular events, then cellular events:

- 1 Vasodilation (histamine, prostaglandins) → redness, heat.
- 2 Increased vascular permeability → plasma proteins and fluid leak out → swelling, and pain from pressure on nerve endings.
- 3 Cellular events — margination (WBCs line the vessel wall) → rolling → adhesion → diapedesis (squeezing through the wall) → chemotaxis (following chemical trails to the injury) → phagocytosis of microbes and debris.

Mediators (a must-memorise list): histamine (mast cells — immediate vasodilation; blocked by antihistamines), prostaglandins (pain, fever — blocked by NSAIDs via COX), leukotrienes (bronchoconstriction in asthma — blocked by montelukast), cytokines (IL-1, IL-6, TNF- α — fever and systemic effects), complement (C3a, C5a — chemotaxis), kinins (bradykinin — pain; raised by ACE inhibitors, which is why they cause dry cough), platelet-activating factor.

Repair: regeneration (same tissue regrows — liver, skin epithelium) vs fibrosis/scarring (connective tissue patches the gap — heart muscle after MI). The outcome depends on the tissue's regenerative capacity and how much framework survived.

Pharmacy link: NSAIDs and corticosteroids both suppress inflammation but at different levels — NSAIDs block prostaglandin synthesis (COX enzymes), steroids act earlier (phospholipase A₂, plus they suppress multiple cytokines). That is why steroids are broader and heavier-hitting, with heavier side effects.

Haematological diseases — pathophysiology

Iron deficiency anaemia — the commonest anaemia worldwide. Causes: chronic blood loss (menstruation, hookworm, piles), poor intake, pregnancy. Iron is needed for haem → microcytic hypochromic RBCs (small, pale). Features: fatigue, pallor, koilonychia (spoon-shaped nails), pica (craving clay/chalk), angular cheilitis. Treated with ferrous sulphate/fumarate — counsel: blackens stools (harmless), best absorbed on an empty stomach with vitamin C, avoid taking with tea/antacids.

Megaloblastic anaemia (B₁₂ and folic acid deficiency) — both vitamins are needed for DNA synthesis; without them RBC precursors grow but cannot divide → large, immature, macrocytic RBCs with hypersegmented neutrophils. B₁₂ deficiency (pernicious anaemia — no intrinsic factor; strict vegetarian diets) additionally causes neurological damage (tingling, numbness, subacute combined degeneration of the cord) because B₁₂ maintains myelin — folate deficiency never causes neuro signs.

Trap alert: never give folate alone when B₁₂ deficiency is possible — folate corrects the anaemia while the nerve damage marches on silently and irreversibly. This is a favourite clinical-trap question.

Sickle cell anaemia — autosomal recessive; one amino-acid swap in beta-globin (glutamate → valine) creates HbS, which polymerises in low oxygen → RBCs sickle. Consequences: vaso-occlusive painful crises (sickled cells jam small vessels), chronic haemolysis, spleen damage (infection risk — functional asplenia). Common in the tribal belts of Madhya Pradesh, Chhattisgarh, and Maharashtra. Managed with hydroxyurea (raises protective HbF), folic acid, vaccination, and crisis care.

Thalassemia — reduced synthesis of globin chains (not a structural change like sickle cell): beta-thalassemia (too few beta chains → excess alpha chains precipitate and wreck RBCs); alpha-thalassemia similarly. Microcytic hypochromic anaemia — but unlike iron deficiency, iron studies are normal or high. Severe beta-thalassemia major (Cooley's anaemia) needs lifelong transfusion → iron overload → chelation with deferoxamine/deferiprone.

Hereditary and acquired haemolytic anaemias — the syllabus phrase "hereditary acquired anaemia" is ambiguous; it is best read as hereditary haemolytic anaemias and acquired haemolytic anaemias. Hereditary spherocytosis (defective membrane proteins — spectrin/ankyrin → fragile spherical RBCs trapped and destroyed in the spleen; splenectomy cures the anaemia) is the model hereditary example; acquired examples include autoimmune haemolytic anaemia and drug-induced haemolysis.

Haemophilia — X-linked recessive (males affected, females carriers). Haemophilia A — factor VIII deficiency (~85% of cases); Haemophilia B (Christmas disease) — factor IX deficiency. Features: prolonged bleeding after trivial injury, haemarthrosis (bleeding into joints — the knee and ankle classically), easy bruising; aPTT prolonged, PT normal. Treated with factor concentrates; avoid NSAIDs, aspirin, and IM injections.

Anaemia	RBC picture	Key distinguishing feature
Iron deficiency	Microcytic hypochromic	Koilonychia, pica; low ferritin
Megaloblastic (B ₁₂ /folate)	Macrocytic	Hypersegmented neutrophils; neuro signs only in B ₁₂
Sickle cell	Sickle shapes, haemolysis	Vaso-occlusive painful crises; Glu→Val in beta-globin
Thalassemia	Microcytic hypochromic	Iron studies normal/high; chain-synthesis defect
Hereditary spherocytosis	Spherocytes, haemolysis	Splenectomy curative
(Haemophilia — not an anaemia)	Normal RBCs	aPTT prolonged, PT normal; X-linked

Very short questions (2 marks)

- 1 Which tests monitor heparin and warfarin therapy, and why those tests?

- 2 Why is group O the universal red-cell donor?
- 3 Name the five cardinal signs of inflammation.
- 4 Which vitamin deficiency causes neurological symptoms in megaloblastic anaemia, and why does it matter?
- 5 State the three mechanisms of oedema.

Short questions (5 marks)

- 1 Describe the mechanism of blood coagulation through the extrinsic, intrinsic and common pathways, naming the key factors.
- 2 Explain the vascular and cellular events of acute inflammation in sequence, with the mediators involved.
- 3 Compare iron deficiency anaemia and megaloblastic anaemia (cause, RBC picture, clinical features, treatment caution).

Long questions (10 marks)

- 1 Describe the composition and functions of blood. Explain haemopoiesis and haemoglobin formation, including the roles of EPO, iron, vitamin B₁₂ and folic acid.
- 2 Discuss the pathophysiology of sickle cell anaemia, thalassemia and haemophilia, differentiating hereditary from acquired haemolytic anaemias.

How to approach these answers

- Very-short Q1: aPTT for heparin (intrinsic pathway), PT/INR for warfarin (vitamin K-dependent factors) — one line each.
- Very-short Q2: no A/B antigens on O cells, so no recipient antibody attacks them.
- Very-short Q3: rubor, tumor, calor, dolor, functio laesa with the English meaning of each.
- Very-short Q4: B₁₂ — myelin maintenance; the trap is giving folate alone.
- Very-short Q5: increased permeability, low plasma protein, blocked lymph drainage — one example each.
- Short Q1: draw the cascade as a flowchart — extrinsic (III) and intrinsic both feeding factor X → thrombin → fibrin; then add PT/aPTT and vitamin K mapping.
- Short Q2: strict sequence — vasodilation → permeability → margination → diapedesis → chemotaxis → phagocytosis, with one mediator named per step.
- Short Q3: a table — microcytic vs macrocytic, cause, two clinical features each, and the folate-alone caution as the closing line.
- Long Q1: structure — plasma vs formed elements with counts and functions, then haemopoiesis (marrow, stem cells, EPO from kidney), then haemoglobin assembly and iron handling; close with the jaundice link.
- Long Q2: structure — one pathophysiology paragraph per disease with its molecular defect, then a short section contrasting hereditary spherocytosis with acquired haemolytic anaemias; end with the anaemia comparison table.

Unit IV — Peripheral nervous system and special senses

Classification of the peripheral nervous system

The nervous system splits into the CNS (brain + spinal cord — command) and the PNS (nerves and ganglia outside the CNS — communication lines). The PNS has two divisions:

- Somatic (voluntary) — sensory neurons carry information in; motor neurons carry commands out to skeletal muscle. One neuron runs all the way from CNS to muscle; the transmitter at the NMJ is acetylcholine (Unit II applied).
- Autonomic (involuntary) — controls smooth muscle, cardiac muscle, and glands. Always a two-neuron chain: preganglionic neuron → ganglion → postganglionic neuron. Divided into sympathetic and parasympathetic (below); the enteric division runs the gut semi-independently.

Trap alert: the somatic system uses ONE neuron to the muscle; the autonomic uses TWO (pre- and postganglionic). And both autonomic divisions use acetylcholine at the preganglionic step (nicotinic receptors) — they differ only in the postganglionic transmitter. Questions love asking "which transmitter" without specifying which synapse.

Sympathetic vs parasympathetic — the master table

Feature	Sympathetic ("fight or flight")	Parasympathetic ("rest and digest")
Origin	Thoracolumbar (T1-L2)	Craniosacral (CN III, VII, IX, X + S2-S4)
Ganglia	Near the spinal cord (paravertebral chain) — long postganglionic fibres	Near or inside the target organ — short postganglionic fibres
Preganglionic transmitter	Acetylcholine (nicotinic)	Acetylcholine (nicotinic)
Postganglionic transmitter	Noradrenaline (mostly; sweat glands are the exception — ACh)	Acetylcholine (muscarinic)
Heart	Rate ↑, force ↑	Rate ↓
Pupil	Dilates (mydriasis)	Constricts (miosis)
Bronchi	Dilates	Constricts
Gut	Motility ↓, sphincters contract	Motility ↑, secretion ↑
Bladder	Detrusor relaxes, sphincter contracts (holds urine)	Detrusor contracts (voids urine)

Feature	Sympathetic ("fight or flight")	Parasympathetic ("rest and digest")
Salivary glands	Thick, scanty saliva	Profuse watery saliva
Adrenal medulla	Stimulated → adrenaline into blood	No direct supply

Why the effects are opposite but coordinated: the two divisions are rarely both fully on — the body shifts the balance. Exercise tilts sympathetic; a meal tilts parasympathetic.

GPAT angle: this table is a drug-class map. Beta-blockers (propranolol, metoprolol) blunt sympathetic effects on the heart (rate and force fall). Anticholinergics (atropine) block parasympathetic effects — predict the side effects straight from the table: dry mouth, blurred vision (mydriasis), urinary retention, constipation. Salbutamol (β_2 agonist) copies sympathetic bronchodilation in asthma. Pilocarpine (muscarinic agonist) copies parasympathetic — constricts the pupil and is used in glaucoma.

Spinal nerves — origin and functions

31 pairs: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, 1 coccygeal. Each forms from a dorsal (sensory) root and a ventral (motor) root joining at the intervertebral foramen — dorsal = in, ventral = out (mnemonic: "Dorsal Detects, Ventral Volunteers movement"). Named by the vertebra below the exit in the neck (C1–C7) and the vertebra above elsewhere.

Functions: sensory input from skin, muscles, and joints to the cord; motor output to skeletal muscles. A dermatome is the skin strip supplied by one spinal nerve — used clinically to locate cord lesions (shingles erupts along a dermatome).

Key plexuses (networks where fibres regroup): cervical (phrenic nerve → diaphragm — the breathing nerve), brachial (upper limb — birth injury here causes Erb's palsy), lumbar (femoral nerve), sacral (sciatic nerve — the largest nerve in the body; its compression causes sciatica, pain shooting down the leg).

Cranial nerves — the twelve

Arising from the brain (mostly the brainstem), numbered I–XII. Names mnemonic: "Oh, Oh, Oh, To Touch And Feel Very Green Vegetables, AH!"

Nerve	Type	Main functions
I Olfactory	Sensory	Smell
II Optic	Sensory	Vision
III Oculomotor	Motor	Most eye movements; constricts pupil; lifts eyelid
IV Trochlear	Motor	Superior oblique eye muscle

Nerve	Type	Main functions
V Trigeminal	Mixed	Face sensation; muscles of chewing
VI Abducens	Motor	Lateral rectus (abducts the eye)
VII Facial	Mixed	Facial expression; taste, anterior two-thirds of tongue; salivary glands
VIII Vestibulocochlear	Sensory	Hearing + balance
IX Glossopharyngeal	Mixed	Taste, posterior third of tongue; swallowing; parotid gland
X Vagus	Mixed	The wanderer — parasympathetic supply to heart, lungs, most of the gut
XI Accessory (spinal)	Motor	Trapezius, sternocleidomastoid (shrug, head turn)
XII Hypoglossal	Motor	Tongue movements

GPAT angle: the vagus (X) is the parasympathetic workhorse — most parasympathetic drug effects on heart, lungs, and gut run through it. And note: cranial nerves III, VII, IX, X are exactly the cranial outflow of the parasympathetic system in the master table above — the two topics interlock.

The eye — structure and functions

Three coats, outside to inside: sclera (white, tough, protective; continuous with the cornea in front) → choroid (vascular, pigmented; continues forward as ciliary body and iris — the coloured diaphragm controlling pupil size) → retina (photoreceptors).

Front to back: cornea (transparent; provides most of the eye's focusing power) → anterior chamber with aqueous humor (made by the ciliary body, drains through the trabecular meshwork/canal of Schlemm — blockage here raises pressure: glaucoma) → pupil → lens (fine focusing; changes shape for near vision — accommodation, driven by the ciliary muscle) → vitreous humor (gel filling the back, holds the retina in place) → retina.

Retina: rods (dim light, black-and-white; contain rhodopsin, need vitamin A — deficiency causes night blindness) and cones (colour, sharp detail; packed in the fovea at the centre of the macula). The optic disc (blind spot) — where the optic nerve leaves — has no photoreceptors.

Visual pathway: retina → optic nerve → optic chiasma (nasal fibres cross) → optic tract → lateral geniculate body → visual cortex (occipital lobe). Accessory structures: eyelids, lashes, lacrimal (tear) glands, six extraocular muscles (CN III, IV, VI).

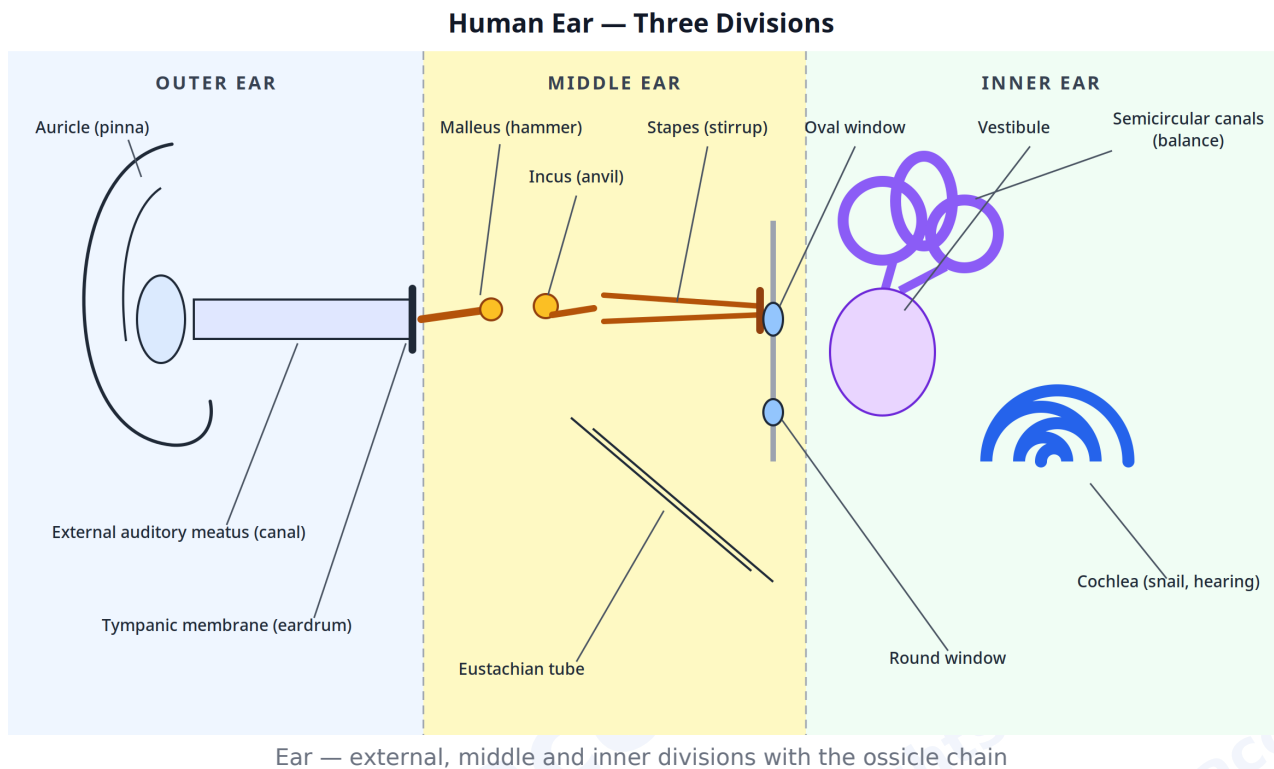
Pharmacy link: glaucoma drugs all target aqueous humor dynamics — timolol (beta-blocker) reduces its production, latanoprost (prostaglandin analogue) increases drainage, pilocarpine opens the drainage angle. And systemic anticholinergics (atropine-like drugs) dilate the pupil and can precipitate angle-closure glaucoma — a counselling point for elderly patients on such drugs.

The ear — structure and functions

- External ear: pinna (funnels sound) → external auditory canal (cerumen/wax — protective) → tympanic membrane (eardrum; vibrates with sound).
- Middle ear: air-filled cavity with three ossicles — malleus (hammer) → incus (anvil) → stapes (stirrup) — a lever chain that amplifies sound from the large eardrum to the small oval window. The Eustachian (auditory) tube connects to the throat and equalises pressure (why ears "pop" in lifts and flights — and why children's colds so often become middle-ear infections: their tubes are shorter and more horizontal).
- Inner ear: cochlea (snail-shaped; hair cells convert vibration to nerve impulses — true hearing), vestibule (utricle + saccule — static balance, head position), semicircular canals (rotational balance). CN VIII (vestibulocochlear) carries both signals.

Hearing loss types: conductive (external/middle ear — wax, otitis media, ossicle damage; often treatable; bone conduction better than air) vs sensorineural (cochlea or nerve — ageing/presbycusis, loud noise, ototoxic drugs — usually permanent).

Pharmacy link: aminoglycosides (gentamicin, streptomycin) and loop diuretics (furosemide) are ototoxic — they damage cochlear hair cells. This is why aminoglycoside courses need hearing vigilance, and why furosemide is pushed slowly IV (rapid pushes raise ototoxicity risk).



Nose and tongue — smell and taste

- **Nose (olfaction):** olfactory receptors in the olfactory epithelium high in the nasal cavity; odorants dissolve in mucus, bind receptors → olfactory nerve (I) → olfactory bulb → cortex. Smell is the only sense that reaches the cortex without relaying through the thalamus — which is why odours trigger memory so powerfully. The nose also warms, moistens, and filters inspired air.
- **Tongue (gustation):** taste buds sit on papillae (fungiform, circumvallate, foliate). Five primary tastes: sweet, salty, sour, bitter, umami. Taste travels via facial (VII) — anterior two-thirds — and glossopharyngeal (IX) — posterior third. Most of what we call "taste" is actually smell — which is why food goes bland with a blocked nose.

Special sense disorders — pathophysiology

- **Glaucoma** — raised intraocular pressure (aqueous humor cannot drain) crushes the optic nerve → gradual peripheral vision loss ("tunnel vision"). Painless and slow, so it is caught late. Open-angle (chronic, commonest) vs angle-closure (acute, painful emergency — red eye, halos, vomiting). Drugs: timolol, latanoprost, pilocarpine, acetazolamide (cuts aqueous production).
- **Cataract** — clouding of the lens (ageing, diabetes, UV, long-term steroids) → painless blurring and glare. No drug reverses it — treatment is surgical lens replacement.
- **Myopia** — eyeball too long (or lens too powerful); distant rays focus in front of the retina → corrected with concave lenses. Contrast: hypermetropia (focus behind the retina — convex lenses), presbyopia (ageing lens loses accommodation — reading glasses).

- Otitis externa — outer canal infection ("swimmer's ear"); pain when the pinna is pulled (the bedside test separating it from media).
- Otitis media — middle-ear infection via the Eustachian tube; common in children; ear pain, fever, possible eardrum perforation.
- Vertigo — a false sense of spinning/rotation from vestibular disturbance (not the same as light-headedness, which is usually cardiovascular). Causes: BPPV (loose otolith crystals — brief episodes on head movement), Ménière's disease (endolymph buildup — vertigo + tinnitus + hearing loss).
- Anosmia — loss of smell: nasal polyps, sinusitis, head injury, viral infections, zinc deficiency. Pharmacy relevance: it kills appetite and weight, and several drugs (including some intranasal ones) list it as an adverse effect.

Trap alert: glaucoma = pressure problem (optic nerve, peripheral vision lost first); cataract = lens problem (blurring, glare). Students swap their mechanisms. And vertigo means the room spins — if the patient says "I feel faint when I stand", that is presyncope, not vertigo.

Very short questions (2 marks)

- 1 Name the cranial nerves carrying parasympathetic outflow (by number).
- 2 State the postganglionic transmitter of the sympathetic and parasympathetic systems.
- 3 What is the function of the Eustachian tube?
- 4 Which lens corrects myopia, and where do distant rays focus in myopia?
- 5 Name the three ossicles in order from eardrum to inner ear.

Short questions (5 marks)

- 1 Compare the sympathetic and parasympathetic nervous systems across origin, transmitters and effects on any four organs.
- 2 Describe the structure of the eye (three coats, humors, retina) and explain how glaucoma develops from it.
- 3 Differentiate conductive from sensorineural hearing loss, with causes and one pharmacy-relevant example.

Long questions (10 marks)

- 1 Classify the peripheral nervous system. Describe the structure and functions of the sympathetic and parasympathetic divisions, with a table of their effects and the drug classes that mimic or block each division.
- 2 Describe the structure and functions of the ear. Discuss the pathophysiology of otitis externa, otitis media and vertigo, distinguishing vertigo from dizziness.

How to approach these answers

- Very-short Q1: III, VII, IX, X — with the word craniosacral.

- Very-short Q2: noradrenaline (sympathetic) vs acetylcholine/muscarinic (parasympathetic); note the preganglionic exception.
- Very-short Q3: equalises middle-ear pressure with the atmosphere; mention the child-infection link in one line.
- Very-short Q4: concave lens; focus in front of the retina.
- Very-short Q5: malleus → incus → stapes, with the one-line job (amplification).
- Short Q1: open with the origin/transmitter table, then four organ rows; close with one drug example per division.
- Short Q2: coats and humors first with the diagram, then the drainage-blockage → pressure → optic nerve chain for glaucoma.
- Short Q3: table — site, air vs bone conduction, causes; close with aminoglycosides/furosemide as the pharmacy link.
- Long Q1: structure — classification flowchart, then the full comparison table, then drug classes mapped row by row (beta-blockers, anticholinergics, salbutamol, pilocarpine); one-line conclusion.
- Long Q2: structure — three divisions of the ear with the diagram, then one paragraph per disorder with cause and key feature, ending with the vertigo-vs-dizziness distinction.

Unit V — Cardiovascular system

Anatomy of the heart

A fist-sized muscular pump in the mediastinum, tilted left, wrapped in the pericardium (fibrous outer sac + serous layers with pericardial fluid for frictionless beating). Wall layers: endocardium (inner lining), myocardium (muscle — thickest in the left ventricle, which does the heaviest work), epicardium (outer layer).

Chambers — right atrium → right ventricle → lungs → left atrium → left ventricle → body. Right side handles deoxygenated blood, left side oxygenated; the septum keeps them apart (a hole here — septal defect — mixes the two).

Valves — one-way gates preventing backflow:

- Atrioventricular (AV) valves: tricuspid (right, 3 cusps), mitral/bicuspid (left, 2 cusps). Anchored by chordae tendineae to papillary muscles — these stop the valves prolapsing into the atria when the ventricles squeeze.
- Semilunar valves: pulmonary (right) and aortic (left), 3 cusps each, no chordae.

Coronary circulation — the heart feeds itself: right and left coronary arteries branch off the aorta just above the aortic valve; blockage here = myocardial infarction. Deoxygenated blood drains via the coronary sinus into the right atrium.

Blood circulation — three circuits

- Pulmonary: right ventricle → pulmonary trunk → lungs (CO₂ out, O₂ in) → pulmonary veins → left atrium.
- Systemic: left ventricle → aorta → body tissues → venae cavae → right atrium.
- Coronary: aorta → coronary arteries → heart muscle → coronary sinus → right atrium.
- Portal: gut → hepatic portal vein → liver → then to the heart. This detour is why oral drugs undergo first-pass metabolism in the liver before reaching the systemic circulation — the entire basis of oral bioavailability.

Trap alert: the pulmonary arteries carry deoxygenated blood and the pulmonary veins carry oxygenated blood — the only vessels where "artery = oxygenated" fails. Examiners set this trap every year. Rule: arteries carry blood away from the heart, veins toward it — oxygenation is a separate question.

Blood vessels — structure and function

Three tunics in arteries and veins: tunica intima (endothelium — the layer where atherosclerosis begins), tunica media (smooth muscle + elastic fibres), tunica externa/adventitia (connective tissue).

Vessel	Wall	Job
Arteries	Thick muscular/elastic; withstand high pressure	Carry blood away from the heart; elastic arteries (aorta) stretch and recoil, smoothing the pulse
Arterioles	Mostly smooth muscle	Main resistance vessels — their constriction/dilation sets blood pressure and local flow
Capillaries	One endothelial cell thick	Exchange site — O ₂ , nutrients, waste by diffusion and filtration
Veins	Thin walls, wide lumens, valves	Carry blood toward the heart; reservoirs holding ~60% of blood volume

Varicose veins = failed venous valves; skeletal-muscle contraction ("muscle pump") normally helps venous return, which is why long immobility swells the legs.

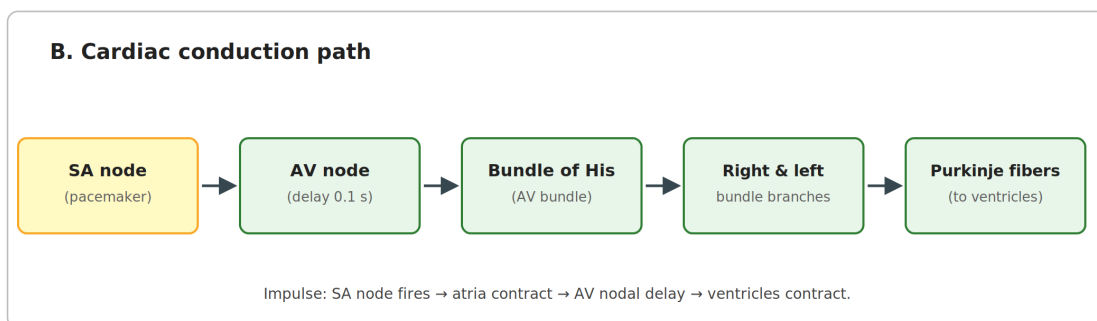
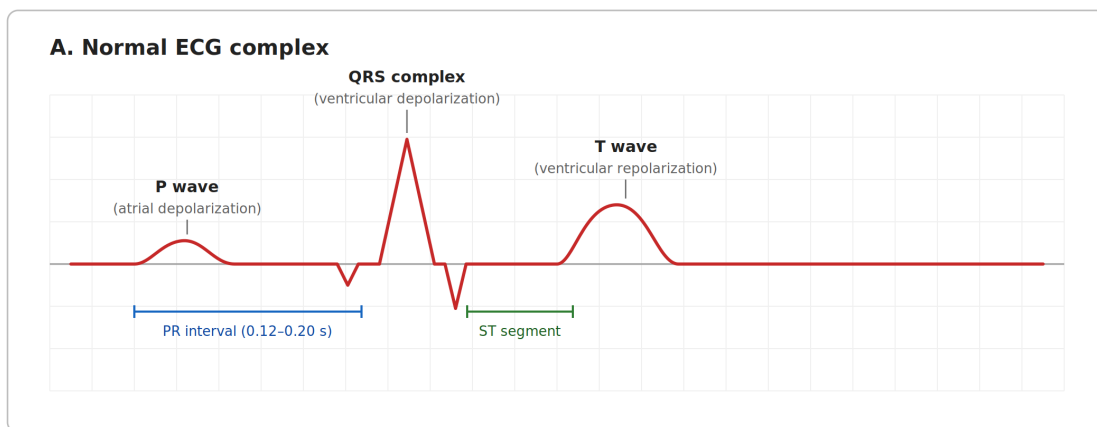
Pharmacy link: most blood-pressure drugs act on the arterioles — calcium-channel blockers and ACE inhibitors dilate them (resistance falls, pressure falls). Diuretics instead shrink the volume inside the vessels. Two different handles on the same equation (below).

Conduction system and the heartbeat

The heart beats by itself (autorhythmic) — nerves only adjust the rate:

- 1 SA (sinoatrial) node — the pacemaker, in the right atrium wall; fires fastest (intrinsic $\sim 100/\text{min}$, held to ~ 72 by resting vagal tone).
- 2 The impulse sweeps the atria (they contract) $\rightarrow$ reaches the AV node $\rightarrow$ delay of ~ 0.1 s so the ventricles finish filling.
- 3 Down the bundle of His $\rightarrow$ right and left bundle branches $\rightarrow$ Purkinje fibres $\rightarrow$ ventricles contract from the apex upward, wringing blood out efficiently.

ANS regulation: sympathetic (noradrenaline on β_1 receptors) $\rightarrow$ faster rate, stronger contraction; parasympathetic (vagus, acetylcholine) $\rightarrow$ slower rate. Drugs: beta-blockers (metoprolol) slow the heart; atropine blocks vagal slowing (used in bradycardia); digoxin boosts vagal tone and contractility.



Cardiac conduction system — SA node to Purkinje fibres, and the ECG waves they produce

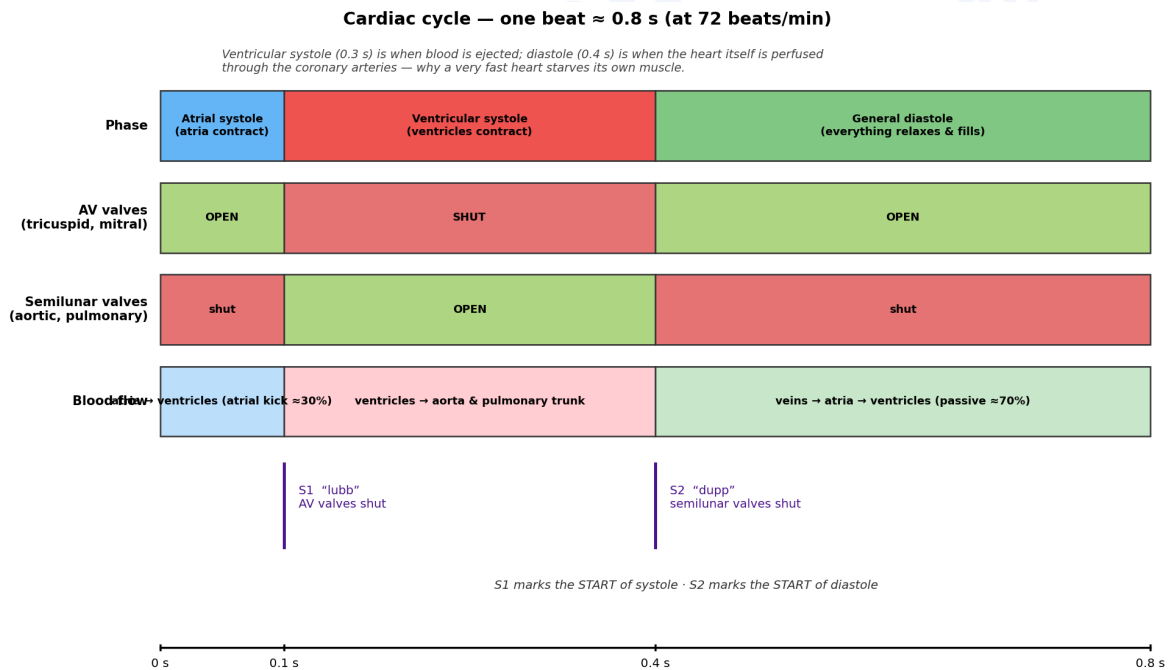
Trap alert: the SA node sets the rate (pacemaker); the AV node sets the timing (the delay). Students swap their roles. If the SA node fails, the AV node can take over — but at a slower escape rate ($\sim 40\text{--}60/\text{min}$); below that, Purkinje fibres pace at $\sim 20\text{--}40$. That hierarchy is the logic behind heart blocks and pacemakers.

Cardiac cycle — one beat in 0.8 s

At 72 beats/min, each cycle is ~ 0.8 s:

- 1 Atrial systole (0.1 s) — atria contract, topping up the ventricles ("atrial kick" $\approx 30\%$ of filling); AV valves open.
- 2 Ventricular systole (0.3 s) — ventricles contract; AV valves slam shut (S_1 — "lubb", marking the start of systole); pressure forces the semilunar valves open; blood ejects into the aorta and pulmonary trunk.
- 3 General diastole (0.4 s) — everything relaxes; semilunar valves shut (S_2 — "dupp", marking the start of diastole); AV valves reopen; ventricles fill — $\sim 70\%$ passively, plus the atrial kick.

Heart sounds: S_1 = AV valves closing; S_2 = semilunar valves closing. Murmurs are abnormal whooshes from turbulent flow — valve stenosis (narrowed) or regurgitation (leaky). Note the coronary arteries fill during diastole — when the heart muscle is relaxed — which is why a very fast heart (short diastole) starves its own muscle of blood.



Cardiac cycle — phases, valve states, blood flow, and heart sounds across 0.8 s

Cardiac output — the master equation

Cardiac output (CO) = heart rate $\times$ stroke volume $\approx 72 \times 70$ mL ≈ 5 L/min at rest — the whole blood volume, every minute.

Stroke volume depends on three determinants — and every heart-failure drug pulls one of these three levers:

- Preload — venous return / end-diastolic volume. More filling $\rightarrow$ more stretch $\rightarrow$ stronger contraction (Frank-Starling law: the heart pumps out what it receives). Diuretics reduce preload.

- Afterload — the resistance the ventricle pumps against (high BP = high afterload = lower stroke volume). Vasodilators reduce afterload.
- Contractility — the muscle's intrinsic strength, raised by sympathetic stimulation and digoxin, lowered by heart failure and beta-blockers.

Ejection fraction = stroke volume ÷ end-diastolic volume (~55–70%) — the single number that defines systolic heart failure.

GPAT angle: map the heart-failure drugs onto $CO = HR \times SV$: diuretics ↓ preload, ACE inhibitors/vasodilators ↓ afterload, digoxin ↑ contractility, beta-blockers ↓ HR (and block the harmful chronic sympathetic drive). One equation, four drug classes — this mapping is asked directly.

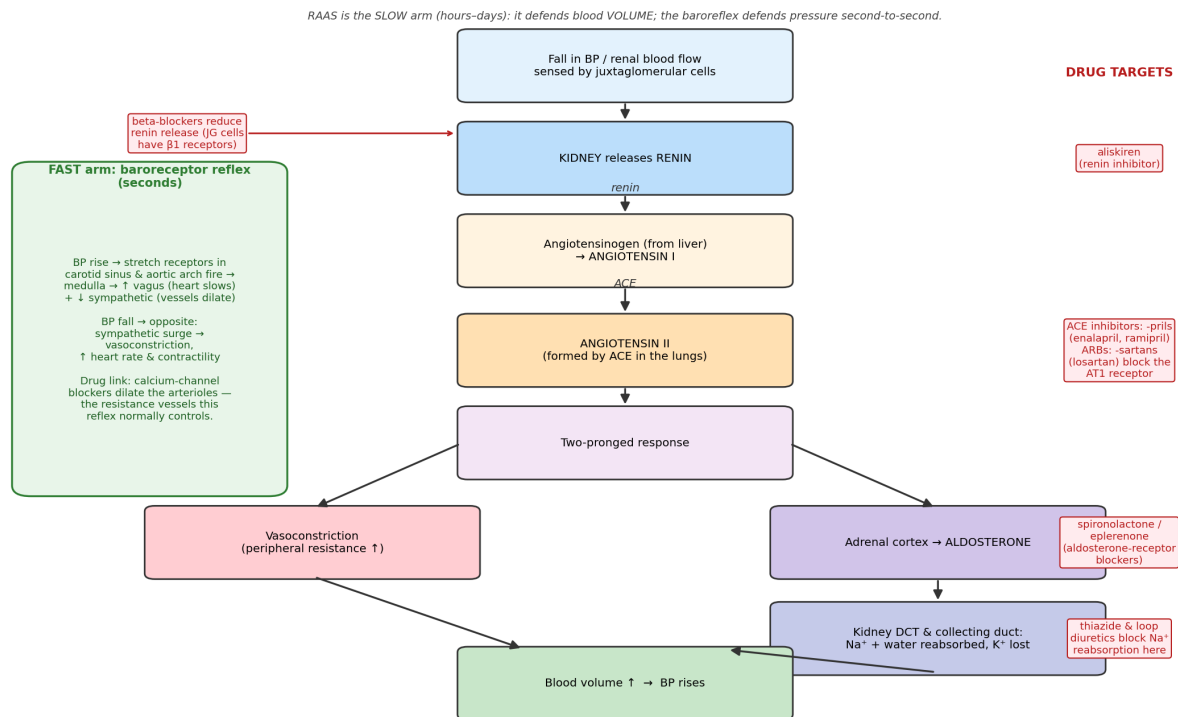
Regulation of blood pressure

BP = cardiac output × peripheral resistance. Normal ~120/80 mmHg (systolic/diastolic).

Short-term (seconds–minutes) — the baroreceptor reflex: stretch receptors in the carotid sinus and aortic arch sense pressure → signals via the vagus and glossopharyngeal nerves to the medulla → BP high → ↑ vagal (heart slows) + ↓ sympathetic (vessels dilate); BP low → sympathetic surge (vasoconstriction, faster stronger heart). Chemoreceptors back it up, responding to low O_2 / high CO_2 / low pH.

Long-term (hours–days) — RAAS: low renal blood flow → juxtaglomerular cells release renin → converts angiotensinogen (liver) → angiotensin I → ACE (lungs) → angiotensin II → intense vasoconstriction + adrenal release of aldosterone → kidney reabsorbs Na^+ and water (losing K^+) → blood volume rises → BP rises. Supporting cast: ADH (water reabsorption when osmolality rises) and ANP (released by stretched atria — the opposite of RAAS: it dumps Na^+ and water).

Blood-pressure regulation: RAAS drug-target map + the fast baroreceptor reflex



BP regulation — RAAS drug-target map plus the fast baroreceptor reflex

GPAT angle: RAAS is the most drug-targeted pathway in this entire subject. Walk it with the drugs: aliskiren blocks renin; ACE inhibitors (-prils: enalapril, ramipril) block angiotensin II formation — and raise bradykinin, hence the dry cough; ARBs (-sartans: losartan) block the AT1 receptor — no cough; spironolactone/eplerenone block aldosterone (K^+ -sparing); thiazide/loop diuretics block Na^+ reabsorption downstream; beta-blockers reduce renin release (JG cells carry β_1 receptors). Learn the pathway once and six drug classes fall into place.

Pulse and ECG — why each wave exists

- Pulse — the pressure wave felt where an artery crosses bone (radial artery at the wrist is standard). Normal 60–100/min; note rate, rhythm, and volume. A pulse deficit (apex beat faster than the radial pulse) points to atrial fibrillation.
- ECG — the heart's electrical activity, recorded via limb and chest leads. Each wave exists because a specific part depolarises or repolarises:
- P wave — atrial depolarisation (atrial contraction follows).
- QRS complex — ventricular depolarisation (the tall spike; ventricular contraction follows). A wide, bizarre QRS means the impulse bypassed the normal conduction path — bundle-branch block or a ventricular ectopic.
- T wave — ventricular repolarisation (recovery).
- PR interval — the AV nodal delay; prolonged in heart block.

- ST segment — elevation = acute MI; depression = ischaemia.

Normal sinus rhythm: every P followed by a QRS, regular, 60–100/min. (See the conduction diagram above — the ECG is simply the electrical shadow of the SA → AV → His → Purkinje sequence.)

Hypertension — pathophysiology

- Definition: sustained BP $\geq$ 140/90 mmHg on more than one occasion.
- Types: primary (essential) — ~90–95%; no single cause, but a risk-factor cluster: age, family history, obesity, high salt, smoking, alcohol, stress, inactivity. Secondary — ~5–10%; identifiable cause: kidney disease, primary aldosteronism, Cushing's, pheochromocytoma, coarctation of the aorta, drugs (NSAIDs, steroids, oral contraceptives).
- Pathogenesis: raised cardiac output and/or peripheral resistance — overactive sympathetic tone, RAAS overactivity, endothelial dysfunction, salt/water retention. Any combination of the handles in the BP equation.
- Why it matters — "the silent killer": usually symptomless until target-organ damage: stroke, myocardial infarction, heart failure, chronic kidney disease, retinopathy. Malignant hypertension adds papilloedema and encephalopathy.

Pharmacy link: lifestyle first (salt, weight, exercise, alcohol, smoking). Then classes matched to mechanism: thiazide diuretics, ACE inhibitors/ARBs, calcium-channel blockers, beta-blockers. Hypertensive emergency needs IV drugs (nitroprusside, labetalol) — oral drugs are too slow when organs are at immediate risk.

Cardiac arrhythmias — pathophysiology

Any abnormality of rate, rhythm, or conduction:

- Sinus tachycardia (>100 /min) — fever, anxiety, exercise, anaemia; sinus bradycardia (<60 /min) — athletes, beta-blockers, hypothyroidism.
- Atrial fibrillation (AF) — chaotic atrial activity, irregularly irregular pulse, loss of the atrial kick. The danger is not the rate — it is clot forming in the quivering atria → stroke. Hence anticoagulation (warfarin/DOACs), linking straight back to Unit III.
- Atrial flutter — sawtooth baseline, fast regular atrial rate.
- Ventricular tachycardia / ventricular fibrillation — VF is chaotic ventricular quivering with zero cardiac output = cardiac arrest; the treatment is immediate defibrillation (an unsynchronised shock resets the rhythm).
- Heart blocks — AV conduction fails: first-degree (long PR), second-degree (dropped beats), third-degree/complete (atria and ventricles beat independently — needs a pacemaker).

- Extrasystoles (ectopic beats) — premature beats from atria or ventricles; often benign, felt as "skipped beats".

Pharmacy link: antiarrhythmics map onto the conduction system: amiodarone (broad — K^+ channel blockade plus more), lidocaine (Na^+ channels — ventricular arrhythmias), verapamil (Ca^{2+} channels — slows the AV node, used in supraventricular tachycardia), adenosine (brief AV nodal block — terminates SVT). You cannot place these drugs without the SA → AV → His → Purkinje order from above.

Congestive heart failure — pathophysiology

- Definition: the heart cannot pump enough to meet the body's needs — a failing pump, not a stopped one.
- Left-sided failure — blood dams back into the lungs: dyspnoea, orthopnoea (breathless lying flat), paroxysmal nocturnal dyspnoea (waking gasping at night), pulmonary oedema (crackles), fatigue. Causes: hypertension, MI, valve disease.
- Right-sided failure — blood dams back into the systemic veins: pedal oedema, raised jugular venous pressure, tender hepatomegaly, ascites. Often follows left-sided failure (via pulmonary hypertension) or chronic lung disease (cor pulmonale).
- The vicious cycle: an initial insult (MI, chronic hypertension) drops output → the body compensates — sympathetic activation + RAAS activation (retain salt/water, vasoconstrict) + ventricular remodelling (hypertrophy, dilation). Helpful for days, harmful for months: the extra load exhausts the failing muscle further. In CHF, the compensation becomes the disease.
- Systolic failure (low ejection fraction — weak squeeze) vs diastolic failure (preserved EF — stiff ventricle that cannot fill).

Pharmacy link: treatment unloads the heart and blocks the harmful compensation: diuretics (↓ preload, clear oedema), ACE inhibitors/ARBs + beta-blockers (block RAAS and sympathetic overdrive — the combination proven to prolong life), digoxin (↑ contractility, controls AF rate), ARNIs (sacubitril/valsartan) in modern guidelines. Notice the paradox students must grasp: beta-blockers worsen acute failure but prolong life in chronic stable failure — because they block the toxic chronic sympathetic drive.

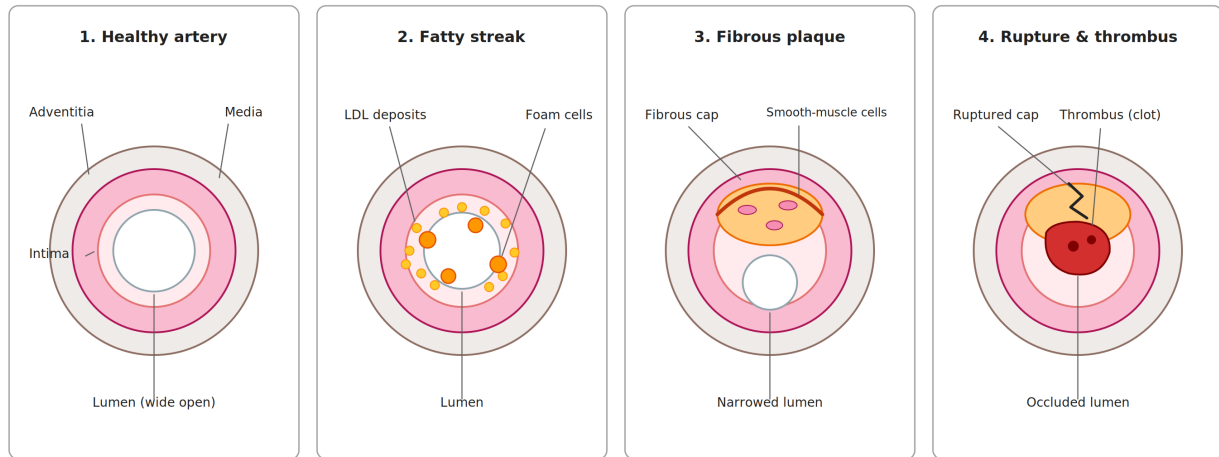
Ischemic heart disease — angina, MI, atherosclerosis, CAD

Atherosclerosis — the root process, in four stages:

- 1 Endothelial injury (hypertension, smoking, high LDL, diabetes) lets LDL into the intima.
- 2 LDL oxidises → monocytes enter, become macrophages, gorge on lipid → foam cells → fatty streak.
- 3 Smooth-muscle proliferation + collagen → fibrous plaque with a lipid core.

- 4 Plaque rupture exposes thrombogenic material → thrombus → occlusion. Stable plaques narrow the lumen (stable angina); ruptured plaques occlude suddenly (MI).

Atherosclerosis: Sequence of Plaque Formation



LDL = low-density lipoprotein; foam cells = lipid-laden macrophages.

Atherosclerosis sequence — from endothelial injury to plaque rupture and thrombus

Angina pectoris — chest pain when myocardial oxygen demand exceeds supply, relieved by rest or nitroglycerin:

- Stable angina — predictable, on exertion, relieved by rest; fixed plaque narrowing.
- Unstable angina — new, more severe, or occurring at rest; plaque disruption without complete occlusion — a pre-infarction warning.
- Prinzmetal (variant) angina — coronary spasm, often at rest, can strike normal-looking coronaries; relieved by calcium-channel blockers.

Myocardial infarction — prolonged ischaemia kills heart muscle. Usually plaque rupture + thrombus in a coronary artery. Features: severe crushing retrosternal pain radiating to the left arm/jaw, sweating, nausea, breathlessness — not relieved by rest or nitrates (that unresponsiveness is what separates it from angina). Diagnosis: ECG (ST elevation in STEMI) + cardiac markers — troponin I/T (most specific, rises in 3–6 hours, stays days) and CK-MB. Complications: arrhythmias (commonest cause of early death), heart failure, cardiogenic shock, wall rupture. Treatment: aspirin + clopidogrel (antiplatelet — Unit III), thrombolytics (streptokinase — recall fibrinolysis) or primary angioplasty (PCI). "Time is muscle" — every minute of delay kills more myocardium.

Coronary artery disease (CAD) — the umbrella term for atherosclerotic coronary disease presenting as angina, MI, or sudden death. Modifiable risk factors — smoking, hypertension, diabetes, dyslipidaemia, obesity, inactivity — are the prevention message pharmacists counsel on at every dispensing counter.

Trap alert: unstable angina vs MI — both are acute coronary syndromes from plaque disruption, but MI has myocardial necrosis (troponin rises, ST elevation in STEMI) while unstable angina does not (no marker rise, no ST elevation). The troponin result is the dividing line examiners test.

Very short questions (2 marks)

- 1 Trace the path of blood through the heart starting at the venae cavae.
- 2 State the order of the cardiac conduction system.
- 3 What does each wave of a normal ECG represent (P, QRS, T)?
- 4 Define hypertension with its cutoff value.
- 5 Why is troponin the preferred marker for MI?

Short questions (5 marks)

- 1 Describe the cardiac cycle with its three phases, valve actions and heart sounds.
- 2 Explain short-term and long-term regulation of blood pressure (baroreceptors and RAAS).
- 3 Differentiate left-sided from right-sided heart failure across clinical features.

Long questions (10 marks)

- 1 Describe the anatomy of the heart (chambers, valves, coronary circulation) and the conduction system. Explain how the autonomic nervous system regulates the heartbeat, with drug examples.
- 2 Discuss the pathophysiology of atherosclerosis and describe how it leads to stable angina, unstable angina and myocardial infarction. Include diagnosis and treatment of MI.

How to approach these answers

- Very-short Q1: venae cavae → right atrium → tricuspid → right ventricle → pulmonary valve → lungs → pulmonary veins → left atrium → mitral → left ventricle → aortic valve → aorta.
- Very-short Q2: SA node → atria → AV node (delay) → bundle of His → bundle branches → Purkinje fibres.
- Very-short Q3: P = atrial depolarisation, QRS = ventricular depolarisation, T = ventricular repolarisation — one line each.
- Very-short Q4: sustained $\geq 140/90$ mmHg on more than one occasion.
- Very-short Q5: cardiac-specific and stays elevated for days, unlike CK-MB.
- Short Q1: use the 0.8 s timeline — three phases with valve open/shut states, S₁/S₂ placement, and the atrial-kick percentages.
- Short Q2: two halves — baroreceptor reflex (seconds, neural) then RAAS step by step (hours-days, hormonal); close with one drug class per RAAS step.

- Short Q3: a table — left = lungs (dyspnoea, orthopnoea, crackles), right = systemic veins (oedema, JVP, hepatomegaly); mention the usual left-to-right progression.
- Long Q1: structure — heart anatomy with the diagram, then conduction order, then sympathetic vs vagal effects with beta-blockers, atropine and digoxin mapped; conclusion tying rate control to drug action.
- Long Q2: structure — atherosclerosis in four stages with the diagram, then angina types in a table, then MI (features, ECG, troponin, treatment with "time is muscle"); close with modifiable risk factors.

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