CHAPTER 1

ANATOMY

~25% of exam | ~45 questions | 6 sub-sections

1.1 UPPER LIMB

Pectoral Region

Muscles

Muscle	Action	Nerve Supply
Pectoralis major	Adduction, medial rotation, flexion of shoulder	Medial & lateral pectoral nerves
Pectoralis minor	Protracts & depresses scapula; accessory muscle of respiration	Medial pectoral nerve
Trapezius	Upper: elevates scapula. Middle: retracts. Lower: depresses	Spinal accessory nerve (CN XI) + C3–C4
Latissimus dorsi	Extension, adduction, medial rotation of shoulder	Thoracodorsal nerve (C6–8)
Serratus anterior	Protracts scapula; holds scapula against chest wall	Long thoracic nerve (C5–7)

⚡ **EXAM TIP: Long thoracic nerve palsy → winging of scapula (serratus anterior paralysis). Spinal accessory nerve palsy → shoulder drop + difficulty shrugging (trapezius weakness). Know which nerve = which deficit.**

Pectoral Joints

Sternoclavicular Joint (SCJ): Synovial (atypical — contains articular disc). Only synovial joint connecting upper limb to axial skeleton. Strong ligaments make dislocation rare (clavicle fracture more common). Costoclavicular ligament = most important stabiliser.

Acromioclavicular Joint (ACJ): Synovial plane joint. Coracoclavicular ligament (trapezoid + conoid) = main stabiliser. Transmits forces from upper limb to axial skeleton. Injured by fall onto point of shoulder.

Axilla & Brachial Plexus

The axilla is a pyramidal space transmitting the neurovascular bundle from neck to upper limb. Contains the axillary artery (continuation of subclavian at outer border of 1st rib, becomes brachial artery at lower border of teres major), giving rise to the circumflex humeral arteries (supply surgical neck of humerus). Detailed branch knowledge NOT required.

Brachial Plexus

Roots: C5, C6, C7, C8, T1. Structure: Roots → Trunks → Divisions → Cords → Branches.

Mnemonic: "Robert Taylor Drinks Cold Beer"

Exam scope: Root derivation and broad trunk/division/cord structure required. Detailed cord-to-nerve mapping NOT required. Appreciate potential for damage based on position in axilla.

Brachial Plexus Injuries

Injury	Roots	Mechanism	Clinical Presentation
Erb–Duchenne palsy	C5–C6 (upper trunk)	Birth injury (shoulder dystocia), motorcycle fall	Waiter's tip: arm adducted, medially rotated, forearm pronated, wrist flexed
Klumpke's palsy	C8–T1 (lower trunk)	Upward traction on arm, birth injury (breech)	Claw hand. May have Horner's syndrome (T1 sympathetic damage)
Complete plexus injury	C5–T1	Severe traction	Flail arm; total motor + sensory loss in upper limb

💡 **HIGH YIELD: Erb's palsy = waiter's tip (C5–C6). Klumpke's = claw hand ± Horner's (C8–T1). These are repeatedly tested distinctions.**

Breast & Chest Drain Landmarks

Lymphatic Drainage of the Breast

Lateral quadrants (75%): Drain to axillary lymph nodes (anterior/pectoral group).

Medial quadrants: Drain to parasternal (internal thoracic) nodes.

Inferior quadrants: May drain to abdominal (subdiaphragmatic) nodes.

Some drainage crosses to the contralateral breast.

Chest Drain Insertion

Safe triangle: Bordered by anterior border of latissimus dorsi, lateral border of pectoralis major, a horizontal line at the level of the nipple (5th intercostal space), and the base of the axilla.

Insertion site: 5th intercostal space, mid-axillary line.

Technique: Insert just ABOVE the rib — the neurovascular bundle (VAN) runs in the costal groove on the inferior border of the rib above.

> 💡 **HIGH YIELD: Chest drain = 5th ICS, mid-axillary line, safe triangle. Insert above rib (VAN runs below). Tested in nearly every sitting.**

Shoulder

Rotator Cuff Muscles

Mnemonic: SITS = Supraspinatus, Infraspinatus, Teres minor, Subscapularis

Muscle	Action	Nerve	Clinical Test
Supraspinatus	Initiates abduction (0–15°)	Suprascapular nerve (C5–6)	Empty can test (Jobe's)
Infraspinatus	External rotation	Suprascapular nerve (C5–6)	Resisted external rotation
Teres minor	External rotation	Axillary nerve (C5–6)	Hornblower's test
Subscapularis	Internal rotation	Upper & lower subscapular nerves	Lift-off test (Gerber's)

> ⚡ **EXAM TIP: Lift-off test = subscapularis. Empty can = supraspinatus. Past paper recall: "Lift-off test — which muscle?" → Subscapularis.**

Shoulder Joint

Type: Synovial ball-and-socket (most mobile joint in the body). Stability sacrificed for mobility — shallow glenoid fossa, relies on soft tissues.

Stability factors: Glenoid labrum, rotator cuff muscles, coracoacromial arch (coracoacromial ligament + coracoid + acromion), glenohumeral ligaments, long head of biceps.

Axillary nerve: Supplies deltoid and teres minor. Vulnerable in anterior shoulder dislocation and surgical neck fractures. Damage → loss of shoulder abduction (15–180°) + regimental badge anaesthesia.

Arm, Elbow & Forearm

Anterior Arm

Muscles: Coracobrachialis (flexion/adduction, musculocutaneous nerve), Biceps (flexion + supination, musculocutaneous), Brachialis (main elbow flexor, musculocutaneous).

Brachial artery: Continuation of axillary artery at lower border of teres major. Palpable medial to biceps tendon at elbow (BP measurement site). Divides into radial and ulnar arteries at the cubital fossa. Venae comitantes accompany it.

Median nerve: From medial + lateral cords. Gives NO branches in the arm. Crosses from lateral to medial side midway down arm.

Ulnar nerve: Gives NO branches in the arm. Passes behind medial epicondyle ("funny bone").

Elbow Joint

Type: Synovial hinge joint (+ pivot for pronation/supination). Three articulations in one capsule: Humeroulnar (hinge), Humeroradial (hinge), Superior radioulnar (pivot).

Movements: Flexion — brachialis (main), biceps, brachioradialis. Extension — triceps (main). Carrying angle ~5–15° valgus (greater in females). Increased carrying angle → ulnar nerve palsy (cubitus valgus).

Posterior Arm — Radial Nerve

Course: Runs in the radial (spiral) groove on posterior humerus, close to bone. Supplies all 3 heads of triceps. Continues as posterior interosseous nerve (deep branch) and superficial branch in forearm.

Injury: Midshaft humeral fracture → radial nerve palsy → wrist drop + loss of finger/thumb extension + sensory loss over anatomical snuffbox.

> 💡 **HIGH YIELD: Radial nerve in spiral groove → vulnerable in midshaft humeral fracture → WRIST DROP. One of the most commonly tested nerve injuries.**

Anterior Forearm

Common flexor origin: Medial epicondyle. Median nerve supplies ALL anterior forearm muscles EXCEPT FCU and medial half of FDP (ulnar nerve).

Anterior interosseous nerve (AIN): Pure motor branch of median nerve; supplies FPL, lateral FDP, pronator quadratus.

Supination: Supinator + biceps brachii (most powerful when elbow flexed). Pronation: pronator teres + pronator quadratus.

Posterior Forearm & Anatomical Snuffbox

All extensors: Supplied by radial nerve or its deep branch (posterior interosseous nerve). Common extensor origin: lateral epicondyle.

Anatomical snuffbox: Lateral borders: APL + EPB. Medial border: EPL. Floor: scaphoid and trapezium. Contents: radial artery (palpable), cephalic vein origin, superficial branch of radial nerve.

De Quervain's: 1st extensor compartment (APL + EPB). EPL tendon can rupture in Colles' fracture.

> ⚡ **EXAM TIP: Anatomical snuffbox floor = scaphoid. Tenderness here after FOOSH = suspected scaphoid fracture. Radial artery crosses the floor.**

Wrist & Hand

Carpal Tunnel

Boundaries: Flexor retinaculum bridges from scaphoid tubercle + trapezium (laterally) to pisiform + hook of hamate (medially).

10 structures pass through: Median nerve (most superficial), 4 FDS tendons, 4 FDP tendons, FPL tendon.

Structures ABOVE retinaculum: Ulnar nerve + ulnar artery (Guyon's canal), palmar cutaneous branch of median nerve, palmaris longus tendon.

> ⚡ **EXAM TIP: Carpal tunnel = median nerve + 9 tendons. Ulnar nerve passes ABOVE (Guyon's canal), NOT through the carpal tunnel. Common exam trick.**

Hand Innervation Summary

Median nerve: Lateral 3.5 digits (thumb, index, middle, lateral half of ring) — palmar surface + fingertips. Motor: thenar muscles (EXCEPT adductor pollicis), lateral 2 lumbricals.

Ulnar nerve: Medial 1.5 digits (little finger, medial half of ring). Motor: hypothenar muscles, interossei, medial 2 lumbricals, adductor pollicis.

Lumbricals: Flex MCPs + extend IPs ("writing position"). Lateral 2 = median nerve. Medial 2 = ulnar nerve.

Flexor Tendon Zones (Verdan)

Zone II ("no man's land"): A1 pulley to FDS insertion. Both FDS + FDP in fibrous sheath. Worst prognosis for repair.

Upper Limb Nerve Injuries — Complete Summary

Nerve	Root	Injury Mechanism	Motor Loss	Sensory Loss	Deformity
Axillary	C5–C6	Anterior shoulder dislocation, surgical neck fracture	Deltoid (abduction 15–180°), teres minor	Regimental badge area (lateral deltoid)	Flattened shoulder
Radial	C5–T1	Midshaft humeral fracture, "Saturday night palsy"	Wrist extensors, finger extensors, thumb extensors, triceps (high)	1st dorsal web space (anatomical snuffbox)	Wrist drop

Median (at wrist)	C6–T1	Carpal tunnel syndrome, wrist laceration	Thenar muscles (opponens, APB, FPB), lateral 2 lumbricals	Lateral 3.5 digits (palmar)	Ape hand (thenar wasting, loss of opposition)
Median (at elbow)	C6–T1	Supracondylar fracture (children)	All anterior forearm muscles (except FCU, medial FDP) + hand losses	As above + palmar cutaneous branch	Hand of benediction (can't flex index + middle fingers)
Ulnar (at wrist)	C8–T1	Guyon's canal, hook of hamate fracture	Interossei, medial 2 lumbricals, hypothenar, adductor pollicis	Medial 1.5 digits (palmar + dorsal)	Ulnar claw (ring + little fingers)
Ulnar (at elbow)	C8–T1	Medial epicondyle fracture, cubitus valgus	As wrist + FCU + medial FDP	As wrist + dorsal branch territory	Ulnar claw (LESS marked paradoxically)
Musculocutaneous	C5–C7	Shoulder surgery, stab wound	Biceps, brachialis, coracobrachialis	Lateral forearm (lateral cutaneous nerve)	Weak elbow flexion + supination

💡 **HIGH YIELD: Wrist drop = radial nerve. Ape hand = median at wrist. Hand of benediction = median at elbow. Claw hand = ulnar. Regimental badge = axillary. These are HOT exam topics — asked in almost every sitting.**

⚡ **EXAM TIP: Ulnar claw is MORE marked with LOW (wrist) lesions than HIGH (elbow) lesions. This is the "ulnar paradox" — high lesions also paralyse FDP to ring/little, so there is less unopposed flexion at the DIP/PIP.**

Rapid Recall — Upper Limb

Topic / Prompt	Key Fact / Answer
Brachial plexus roots	C5, C6, C7, C8, T1
Erb's palsy (C5–C6)	Waiter's tip: arm adducted, medially rotated, forearm pronated
Klumpke's palsy (C8–T1)	Claw hand ± Horner's syndrome
SCJ	Only synovial joint connecting upper limb to axial skeleton
ACJ main stabiliser	Coracoclavicular ligament (trapezoid + conoid)
Winging of scapula	Long thoracic nerve palsy → serratus anterior paralysis
Rotator cuff (SITS)	Supraspinatus, Infraspinatus, Teres minor, Subscapularis
Lift-off test	Subscapularis
Axillary nerve damage	Loss of abduction (deltoid) + regimental badge anaesthesia
Radial nerve injury	Wrist drop (midshaft humerus fracture)
Median nerve at wrist	Ape hand + thenar wasting (carpal tunnel)
Median nerve at elbow	Hand of benediction (supracondylar fracture)
Ulnar nerve at wrist	Claw hand (ring + little fingers hyperextended at MCP)
Ulnar paradox	Claw WORSE with LOW (wrist) lesion than high (elbow) lesion
Carpal tunnel contents	Median nerve + 4 FDS + 4 FDP + FPL (10 total)
Ulnar nerve at wrist	Passes through Guyon's canal (ABOVE flexor retinaculum)
Anatomical snuffbox floor	Scaphoid + trapezium
Snuffbox contents	Radial artery, cephalic vein origin, superficial radial nerve
Chest drain insertion	5th ICS, mid-axillary line, insert above rib (VAN below)
Breast lymph drainage (75%)	Axillary nodes (lateral quadrants)
Carrying angle	5–15° valgus; increased = ulnar nerve palsy (cubitus valgus)
Cubital fossa (lateral to medial)	Radial nerve, Biceps tendon, Brachial artery, Median nerve
Zone II (no man's land)	FDS + FDP in fibrous sheath; worst prognosis

De Quervain’s	1st extensor compartment (APL + EPB)

1.2 LOWER LIMB

Femoral Triangle & Femoral Sheath

Femoral Sheath

Origin: Prolongation of extraperitoneal fascia (transversalis anteriorly, iliopsoas posteriorly) into the thigh.

3 compartments: Lateral = femoral artery. Intermediate = femoral vein. Medial = femoral canal (contains lymph node of Cloquet).

Femoral nerve: NOT in the femoral sheath — lies lateral to it.

> 💡 **HIGH YIELD: NAVY mnemonic (lateral to medial at inguinal ligament): Nerve → Artery → Vein → Y-fronts (lymphatics/canal). The femoral NERVE is OUTSIDE the sheath. Tested repeatedly.**

Femoral Ring Boundaries

Anterior: Inguinal ligament. Posterior: Pectineal ligament (Cooper's). Medial: Lacunar ligament. Lateral: Femoral vein.

> ⚡ **EXAM TIP: Femoral hernia passes through the femoral canal (medial compartment of sheath). More common in women. Narrow neck → higher risk of strangulation than inguinal hernia.**

Femoral Artery

Surface marking: Mid-inguinal point (midpoint between ASIS and pubic symphysis). Note: this is NOT the same as the midpoint of the inguinal ligament (ASIS to pubic tubercle).

Femoral Nerve

Derivation: L2, L3, L4 (posterior divisions).

Motor: Quadriceps (knee extension), sartorius, pectineus, iliacus.

Sensory: Anterior thigh + saphenous nerve (longest cutaneous nerve — supplies medial leg and foot).

Hip Joint & Gluteal Region

Gluteal Muscles

Muscle	Action	Nerve
Gluteus maximus	Extension + lateral rotation of hip	Inferior gluteal nerve
Gluteus medius	Abduction + medial rotation of hip	Superior gluteal nerve
Gluteus minimus	Abduction + medial rotation of hip	Superior gluteal nerve
Piriformis	Lateral rotation + abduction when hip flexed	Nerve to piriformis (S1–S2)

> ⚡ **EXAM TIP: Trendelenburg sign = superior gluteal nerve damage → gluteus medius/minimus weakness → pelvis drops on the OPPOSITE side when standing on affected leg.**

Sciatic Nerve

Derivation: L4–S3 (largest nerve in the body).

Entry: Greater sciatic foramen, BELOW piriformis.

Surface marking: Midpoint between ischial tuberosity and greater trochanter (buttock); midline of posterior thigh.

Division: Tibial nerve + common peroneal nerve (usually at apex of popliteal fossa).

IM injection safe zone: Upper outer quadrant of buttock (to avoid sciatic nerve).

Hip Joint

Type: Synovial ball-and-socket. Acetabulum formed by ilium, ischium, pubis. Deepened by acetabular labrum.

Blood supply: Retinacular arteries from medial + lateral circumflex femoral arteries (branches of profunda femoris) = MAIN supply in adults. Artery of ligamentum teres (obturator artery) = important in children.

Nerve supply: Hilton's law — femoral, obturator, sciatic, nerve to quadratus femoris.

> 💡 **HIGH YIELD: Intracapsular neck of femur fractures disrupt retinacular arteries → avascular necrosis (AVN) of femoral head. This is why displaced intracapsular fractures require hip replacement rather than fixation.**

Posterior Thigh & Popliteal Fossa

Hamstrings

Muscle	Action	Nerve
Biceps femoris (long head)	Flexion of knee, extension of hip, lateral rotation	Tibial division of sciatic
Biceps femoris (short head)	Flexion of knee	Common peroneal division of sciatic
Semitendinosus	Flexion of knee, extension of hip, medial rotation	Tibial division of sciatic
Semimembranosus	Flexion of knee, extension of hip, medial rotation	Tibial division of sciatic

Pes anserinus: “Say Grace before Tea” = Sartorius, Gracilis, semiTendinosus — insert together on medial proximal tibia.

Popliteal Fossa

Boundaries: Superomedial: semimembranosus (+ semitendinosus). Superolateral: biceps femoris. Inferomedial + inferolateral: medial and lateral heads of gastrocnemius. Floor: femur + posterior knee capsule. Roof: popliteal fascia.

Contents (superficial to deep): Tibial nerve (most superficial) → Popliteal vein → Popliteal artery (deepest, closest to bone).

Common peroneal nerve: Follows medial border of biceps femoris laterally, then wraps around the neck of the fibula.

> 💡 **HIGH YIELD: Popliteal fossa boundaries: Superomedial = semimembranosus. Superolateral = biceps femoris. Asked in multiple past papers.**

Knee Joint

Ligaments: ACL = prevents anterior tibial displacement (positive anterior drawer). PCL = prevents posterior tibial displacement (posterior drawer). MCL = resists valgus stress. LCL = resists varus stress.

Menisci: Medial = larger, C-shaped, attached to MCL (less mobile, more commonly torn). Lateral = smaller, more circular, not attached to LCL (more mobile, less commonly torn).

Screw-home mechanism: In last 30° of extension, femur medially rotates on tibia, “locking” the knee. Unlocked by popliteus.

> ⚡ **EXAM TIP: ACL injury = positive anterior drawer test + Lachman test. Most common ligament injured in the knee. Medial meniscus is MORE commonly torn than lateral (tethered to MCL = less mobile).**

Leg, Ankle & Foot

Anterior Compartment

Key muscle: Tibialis anterior (dorsiflexion + inversion). Also: EHL, EDL, peroneus tertius.

Nerve supply: Deep peroneal nerve.

Dorsalis pedis: Continuation of anterior tibial artery. Palpable between EHL and EDL tendons on dorsum of foot.

Lateral Compartment

Muscles: Peroneus longus + brevis (eversion + plantarflexion). Pass behind lateral malleolus.

Nerve: Superficial peroneal nerve.

Clinical: Peroneus brevis can avulse base of 5th metatarsal in ankle inversion injury.

Posterior Compartment

Superficial: Gastrocnemius + soleus = triceps surae → Achilles tendon → calcaneus. Plantarflexion.

Deep: FDL, FHL, tibialis posterior (main invertor + arch support).

Tibial nerve: Nerve of posterior compartment. Passes behind medial malleolus with posterior tibial artery (palpable there).

Common Peroneal Nerve

Course: Wraps around the NECK OF THE FIBULA (most vulnerable point).

Injury: Fibula neck fracture, tight cast, prolonged leg crossing → FOOT DROP (loss of dorsiflexion + eversion) + sensory loss over dorsum of foot and lateral leg.

Branches: Deep peroneal (anterior compartment) + superficial peroneal (lateral compartment).

> 💡 **HIGH YIELD: Common peroneal nerve at fibula neck → foot drop. This is a highly tested nerve injury. Remember: deep peroneal = anterior (dorsiflexion); superficial peroneal = lateral (eversion).**

Ankle Joint & Stability

Type: Synovial hinge (dorsiflexion/plantarflexion only). Inversion/eversion occur at subtalar and midtarsal joints.

Ligaments: Deltoid (medial) = strong, resists eversion. Lateral ligaments (ATFL, CFL, PTFL) = weaker, injured in inversion.

Talus stability: Wider anteriorly → in dorsiflexion ankle is MOST STABLE. In plantarflexion → LEAST STABLE (more prone to inversion injuries).

Foot arches: Medial longitudinal arch (higher) supported by spring ligament + tibialis posterior tendon + FHL + plantar aponeurosis. Lateral arch supported by peroneus longus.

Lower Limb Nerve Injuries

Nerve	Root	Injury	Motor Loss	Sensory Loss
Femoral	L2–L4	Pelvic fracture, femoral surgery	Quadriceps (knee extension), hip flexors	Anterior thigh + medial leg (saphenous)
Obturator	L2–L4	Pelvic surgery, obturator hernia	Adductors (hip adduction)	Medial thigh
Lateral cutaneous of thigh	L2–L3	Compression at inguinal ligament	None (pure sensory)	Lateral thigh (meralgia paraesthetica)
Sciatic	L4–S3	Hip surgery, posterior dislocation	All below knee + hamstrings	All below knee (except medial leg)
Common peroneal	L4–S2	Fibula neck fracture/pressure	Dorsiflexion + eversion (foot drop)	Dorsum of foot + lateral leg
Tibial	L4–S3	Popliteal fossa trauma	Plantarflexion + toe flexion + inversion	Sole of foot

Rapid Recall — Lower Limb

Topic / Prompt	Key Fact / Answer
NAVY (lateral to medial)	Nerve, Artery, Vein, Y-fronts (lymphatics)
Femoral nerve	NOT in femoral sheath; L2–L4; knee extension
Femoral artery surface marking	Mid-inguinal point (ASIS to pubic symphysis midpoint)
Femoral canal contents	Lymph node of Cloquet (site of femoral hernia)
Sciatic nerve surface marking	Midpoint ischial tuberosity – greater trochanter
Sciatic nerve: exits below	Piriformis (greater sciatic foramen)
Hip joint blood supply (adult)	Retinacular arteries (medial + lateral circumflex femoral)
Intracapsular NOF fracture risk	AVN of femoral head (retinacular arteries disrupted)
Trendelenburg sign	Superior gluteal nerve damage → gluteus medius weakness
Popliteal fossa (superomedial)	Semimembranosus
Popliteal fossa (superolateral)	Biceps femoris
Deepest structure in popliteal fossa	Popliteal artery (closest to bone)
ACL test	Anterior drawer + Lachman test

Screw-home mechanism	Last 30° extension: femur medially rotates, “locked”
Common peroneal nerve injury	Foot drop (fibula neck fracture/pressure)
Foot drop = loss of	Dorsiflexion (tibialis anterior) + eversion
Ankle: most stable position	Dorsiflexion (wider anterior talus in mortise)
Medial arch key support	Spring ligament + tibialis posterior tendon
Deltoid ligament	Strong medial ankle ligament; resists eversion
Peroneus brevis avulsion	Base of 5th metatarsal (inversion injury)
Saphenous nerve	Terminal branch of femoral; longest cutaneous nerve
Cremasteric reflex nerve	Genitofemoral nerve (L1–L2)
Pes anserinus	Sartorius, Gracilis, Semitendinosus (medial tibia)

1.3 THORAX

Thoracic Wall

Rib Structure

12 pairs: True ribs (1–7) = sternum directly. False ribs (8–10) = indirectly via cartilage. Floating ribs (11–12) = no anterior attachment.

Costal groove: Inferior internal surface of rib shaft. Contains VAN (Vein, Artery, Nerve) from superior to inferior.

1st rib: Articulates with T1 (NOT C7). Shortest, broadest, most curved. Grooves for subclavian artery + vein. Scalene tubercle for scalenus anterior.

⚡ **EXAM TIP: 1st rib articulates with T1, NOT C7. This is a common exam trap. VAN order in costal groove: Vein (top), Artery, Nerve (bottom).**

Intercostal Space

Layers (superficial to deep): Skin → External intercostal → Internal intercostal → VAN bundle → Innermost intercostal → Endothoracic fascia → Parietal pleura.

VAN bundle: Runs in costal groove on the INFERIOR border of the RIB ABOVE, between internal and innermost intercostal layers.

Respiration Mechanics

Pump handle: Upper ribs (1–6) → increases AP diameter.

Bucket handle: Lower ribs (7–10) → increases transverse diameter.

Diaphragm: Primary muscle (~75% tidal volume). External intercostals assist inspiration. Abdominal muscles + internal intercostals for forced expiration.

Diaphragm

Openings & Vertebral Levels

Mnemonic: "I 8 10 Eggs At 12" (IVC at T8, oEsophagus at T10, Aorta at T12)

Opening	Level	Structures Passing Through	Key Detail
Caval opening	T8	IVC + right phrenic nerve	In the central tendon; most anterior
Oesophageal hiatus	T10	Oesophagus + anterior & posterior vagal trunks	In the muscular part (right crus); most common site for hiatus hernia
Aortic hiatus	T12	Aorta + thoracic duct + azygos vein	Behind the median arcuate ligament (not truly in diaphragm); most posterior

💡 **HIGH YIELD: Diaphragm openings are tested in EVERY sitting. T8 = IVC + right phrenic. T10 = oesophagus + vagi. T12 = aorta + thoracic duct + azygos. The aortic hiatus is BEHIND the diaphragm (median arcuate ligament), not through it.**

Phrenic Nerve

Origin: C3, C4, C5 (“C3, 4, 5 keeps the diaphragm alive”).

Course: Descends on scalenus anterior. Right phrenic passes through caval opening. Left phrenic pierces muscular diaphragm.

Referred pain: Central diaphragm irritation (e.g. subphrenic abscess) → shoulder tip pain (C3–C5 dermatomes).

Heart & Great Vessels

Pericardium

Fibrous pericardium: Tough outer layer. Nerve supply = phrenic nerve (pain of pericarditis = sharp, pleuritic, relieved by sitting forward). Distinction from ACS = important.

Serous pericardium: Parietal (lines fibrous) + visceral (epicardium). Between them = pericardial cavity (~15–50 mL fluid).

Heart Borders & Surface Markings

Right border: Right atrium (SVC to IVC).

Inferior border: Right ventricle (mainly).

Left border: Left ventricle (+ left atrium above).

Apex: 5th left intercostal space, mid-clavicular line.

Valve Auscultation

Valve	Surface Marking	Auscultation Site
Aortic	Left sternal border, 3rd ICS	2nd right ICS, right sternal border
Pulmonary	Left sternal border, 3rd ICS	2nd left ICS, left sternal border
Mitral	5th left ICS, mid-clavicular line	Apex (5th left ICS, MCL)
Tricuspid	Left sternal border, 4th–5th ICS	Left lower sternal border, 4th ICS

> ⚡ **EXAM TIP: Aortic valve auscultation = 2nd RIGHT intercostal space. Past paper: "Aortic valve auscultation — location?" → 2nd right ICS.**

Coronary Arteries (Overview)

Origin: Both from aortic root (sinuses of Valsalva), just above aortic valve.

Left coronary: Left anterior descending (LAD) = anterior wall + septum. Circumflex (LCx) = lateral + posterior wall.

Right coronary: RCA = inferior wall + right ventricle. Usually supplies SA node (60%) and AV node (80%).

Pericardiocentesis: Subxiphoid approach, needle angled 45° toward left shoulder. Indication: cardiac tamponade (Beck's triad: hypotension, muffled heart sounds, distended neck veins).

Trachea, Thymus & Oesophagus

Trachea: C6 to T4/5 (carina at sternal angle). 16–20 C-shaped hyaline cartilage rings. Posterior wall = trachealis muscle (no cartilage). Lined by ciliated pseudostratified columnar epithelium.

Thymus: Superior/anterior mediastinum. Largest in children (T-lymphocyte production). Involutes after puberty. Thymoma associated with myasthenia gravis.

Oesophagus: C6 to T10. Pierces diaphragm at T10 (left crus). Points of constriction: cricopharyngeus (C6), aortic arch (T4), left main bronchus (T4/5), diaphragm (T10).

Pleura & Lungs

Parietal pleura: Lines the chest wall. Innervated by intercostal nerves (somatic = sharp, localised pain) + phrenic nerve (central diaphragmatic pleura).

Visceral pleura: Covers the lung surface. Innervated by autonomic nerves (no pain sensation).

Lung lobes: Right = 3 lobes (upper, middle, lower); 2 fissures (oblique + horizontal). Left = 2 lobes (upper, lower); 1 fissure (oblique). Left upper lobe has the lingula.

Lung roots: Connect lung to mediastinum. Contents: main bronchus, pulmonary artery, 2 pulmonary veins, bronchial vessels, nerves, lymph nodes.

Rapid Recall — Thorax

Topic / Prompt	Key Fact / Answer
T8 opening	IVC + right phrenic nerve (central tendon)
T10 opening	Oesophagus + anterior & posterior vagal trunks
T12 opening	Aorta + thoracic duct + azygos vein (behind diaphragm)
Phrenic nerve	C3, C4, C5. Motor to diaphragm. Referred pain = shoulder tip
1st rib articulates with	T1 (NOT C7)
VAN in costal groove	Vein (top), Artery, Nerve (bottom); inferior border of rib above

Pump handle	Upper ribs → increases AP diameter
Bucket handle	Lower ribs → increases transverse diameter
Aortic valve auscultation	2nd right intercostal space, right sternal border
Coronary arteries origin	Aortic root (sinuses of Valsalva)
RCA territory	Inferior wall + SA node (60%) + AV node (80%)
LAD territory	Anterior wall + interventricular septum
Pericardiocentesis	Subxiphoid, 45° toward left shoulder
Beck’s triad	Hypotension, muffled heart sounds, distended neck veins
Trachea extent	C6 to T4/5 (carina at sternal angle)
Right lung	3 lobes, 2 fissures
Left lung	2 lobes, 1 fissure, lingula
Parietal pleura innervation	Intercostal nerves (somatic) + phrenic (central diaphragm)
Visceral pleura	Autonomic only = no pain sensation
Oesophageal constrictions	C6 (cricopharyngeus), T4 (aortic arch/bronchus), T10 (diaphragm)

1.4 ABDOMEN & PELVIS

Anterior Abdominal Wall

Layers: External oblique (superficial) → Internal oblique → Transversus abdominis (deepest). Rectus abdominis lies within the rectus sheath.

Rectus sheath: Above arcuate line: anterior = EO + IO aponeuroses. Posterior = IO + TA aponeuroses. Below arcuate line: ALL aponeuroses pass anterior; posterior wall = transversalis fascia only.

Nerve supply: Segmental: T7–T12 intercostal nerves + L1 (iliohypogastric, ilioinguinal).

Inferior epigastric artery: Runs within rectus sheath posterior to rectus abdominis. Landmark for inguinal hernias: Direct = medial to it. Indirect = lateral to it.

Inguinal Region

Inguinal Canal

Length: ~4 cm. Transmits spermatic cord (males) or round ligament (females).

Deep ring: In transversalis fascia, lateral to inferior epigastric artery.

Superficial ring: In external oblique aponeurosis, above and medial to pubic tubercle.

Walls: Anterior = EO aponeurosis. Posterior = transversalis fascia (+ conjoint tendon medially). Roof = internal oblique + transversus arching fibres. Floor = inguinal ligament + lacunar ligament medially.

Inguinal vs Femoral Hernia

Feature	Indirect Inguinal	Direct Inguinal	Femoral
Route	Through deep ring → canal → superficial ring	Through posterior wall (Hesselbach's triangle)	Through femoral canal (below inguinal ligament)
Relation to inf. epigastric a.	LATERAL	MEDIAL	Below and lateral
Relation to pubic tubercle	Above and medial	Above and medial	Below and lateral
Age/sex	Young males; most common hernia	Older males	Older females; narrowest neck
Strangulation risk	Moderate	Low (wide neck)	HIGH (narrow rigid femoral ring)
Sac covering	Has 3 coverings of spermatic cord	No cord coverings	No cord coverings

💡 **HIGH YIELD: Inguinal vs femoral hernia distinction is a HOT topic. Indirect = lateral to inferior epigastric artery, through deep ring. Direct = medial, through Hesselbach's. Femoral = below inguinal ligament, below and lateral to pubic tubercle. Femoral has highest strangulation risk.**

GI Tract — Arterial Supply

Foregut, Midgut, Hindgut

Division	Artery	Structures Supplied	Referred Pain
Foregut	Coeliac trunk (T12)	Oesophagus (abdominal) to 2nd part of duodenum + liver, gallbladder, spleen, pancreas	Epigastric (T6–T9)
Midgut	Superior mesenteric artery (SMA)	2nd part of duodenum to 2/3 along transverse colon + appendix	Periumbilical (T10)
Hindgut	Inferior mesenteric artery (IMA)	Distal 1/3 transverse colon to upper rectum	Suprapubic (T11–L2)

⚡ **EXAM TIP: SMA supplies midgut = duodenum (2nd part) to 2/3 transverse colon. Past paper: "SMA — which structure does it supply?" → Ascending colon (among others).**

Portal Vein & Portosystemic Anastomoses

Formation: Superior mesenteric vein + splenic vein (behind neck of pancreas).

5 sites of portosystemic anastomosis: 1. Lower oesophagus (oesophageal varices). 2. Rectum (haemorrhoids). 3. Umbilicus (caput medusae). 4. Retroperitoneal (bare area of liver). 5. Patent ductus venosus.

Liver, Spleen & Pancreas

Liver: Surface marking: upper border at 5th rib MCL (right). 4 lobes: right, left, caudate, quadrate. Functionally divided into right and left halves. Portal triad at porta hepatis: hepatic artery, portal vein, bile duct.

Spleen: Lies under ribs 9–11 on left side. Relations: stomach, kidney, splenic flexure, diaphragm. Palpation: enlarged spleen moves toward right iliac fossa (differentiates from kidney).

Pancreas: Head in C-loop of duodenum. Tail reaches splenic hilum. Arterial supply mainly from splenic artery. Referred pain T6–T10.

Kidneys & Ureters

Position: Retroperitoneal. Right lower than left (liver). Move with respiration. T12–L3 (upper pole of right at 12th rib).

Relations: Posterior: diaphragm, quadratus lumborum, psoas. Anterior (right): liver, duodenum, hepatic flexure. Anterior (left): stomach, spleen, splenic flexure, pancreas tail.

Blood supply: Renal arteries (direct from aorta at L1–L2). Segmental supply (end arteries → infarction if blocked).

Referred pain: Renal colic pain via T10–L1 (loin to groin).

Pelvis

Rectum & Anus

PR examination: Anterior: males = prostate + seminal vesicles; females = cervix + posterior fornix of vagina. Posterior: sacrum + coccyx.

Anal canal lymph drainage: Above dentate line → internal iliac nodes. Below dentate line → superficial inguinal nodes (palpable).

Female Reproductive System

Uterus: Relations: bladder (anterior), rectouterine pouch/pouch of Douglas (posterior), ovary and fallopian tubes (lateral).

Ectopic pregnancy sites: Ampulla (most common), isthmus, fimbriae, interstitial.

Uterine artery: In broad ligament. Crosses ABOVE the ureter (“water under the bridge” = ureter at risk in hysterectomy).

Male Urethra

Three parts: Prostatic (widest), membranous (narrowest, through urogenital diaphragm), spongy/penile (longest).

Rapid Recall — Abdomen & Pelvis

Topic / Prompt	Key Fact / Answer
Indirect inguinal hernia	Lateral to inferior epigastric artery, through deep ring
Direct inguinal hernia	Medial to inferior epigastric artery (Hesselbach’s triangle)
Femoral hernia	Below inguinal ligament, below & lateral to pubic tubercle. Highest strangulation risk
Foregut artery	Coeliac trunk (T12) → to 2nd part of duodenum
Midgut artery	SMA → 2nd part duodenum to 2/3 transverse colon
Hindgut artery	IMA → distal 1/3 transverse colon to upper rectum
Appendix blood supply	Appendicular artery (branch of ileocolic, from SMA)
McBurney’s point	1/3 from ASIS to umbilicus

Portal vein formation	SMV + splenic vein (behind neck of pancreas)
Oesophageal varices	Portosystemic anastomosis at lower oesophagus
Testicular lymph drainage	Para-aortic nodes (NOT inguinal — follows testicular artery to aorta)
Scrotal lymph drainage	Superficial inguinal nodes
Ectopic pregnancy (commonest site)	Ampulla of fallopian tube
Ureter at risk in	Hysterectomy (“water under the bridge” — uterine artery crosses above)
Renal colic referred pain	T10–L1 (loin to groin)
Below dentate line drainage	Superficial inguinal nodes
Pancreas head	In concavity (C-loop) of duodenum
Rectus sheath below arcuate line	All aponeuroses anterior; posterior = transversalis fascia only
Inferior epigastric artery	Landmark: direct hernia medial, indirect lateral to it

1.5 HEAD & NECK

Neck — General Topography

Cervical fascia: Deep cervical fascia has 4 components: investing, pretracheal, prevertebral, carotid sheath. Tissue spaces (prevertebral, retropharyngeal, parapharyngeal, submandibular) allow infection spread.

Ludwig's angina: Bilateral submandibular space infection → rapidly spreading cellulitis of floor of mouth → airway compromise. Often from dental infection.

Thyroid & Trachea

Thyroid: Two lobes + isthmus. Isthmus attached to tracheal rings 2–4. Recurrent laryngeal nerve lies in the groove between trachea and oesophagus, posterior to thyroid — at risk in thyroid surgery.

Blood supply: Superior thyroid artery (from external carotid) + inferior thyroid artery (from thyrocervical trunk). Rich vascular supply → haemorrhage risk in trauma.

Trachea (cervical): Anterior to oesophagus. Landmarks for tracheostomy: between 2nd–4th tracheal rings. Isthmus lies anterior at rings 2–4.

> 💡 **HIGH YIELD: Recurrent laryngeal nerve = at risk in thyroid surgery. Unilateral damage → hoarse voice (paralysed cord in paramedian position). Bilateral damage → stridor/airway obstruction (cords adducted).**

Cervical Sympathetic Trunk & Horner's Syndrome

Components: Superior, middle, and inferior cervical ganglia. Somatic branches via grey rami to C1–C8. Visceral branches to cardiac plexus. Vascular branches — especially to dilator pupillae.

Horner's syndrome: Disruption of sympathetic supply to the eye. Triad: MIOSIS (small pupil) + PTOSIS (partial, as Müller's muscle only) + ANHIDROSIS (loss of sweating on ipsilateral face).

Causes: Pancoast tumour (lung apex), brainstem stroke, carotid dissection, neck surgery, Klumpke's palsy (C8–T1).

> ⚡ **EXAM TIP: Horner's syndrome: Miosis + Ptosis + Anhidrosis. Can be caused by Pancoast tumour, carotid dissection, or Klumpke's palsy. Past papers test both the features AND the causes.**

Facial Nerve (CN VII)

UMN vs LMN Facial Palsy

Feature	UMN Lesion	LMN Lesion
Forehead	SPARED (bilateral cortical supply)	AFFECTED (entire face paralysed)
Lower face	Paralysed (contralateral to lesion)	Paralysed (ipsilateral to lesion)
Common cause	Stroke (contralateral cortex)	Bell's palsy (most common), parotid tumour, middle ear disease
Side affected	Opposite side to brain lesion	Same side as nerve lesion

> 💡 **HIGH YIELD: UMN = forehead SPARED. LMN = ENTIRE face affected. This is the single most tested cranial nerve distinction. Bell's palsy = most common LMN facial palsy.**

Five Branches (from parotid)

Mnemonic: "To Zanzibar By Motor Car" = Temporal, Zygomatic, Buccal, Marginal mandibular, Cervical.

Temporal branch: Frontalis (wrinkling forehead). Past paper: "Wrinkling of forehead — which branch?" → Temporal.

Marginal mandibular: Depressor anguli oris. At risk in submandibular surgery.

Sensory Supply of the Face

Trigeminal Nerve (CN V) Divisions

Division	Foramen	Key Branches	Territory

V1 (Ophthalmic)	Superior orbital fissure	Supraorbital, supratrochlear, lacrimal, infratrochlear, external nasal	Forehead, upper eyelid, nose bridge
V2 (Maxillary)	Foramen rotundum	Infraorbital, zygomaticofacial, zygomaticotemporal	Cheek, upper lip, lateral nose, lower eyelid
V3 (Mandibular)	Foramen ovale	Auriculotemporal, mental, buccal	Lower face, chin, temple, ear (anterior)

⚡ **EXAM TIP: Sensation of upper lip = infraorbital nerve (V2). Nerve block at centre of forehead = supratrochlear (V1). Ear lobule = great auricular nerve (C2–C3), NOT trigeminal. These are all recalled in past papers.**

Cranial Nerves IX–XII

Glossopharyngeal (CN IX)

Key functions: Sensory + taste to posterior 1/3 tongue; afferent limb of gag reflex; carotid sinus (baroreceptor); secretomotor to parotid.

Vagus (CN X)

Key functions: Pharyngeal/laryngeal motor; cardiac parasympathetic; GI parasympathetic; efferent limb of gag reflex.

Unilateral CN X lesion: Uvula deviates AWAY from lesion (pulled by intact side). Hoarse voice (RLN palsy).

⚡ **EXAM TIP: Uvula deviates AWAY from CN X lesion (intact side pulls it). Tongue deviates TOWARDS CN XII lesion (weak genioglossus can't push). These are opposite directions — common exam question.**

Accessory Nerve (CN XI)

Supplies: SCM + trapezius. Vulnerable in posterior triangle surgery/lymph node biopsy.

Lesion: Shoulder drop + difficulty shrugging (trapezius). Weakness turning head to CONTRALATERAL side (SCM).

Hypoglossal Nerve (CN XII)

Supplies: All tongue muscles except palatoglossus.

LMN lesion: Tongue deviates TOWARDS the lesion on protrusion + ipsilateral wasting + fasciculation.

UMN lesion: Tongue deviates AWAY from cortical lesion (= towards weak side). No wasting or fasciculation.

💡 **HIGH YIELD: CN XII LMN: tongue TOWARDS lesion + wasting. CN XII UMN: tongue AWAY from cortex (towards weak side), NO wasting. Past paper tested.**

Orbit & Eye

Orbital muscles: Superior/medial/inferior rectus + inferior oblique = CN III. Superior oblique = CN IV (SO4). Lateral rectus = CN VI (LR6).

CN III palsy: Ptosis, "down and out" eye, dilated pupil (parasympathetic involvement). Dilated pupil = surgical cause (PCA aneurysm compressing parasympathetic fibres on outside of nerve).

CN IV palsy: Difficulty looking down and in. Head tilt away from affected side.

CN VI palsy: Horizontal diplopia (loss of abduction). False localising sign of raised ICP (longest intracranial course).

⚡ **EXAM TIP: Horizontal diplopia = CN VI (abducens, lateral rectus). CN VI palsy = false localising sign of raised ICP. CN III with dilated pupil = surgical (PCA aneurysm). All past paper tested.**

Ear, Tongue & Larynx

Ear innervation: Pinna: great auricular nerve (C2–C3) + auriculotemporal nerve (V3). Ear lobule = great auricular nerve.

Tongue lymph drainage: Tip → submental nodes. Anterior 2/3 → submandibular + deep cervical. Posterior 1/3 → deep cervical (bilateral). Tip has crossover drainage.

Larynx: Skeleton: thyroid, cricoid, epiglottic, arytenoid cartilages. Cricothyroid membrane = surface landmark for emergency airway (cricothyrotomy). Recurrent laryngeal nerve supplies all intrinsic muscles except cricothyroid (external branch of SLN).

Rapid Recall — Head & Neck

Topic / Prompt	Key Fact / Answer
CN VII UMN vs LMN	UMN = forehead SPARED. LMN = entire face affected
Bell's palsy	Most common LMN facial palsy; idiopathic
Temporal branch of CN VII	Wrinkling of forehead
Upper lip sensation	Infraorbital nerve (V2)
Forehead nerve block (centre)	Supratrochlear nerve (V1)
Ear lobule sensation	Great auricular nerve (C2–C3)
Horner's syndrome	Miosis + ptosis + anhidrosis (sympathetic disruption)
Recurrent laryngeal nerve	All intrinsic laryngeal muscles except cricothyroid
Unilateral RLN palsy	Hoarse voice (cord paramedian)
Bilateral RLN palsy	Stridor/airway obstruction (cords adducted)
Uvula deviation	AWAY from CN X lesion
Tongue deviation (LMN XII)	TOWARDS lesion + wasting + fasciculation
Tongue deviation (UMN XII)	AWAY from cortical lesion (towards weak side)
CN III palsy	Ptosis, down-and-out eye, dilated pupil (if surgical)
CN VI palsy	Horizontal diplopia; false localising sign of raised ICP
Gag reflex	Afferent = CN IX. Efferent = CN X
CN XI damage	Shoulder drop (trapezius) + weak contralateral head turning (SCM)
Cricothyroid membrane	Landmark for emergency cricothyrotomy
Tip of tongue lymph	Submental nodes → jugulo-omohyoid (deep cervical)
Ludwig's angina	Bilateral submandibular space infection → floor of mouth cellulitis
Parotid duct	Opens opposite upper 2nd molar (inside cheek)
Cavernous sinus thrombosis	Infection of upper lip/cheek via facial vein → ophthalmic veins

1.6 CENTRAL NERVOUS SYSTEM

Cerebral Hemispheres

Lobes: Frontal (anterior to central sulcus), Parietal (behind central sulcus), Temporal (below lateral sulcus), Occipital (below parieto-occipital sulcus).

Key cortical areas: Broca's area (inferior frontal gyrus) = motor speech (expressive aphasia if damaged). Wernicke's area (superior temporal gyrus) = language comprehension (receptive aphasia). Primary motor cortex = precentral gyrus. Primary sensory cortex = postcentral gyrus.

Internal capsule: Contains motor and sensory projection fibres. Haemorrhage or thrombosis here → contralateral hemiplegia.

Basal ganglia: Supraspinal control of skeletal muscle movement. Loss of dopaminergic neurons in substantia nigra → Parkinson's disease.

Cerebral Blood Supply

Circle of Willis

Location: Around the optic chiasm. Formed by: anterior communicating artery connecting the 2 anterior cerebrals; posterior communicating arteries connecting internal carotids to posterior cerebrals.

Clinical significance: Anastomotic potential (variable). Berry aneurysms at junctions → subarachnoid haemorrhage. Most common site = anterior communicating artery.

Cerebral Arteries

Artery	Source	Territory	Occlusion Effect
Anterior cerebral (ACA)	Internal carotid	Medial cerebral surface; leg motor/sensory cortex	Contralateral leg weakness > arm
Middle cerebral (MCA)	Internal carotid	Lateral surface; motor/sensory (arm/face), Broca's, Wernicke's	Contralateral arm/face weakness; aphasia (dominant hemisphere)
Posterior cerebral (PCA)	Basilar artery	Occipital lobe (visual cortex), inferior temporal	Contralateral homonymous hemianopia with macular sparing

⚡ **EXAM TIP: MCA = most commonly occluded by embolism. Arm + face > leg weakness. Aphasia if dominant hemisphere. PCA occlusion = visual loss with macular sparing.**

Intracranial Haemorrhage

Type	Artery	Location	CT Appearance	Key Feature
Extradural	Middle meningeal artery	Between skull and dura	Biconvex/lenticular (lens-shaped)	Lucid interval; temporal bone fracture; does NOT cross suture lines
Subdural	Bridging veins	Between dura and arachnoid	Crescent-shaped	Crosses suture lines; elderly/alcoholics/anticoagulated; acute or chronic
Subarachnoid	Berry aneurysm (Circle of Willis)	Subarachnoid space	Blood in basal cisterns + sulci	Thunderclap headache; sentinel bleed; meningism
Intracerebral	Charcot-Bouchard microaneurysms	Within brain parenchyma	Hyperdense area in brain	Hypertension; basal ganglia most common site

💡 **HIGH YIELD: Extradural = biconvex, middle meningeal, lucid interval, does NOT cross sutures. Subdural = crescent, bridging veins, crosses sutures. SAH = thunderclap headache, berry aneurysm.**

Meninges & Ventricular System

Meninges: Dura mater (tough, outer) → Arachnoid mater (middle, avascular) → Pia mater (delicate, adherent to brain surface). CSF in subarachnoid space (between arachnoid and pia).

Ventricles: Lateral ventricles (C-shaped, in hemispheres) → interventricular foramen (of Monro) → 3rd ventricle → cerebral aqueduct → 4th ventricle → exits via foramina of Luschka and Magendie.

CSF production: Choroid plexuses (mainly lateral ventricles). Absorbed by arachnoid granulations into superior sagittal sinus.

Lumbar puncture: L3/4 or L4/5 interspace (below conus medullaris at L1/2). Layers pierced: skin → supraspinous ligament → interspinous ligament → ligamentum flavum ("give") → epidural space → dura → arachnoid → subarachnoid space.

Spinal Cord

Key tracts: Dorsal columns = proprioception + vibration + fine touch (cross in medulla). Lateral corticospinal = motor (crosses in medullary pyramids). Spinothalamic = pain + temperature (cross at/near entry level in cord).

Spinal Cord Syndromes

Syndrome	Lesion	Motor	Sensory	Key Feature
Brown-Séquard	Hemisection	IPSILATERAL motor loss (corticospinal)	IPSILATERAL proprioception loss + CONTRALATERAL pain/temp loss	Hemisection; knife wound
Central cord	Central cord damage	Upper limbs > lower limbs	Variable; cape-like distribution	Hyperextension injury in elderly with cervical spondylosis
Anterior cord	Anterior spinal artery occlusion	Complete motor loss below	Pain + temperature lost; proprioception PRESERVED	Aortic surgery complication
Cauda equina	Below L1/2 (nerve roots)	LMN bilateral leg weakness	Saddle anaesthesia; urinary retention	SURGICAL EMERGENCY; LMN signs

> 💡 **HIGH YIELD: Brown-Séquard: ipsilateral motor + proprioception, contralateral pain/temp. Central cord: arms > legs (hyperextension in elderly). Anterior cord: motor + pain/temp lost, proprioception preserved. Cauda equina: saddle anaesthesia + LMN = surgical emergency.**

Rapid Recall — CNS

Topic / Prompt	Key Fact / Answer
Broca's area	Inferior frontal gyrus; expressive (motor) aphasia
Wernicke's area	Superior temporal gyrus; receptive (sensory) aphasia
Internal capsule haemorrhage	Contralateral hemiplegia
Circle of Willis aneurysm	Most common at anterior communicating artery → SAH
MCA occlusion	Contralateral face + arm weakness; aphasia (dominant)
PCA occlusion	Contralateral homonymous hemianopia with macular sparing
Extradural haemorrhage	Middle meningeal artery; biconvex; lucid interval; does NOT cross sutures
Subdural haemorrhage	Bridging veins; crescent-shaped; crosses sutures; elderly
SAH	Thunderclap headache; berry aneurysm (Circle of Willis)
CSF production	Choroid plexuses (lateral ventricles mainly)
Lumbar puncture level	L3/4 or L4/5 (below conus medullaris at L1/2)
Dorsal columns	Proprioception + vibration; cross in medulla
Spinothalamic tract	Pain + temperature; cross at cord level
Brown-Séquard	Ipsilateral motor + proprioception; contralateral pain/temp
Central cord syndrome	Arms > legs; hyperextension in elderly
Anterior cord syndrome	Motor + pain/temp lost; proprioception preserved
Cauda equina syndrome	Saddle anaesthesia + urinary retention + LMN; surgical emergency
Papilloedema mechanism	Optic nerve has subarachnoid space → raised ICP transmitted
RAPD	Abnormal pupil dilates when light swung to it (CN II lesion)
Substantia nigra	Dopaminergic neurons; loss → Parkinson's disease

CHAPTER 2
PHYSIOLOGY

~25% of exam | ~45 questions | 6 sub-sections

2.1 BASIC CELLULAR PHYSIOLOGY

Homeostasis & Feedback

Negative feedback: STABLE and corrective. The response opposes the stimulus. Controls most physiological systems (e.g. thermoregulation, blood glucose, BP).

Positive feedback: UNSTABLE and self-amplifying. Response enhances the stimulus until an external event stops it. Examples: blood clotting cascade, oxytocin in labour, action potential upstroke (Na+ influx).

⚡ **EXAM TIP: Positive feedback is UNSTABLE. Negative feedback is STABLE. Positive feedback examples (clotting, labour, action potential) are commonly tested.**

Osmosis, Tonicity & Osmolality

Osmosis: Net movement of water across a semi-permeable membrane from LOW solute to HIGH solute concentration.

Tonicity: Isotonic = no net water movement. Hypotonic = water INTO cell (swells). Hypertonic = water OUT of cell (shrinks).

Osmolality: Normal plasma = 285–295 mOsm/kg. Calculated = $2(Na^+)$ + urea + glucose.

Osmolar gap: Measured – calculated. Normal <10. Raised = unmeasured osmoles (methanol, ethylene glycol, ethanol).

💡 **HIGH YIELD: Raised osmolar gap + metabolic acidosis = toxic alcohol poisoning (methanol, ethylene glycol). 0.9% NaCl is isotonic. 5% dextrose becomes hypotonic once glucose metabolised.**

Body Fluid Compartments & Na-K ATPase

TBW: ~60% body weight in males (~50% females). ICF = 2/3 of TBW. ECF = 1/3 (plasma + interstitial).

Na-K ATPase: 3 Na^+ OUT, 2 K^+ IN per ATP. Electrogenic (net +1 charge out). Maintains concentration gradients for all cellular transport. Uses ~30% of basal metabolic energy. Inhibited by digoxin.

Digoxin mechanism: Inhibits Na-K ATPase → ↑ intracellular Na^+ → Na/Ca exchanger less effective → ↑ intracellular Ca^{2+} → increased contractility.

💡 **HIGH YIELD: Na-K ATPase: 3 Na^+ out, 2 K^+ in. Drives virtually all secondary active transport. Digoxin inhibits it → positive inotropy. Tested repeatedly.**

Cell Membrane & Transport

Phospholipid bilayer: Fluid mosaic model. Integral proteins (span membrane) and peripheral proteins. Cholesterol regulates fluidity.

GPCRs: 7-transmembrane domain receptors. Largest receptor family. Ligand → G-protein (GDP→GTP) → second messenger → cellular response.

Ion channels: Voltage-gated Na^+ channels = rapid depolarisation. Blocked by local anaesthetics (lidocaine). Ca^{2+} channels = target of CCBs (verapamil, nifedipine).

Vessel Fluid Dynamics

Poiseuille's relationship: Flow $\propto r^4$. Radius is the most powerful determinant. Halving radius reduces flow by 16×. Explains dramatic effects of bronchospasm and vasoconstriction.

Laplace's law: Wall tension = Pressure × Radius / Wall thickness. Aneurysms enlarge progressively (increased radius → increased tension). Surfactant reduces alveolar surface tension to prevent collapse.

⚡ **EXAM TIP: Flow $\propto r^4$ (Poiseuille). Small airway narrowing → massive resistance increase. This is why bronchospasm is so dangerous. Laplace explains aneurysm rupture.**

Oncotic Pressure & Starling Forces

Oncotic pressure: ~25 mmHg. Albumin = ~80% of plasma oncotic pressure. Low albumin → oedema.

Starling equation: Net filtration = $Kf[(Pc–Pi) – (\pi c–\pi i)]$. Arterial end: filtration out. Venous end: reabsorption. ~10% drained by lymphatics.

Oedema causes: ↑ hydrostatic pressure (heart failure), ↓ oncotic pressure (nephrotic, liver failure), ↑ permeability (sepsis, burns), lymphatic obstruction.

Blood & Haemostasis

RBCs: 120-day lifespan. EPO from kidney (peritubular fibroblasts) in response to hypoxia. Spleen removes old RBCs.

WBCs: Neutrophilia = bacterial. Lymphocytosis = viral. Eosinophilia = parasites/allergy.

Haemostasis: 1. Vessel injury → 2. Platelet adhesion (via vWF to collagen) → 3. Activation (TXA2, ADP) → 4. Aggregation (fibrinogen bridges via GPIIb/IIIa) → 5. Coagulation cascade → fibrin clot.

> 💡 **HIGH YIELD: Platelet adhesion = vWF + GPIb. Aggregation = fibrinogen + GPIIb/IIIa. Aspirin blocks TXA2. Clopidogrel blocks ADP (P2Y12). Abciximab blocks GPIIb/IIIa. All reduce platelet function.**

Action Potential & Autonomic NS

Resting membrane potential: ~−70 mV. Maintained by Na-K ATPase and K^+ leak channels.

Action potential: All-or-nothing. Depolarisation: voltage-gated Na^+ channels open → rapid influx. Repolarisation: Na^+ channels inactivate + K^+ channels open. Absolute refractory period prevents backward propagation.

Saltatory conduction: In myelinated nerves, AP jumps between nodes of Ranvier → faster conduction (up to 120 m/s). Demyelination (MS, GBS) slows conduction.

Autonomic Nervous System

Feature	Sympathetic	Parasympathetic
Preganglionic NT	Acetylcholine (nicotinic)	Acetylcholine (nicotinic)
Postganglionic NT	Noradrenaline (adrenergic)	Acetylcholine (muscarinic)
Exception	Sweat glands: ACh (muscarinic)	None
Heart	Increases rate + force (β1)	Decreases rate (M2, vagus)
Bronchi	Bronchodilation (β2)	Bronchoconstriction (M3)
Pupils	Mydriasis (α1, dilator pupillae)	Miosis (M3, sphincter pupillae)
GI motility	Decreases	Increases
Bladder	Relaxes detrusor (β2/β3)	Contracts detrusor (M3)

> 💡 **HIGH YIELD: Sympathetic postganglionic = noradrenaline (except sweat glands = ACh). Parasympathetic = ACh at both synapses. β1 = heart. β2 = bronchi + uterus. α1 = vasoconstriction. This is the MOST tested physiology topic.**

> ⚡ **EXAM TIP: Atropine (muscarinic antagonist) → tachycardia, mydriasis, dry mouth, urinary retention, reduced gut motility. β-blockers: β1-selective (atenolol, bisoprolol) safer in asthma than non-selective (propranolol).**

Rapid Recall — Basic Cellular

Topic / Prompt	Key Fact / Answer
Na-K ATPase	3 Na^+ out, 2 K^+ in per ATP. Inhibited by digoxin
Positive feedback examples	Clotting cascade, labour (oxytocin), AP upstroke
Plasma osmolality	285–295 mOsm/kg. Calculated: 2(Na) + urea + glucose
Raised osmolar gap + acidosis	Toxic alcohols (methanol, ethylene glycol)
Albumin	~80% of oncotic pressure. Low = oedema
Flow ∝ r^4	Halving radius → 16× reduced flow
Laplace's law	T = P×r. Aneurysms enlarge progressively
EPO source	Kidney (peritubular fibroblasts)
Platelet adhesion	vWF + GPIb receptor
Platelet aggregation	Fibrinogen + GPIIb/IIIa
Sympathetic postganglionic NT	Noradrenaline (exception: sweat glands = ACh)

β1 receptor	↑ HR + contractility (heart)
β2 receptor	Bronchodilation + uterine relaxation
α1 receptor	Vasoconstriction + mydriasis
Muscarinic effects	Miosis, bradycardia, bronchoconstriction, ↑ GI motility
Saltatory conduction	AP jumps between nodes of Ranvier in myelinated nerves
Resting membrane potential	~−70 mV (K^+ leak channels + Na-K ATPase)

2.2 RESPIRATORY PHYSIOLOGY

Lung Volumes

FRC: ERV + RV. Volume at end of normal expiration. Elastic recoil of lung inward = chest wall spring outward. Provides O_2 reserve during apnoea.

Cannot be measured by spirometry: RV, FRC, TLC. Require body plethysmography or helium dilution.

Dead space: Anatomical ~150 mL. Alveolar ventilation = (TV – dead space) × RR. Rapid shallow breathing increases dead space proportion.

Obstructive: FEV1/FVC <0.70 (asthma, COPD). Restrictive: normal/high ratio, reduced volumes (fibrosis, kyphoscoliosis).

> 💡 **HIGH YIELD: FRC = ERV + RV. Cannot measure RV by spirometry. Obstructive = low FEV1/FVC. Restrictive = normal ratio, reduced volumes. Tested in every sitting.**

Surfactant & Compliance

Surfactant: Produced by Type II pneumocytes from ~24 weeks; mature by ~35 weeks. Mainly DPPC. Reduces surface tension → prevents atelectasis, increases compliance.

Deficiency: Neonatal RDS (premature). ARDS (adults). Antenatal corticosteroids accelerate production.

Compliance: High = easy expansion (emphysema). Low = resists expansion (fibrosis, ARDS, pulmonary oedema).

> ⚡ **EXAM TIP: Type II pneumocytes produce surfactant AND regenerate Type I cells. Surfactant deficiency = neonatal RDS. Antenatal steroids promote maturation. Static compliance reduced in restrictive disease.**

Gas Transport & O_2-Hb Dissociation Curve

Alveolar gas equation: $PAO_2 = PiO_2 – (PACO_2/R)$. Normal $PAO_2 \approx 100$ mmHg. $PiO_2 \approx 150$ mmHg. R = 0.8.

Henry's law: Dissolved gas ∝ partial pressure. Basis of hyperbaric O_2 therapy.

O_2-Hb curve: Sigmoid (cooperative binding). P50 = 26.6 mmHg. At PO_2 100: ~97% sat. At PO_2 40 (venous): ~75% sat.

Shifts of the O_2-Hb Dissociation Curve

RIGHT Shift (↓ affinity, ↑ O_2 unloading)	LEFT Shift (↑ affinity, ↓ O_2 unloading)
↑ CO_2 (Bohr effect)	↓ CO_2
↑ H^+ (acidosis)	↓ H^+ (alkalosis)
↑ 2,3-DPG	↓ 2,3-DPG
↑ Temperature	↓ Temperature
Exercise	Fetal haemoglobin (HbF)
Anaemia (compensatory)	Carbon monoxide (CO)
	Methaemoglobin

> 💡 **HIGH YIELD: RIGHT shift = "CADET face Right": CO_2, Acid, 2,3-DPG, Exercise, Temperature. Favours O_2 delivery to tissues. LEFT shift = tighter binding. HbF = left-shifted (higher affinity for placental O_2 transfer). This is the single most tested respiratory topic.**

> ⚡ **EXAM TIP: Bohr effect: ↑CO_2 shifts curve RIGHT → O_2 unloading in tissues. Haldane effect: deoxyHb carries MORE CO_2. In anaemia: PaO_2 and SaO_2 are NORMAL but O_2 CONTENT is reduced. Pulse oximetry shows normal SpO_2 despite severe anaemia.**

CO_2 Transport & Chloride Shift

Three forms: 1. Dissolved (~7%). 2. Bound to Hb as carbaminohaemoglobin (~23%). 3. As HCO_3^- (~70%, main form).

Chloride shift: In tissues: $CO_2 \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$ (carbonic anhydrase in RBCs). HCO_3^- exits RBC, Cl^- enters to maintain electroneutrality. Reverses in lungs.

Control of Respiration

Primary drive (health): CO_2 via central chemoreceptors. CO_2 crosses BBB → H^+ in CSF → stimulates ventilation.

Peripheral chemoreceptors: Carotid body (CN IX) + aortic body (CN X). Respond to ↓PaO_2 (<8 kPa), ↑$PaCO_2$, ↑H^+.

Hypoxic drive: In chronic CO_2 retention (severe COPD), central receptors desensitised. Patient relies on hypoxic drive. High-flow O_2 may abolish this → hypoventilation. Target SpO_2 88–92%.

> 💡 **HIGH YIELD: CO_2 is the primary respiratory drive (via central chemoreceptors responding to CSF H^+). In chronic COPD: hypoxic drive dominates. High-flow O_2 → CO_2 narcosis. Target 88–92%.**

J receptors: Stimulated by pulmonary oedema/PE → tachypnoea. Explains rapid breathing despite adequate PO_2.

V/Q Matching

Normal V/Q: ~0.8. Ideal = 1.0. In upright lung: perfusion increases more than ventilation from apex to base.

V/Q = 0 (shunt): Perfusion without ventilation (e.g. consolidation, ARDS). Blood bypasses gas exchange.

V/Q = ∞ (dead space): Ventilation without perfusion (e.g. PE). Wasted ventilation.

Key concept: V/Q mismatch causes hypoxaemia more readily than hypercapnia (body can blow off CO_2 but cannot load extra O_2 onto already-saturated Hb).

True shunt: REFRACTORY to supplemental O_2. If PaO_2 does not improve with 100% O_2 → significant shunt.

HPV: Hypoxic pulmonary vasoconstriction: alveolar hypoxia → local vasoconstriction (opposite to systemic). Diverts blood to better-ventilated areas. Chronic → pulmonary HTN → cor pulmonale.

> ⚡ **EXAM TIP: True shunt = refractory to O_2 (ARDS, R→L cardiac shunt). V/Q mismatch responds to O_2. HPV = unique pulmonary response (vasoconstriction to hypoxia). Chronic HPV → cor pulmonale.**

Rapid Recall — Respiratory

Topic / Prompt	Key Fact / Answer
FRC	ERV + RV. Cannot measure RV/FRC/TLC by spirometry
Obstructive pattern	FEV1/FVC <0.70
Restrictive pattern	Normal/high ratio, reduced volumes
Type II pneumocytes	Produce surfactant + regenerate Type I
Surfactant deficiency	Neonatal RDS (premature), ARDS (adults)
RIGHT shift (CADET)	CO_2, Acid, 2,3-DPG, Exercise, Temperature
LEFT shift	HbF, CO, alkalosis, hypothermia, metHb
Bohr effect	CO_2 affects O_2 binding (RIGHT shift in tissues)
Haldane effect	O_2 affects CO_2 binding (deoxyHb carries more CO_2)
Anaemia: PaO_2 + SaO_2	NORMAL. O_2 content REDUCED
Chloride shift	HCO_3^- out of RBC, Cl^- in (tissues). Reverses in lungs
Primary respiratory drive	CO_2 via central chemoreceptors (CSF H^+)
Hypoxic drive	Peripheral chemoreceptors. Dominates in chronic COPD
Target SpO_2 in COPD	88–92% (avoid abolishing hypoxic drive)
True shunt	Refractory to supplemental O_2
HPV	Pulmonary vasoconstriction to hypoxia (opposite to systemic)
Alveolar gas equation	$PAO_2 = PiO_2 – (PACO_2/R)$
Henry's law	Dissolved gas ∝ partial pressure
J receptors	Tachypnoea in pulmonary oedema/PE
CO_2 transport (main form)	HCO_3^- (~70%)

2.3 CARDIOVASCULAR PHYSIOLOGY

Haemodynamic Equations

MAP: = Diastolic + 1/3(Pulse Pressure). Example: 120/80 → MAP = 80 + 13 = ~93 mmHg. Weighted towards diastolic (diastole is 2/3 of cycle).

MAP = CO × SVR: The fundamental equation. MAP falls if CO drops (hypovolaemic, cardiogenic) or SVR drops (septic/distributive).

CO = HR × SV: Normal ~5 L/min. SV ~70 mL. SV depends on: Preload, Contractility, Afterload.

> 💡 **HIGH YIELD: MAP = CO × SVR. CO = HR × SV. SV = f(preload, contractility, afterload). This is the basis for understanding ALL types of shock. Tested in nearly every sitting.**

Cardiac Conduction

Pathway: SA node → atrial myocytes → AV node → Bundle of His → L+R bundle branches → Purkinje fibres → ventricular myocytes.

AV node delay: PR interval. Allows atrial contraction to complete before ventricular contraction (atrial kick = ~20–30% of filling). Lost in AF → reduced CO.

SA node rate: Intrinsic ~100 bpm. Vagal tone reduces to 60–100 bpm at rest.

Accessory pathways: Bundle of Kent (WPW) bypasses AV node → pre-excitation (short PR, delta wave).

> ⚡ **EXAM TIP: AV node = only normal electrical connection between atria and ventricles (annulus fibrosus insulates). Accessory pathway (WPW) = short PR + delta wave. AV delay is essential for atrial kick.**

Cardiac Action Potential

Ventricular Myocyte AP

Phase	Mechanism	Clinical Relevance
Phase 0: Rapid depolarisation	Fast Na^+ channel opening	Blocked by Class I antiarrhythmics
Phase 1: Partial repolarisation	Transient K^+ efflux	Brief
Phase 2: PLATEAU	L-type Ca^{2+} influx	KEY feature. Prolongs refractory period → prevents tetanus. Blocked by CCBs
Phase 3: Repolarisation	K^+ efflux (delayed rectifier)	Blocked by Class III (amiodarone) → prolongs QT
Phase 4: Resting	Stable at ~−90 mV	K^+ leak channels maintain

> 💡 **HIGH YIELD: Phase 2 PLATEAU (Ca^{2+} influx) is the key cardiac AP feature. Prevents tetanic contraction + allows ventricular filling. This is tested repeatedly. Without the plateau, the heart would tetanise like skeletal muscle.**

SA Node (Pacemaker) AP

No fast Na^+ channels: Upstroke is slow, Ca^{2+}-dependent.

Pacemaker potential (Phase 4): Slow spontaneous depolarisation via If (funny current) + T-type Ca^{2+} channels.

Chronotropes: Change slope of Phase 4. Steeper = faster rate. Flatter = slower.

Ivabradine: Selectively blocks If → slows HR without affecting contractility.

> ⚡ **EXAM TIP: SA node: NO fast Na^+ channels. Pacemaker potential = If (funny current). Ivabradine blocks If. Chronotropes change Phase 4 slope. Past paper: "What causes automaticity in SA node?" → funny current/If.**

Heart Sounds & Cardiac Cycle

S1: Mitral + tricuspid valve closure (start of systole/isovolumetric contraction).

S2: Aortic + pulmonary valve closure (start of diastole/isovolumetric relaxation).

S3: Rapid ventricular filling into a volume-overloaded ventricle. Pathological in adults (heart failure, MR).

S4: Atrial contraction into a stiff ventricle (LVH, aortic stenosis). Absent in AF (no atrial contraction).

Dicrotic notch: Brief pressure rise on aortic pressure trace when aortic valve closes. Represents elastic recoil of aorta.

Isovolumetric phases: ALL valves closed. Volume unchanged. Pressure rises (contraction) or falls (relaxation) rapidly.

> 💡 **HIGH YIELD: S3 = volume overload (HF). S4 = stiff ventricle (LVH, AS). S4 absent in AF. Dicrotic notch = aortic valve closure. Isovolumetric = all valves closed. These are tested in EVERY sitting.**

Frank–Starling Law & Cardiac Output

Starling law: Force of contraction ∝ initial muscle fibre length. ↑ preload → ↑ EDV → ↑ stretch → ↑ SV.

Starling curve: Ascending limb = normal. Plateau = optimal. Descending limb = heart failure (overstretching).

Inotropes: Shift curve UPWARD (higher SV for same preload). Heart failure: curve shifts DOWN and RIGHT.

Baroreceptor reflex: Carotid sinus (CN IX) + aortic arch (CN X). ↓BP → ↑ sympathetic → ↑HR, ↑contractility, vasoconstriction.

> ⚡ **EXAM TIP: Starling ensures L and R output are matched. If LV fails to match RV → pulmonary oedema. Baroreceptors: carotid sinus = CN IX, aortic arch = CN X.**

Regional Circulations

Coronary: Flow highest in DIASTOLE (myocardial compression in systole). O_2 extraction ~70–80% at rest → cannot extract more → must increase FLOW. Tachycardia shortens diastole → ischaemia risk.

Cerebral: Autoregulation MAP 60–160. CO_2 is key regulator: ↑$PaCO_2$ → vasodilation → ↑CBF. Hyperventilation (↓CO_2) → vasoconstriction → ↓ICP.

Shock types: Distributive (sepsis): low SVR, CO normal/high (warm). Hypovolaemic/cardiogenic: low CO, high SVR (cold, vasoconstricted).

> 💡 **HIGH YIELD: Coronary flow = mainly DIASTOLE. Tachycardia reduces coronary perfusion. Cerebral: CO_2 is key regulator. Hyperventilation → ↓ICP (temporary measure). These are past paper favourites.**

Rapid Recall — Cardiovascular

Topic / Prompt	Key Fact / Answer
MAP equation	Diastolic + 1/3(Pulse Pressure)
MAP = CO × SVR	Fundamental haemodynamic equation
CO = HR × SV	Normal CO ~5 L/min
SV determinants	Preload, Contractility, Afterload
SA node intrinsic rate	~100 bpm (vagal tone slows to 60–100)
AV node delay purpose	Atrial kick (~20–30% of ventricular filling)
Phase 2 plateau	Ca^{2+} influx. Prevents tetanus. KEY cardiac feature
Pacemaker potential (If)	Funny current. Blocked by ivabradine
S1	MV + TV closure (start of systole)
S2	AoV + PV closure (start of diastole)
S3	Rapid filling of dilated ventricle (HF, MR)
S4	Atrial contraction into stiff ventricle (LVH, AS). Absent in AF
Dicrotic notch	Aortic valve closure (elastic recoil)
Frank–Starling	Force ∝ fibre length. ↑ preload → ↑ SV
Starling curve: inotropes	Shift curve UPWARD
Baroreceptors	Carotid sinus = CN IX. Aortic arch = CN X
Coronary blood flow	Mainly in DIASTOLE. High O_2 extraction at rest
Cerebral blood flow regulator	CO_2 (↑CO_2 = vasodilation = ↑CBF)
Distributive shock	Low SVR, CO normal/high (warm)
Cardiogenic shock	Low CO, high SVR (cold, clamped)

2.4 GI PHYSIOLOGY

Gut Wall & Enteric Nervous System

Layers: Mucosa → Submucosa → Muscularis externa → Serosa/Adventitia.

Auerbach's plexus: Between muscle layers. Controls MOTILITY.

Meissner's plexus: In submucosa. Controls SECRETION.

Hirschsprung's: Absent ganglion cells → functional obstruction.

⚡ **EXAM TIP: Auerbach's = motility (between muscle layers). Meissner's = secretion (submucosa). Hirschsprung's = absent ganglia. All commonly tested.**

Stomach

Gastric Secretory Cells

Cell Type	Location	Product	Function
Parietal cells	Body/fundus	HCl + Intrinsic Factor	Acid digestion; IF for B12 absorption
Chief cells	Body/fundus	Pepsinogen	Converted to pepsin by acid; protein digestion
G cells	Antrum	Gastrin	Stimulates parietal cells; ↑ acid secretion
D cells	Antrum/duodenum	Somatostatin	Inhibits gastrin + acid secretion
ECL cells	Body/fundus	Histamine	Paracrine stimulation of parietal cells (H2)
Mucous neck cells	Throughout	Mucus + HCO_3^-	Mucosal barrier protection

💡 **HIGH YIELD: Parietal cells: HCl via H-K-ATPase (proton pump) + Intrinsic Factor (for B12). Three stimulants: ACh (M3, vagus), gastrin (CCK-B), histamine (H2). PPIs block H-K-ATPase = most potent acid suppression. This is the most tested GI topic.**

GI Hormones

Hormone	Source	Stimulus	Actions
Gastrin	G cells (antrum)	Protein, distension, vagal	Stimulates acid + pepsinogen; ↑ gastric motility
Secretin	S cells (duodenum)	ACID in duodenum	Stimulates pancreatic HCO_3^-; inhibits gastrin
CCK	I cells (duodenum/jejunum)	FAT + protein	Stimulates pancreatic enzymes + gallbladder contraction; relaxes sphincter of Oddi
GIP	K cells (duodenum/jejunum)	Glucose, fat	Incretin: augments insulin release; inhibits gastric acid
GLP-1	L cells (ileum/colon)	Glucose, fat	Incretin: augments insulin; delays gastric emptying; ↓ appetite
Motilin	M cells (duodenum/jejunum)	Fasting	Stimulates MMC (migrating motor complex); gastric emptying
Somatostatin	D cells (throughout)	Acid, fat	Inhibits most GI hormones + acid secretion

💡 **HIGH YIELD: Secretin = ACID → HCO_3^-. CCK = FAT/PROTEIN → enzymes + gallbladder. These two are the most frequently tested GI hormones. GIP + GLP-1 = incretins (augment insulin). Past paper: "Acid enters duodenum — which hormone?" → Secretin.**

Small Intestine: Absorption

SGLT1: Na^+/glucose cotransporter on apical membrane. Basis of oral rehydration therapy (glucose enhances Na^+ and water absorption).

Iron: Absorbed in duodenum. Fe^{3+} → Fe^{2+} (by DcytB, aided by vitamin C) → DMT1 → ferroportin → transferrin. Hepcidin regulates (degrades ferroportin).

Fat: Bile salts emulsify → lipase + colipase digest → micelles transport → chylomicrons → lacteals → lymph (bypass liver).

Fat-soluble vitamins: A, D, E, K. Absorbed with fat. Deficiency in biliary obstruction, coeliac, pancreatic insufficiency.

Terminal ileum: Absorbs bile salts (enterohepatic circulation) + vitamin B12 (with intrinsic factor).

> ⚡ **EXAM TIP: Terminal ileum = B12 + bile salt absorption. Resection/disease (Crohn's) → B12 deficiency + bile salt malabsorption → steatorrhoea. Iron = duodenum. Calcium = duodenum/proximal jejunum.**

Liver & Gallbladder

Portal triad: Hepatic artery + portal vein + bile ductule (at lobule corners).

Liver functions: Metabolism (glucose, protein, lipid), detoxification, bile production, clotting factor synthesis, albumin, storage (glycogen, iron, vitamins).

Bile: Contains bile salts, phospholipids, cholesterol, bilirubin. Concentrated in gallbladder. CCK contracts gallbladder + relaxes sphincter of Oddi.

Bilirubin: Unconjugated (fat-soluble, albumin-bound) → conjugated in liver (water-soluble, glucuronic acid) → excreted in bile → urobilinogen (gut bacteria) → stercobilin (faeces) + urobilin (urine).

Rapid Recall — GI

Topic / Prompt	Key Fact / Answer
Parietal cells produce	HCl (H-K-ATPase) + Intrinsic Factor
Intrinsic factor function	Essential for B12 absorption in terminal ileum
3 stimulants of acid secretion	ACh (M3), gastrin (CCK-B), histamine (H2)
PPIs mechanism	Irreversibly block H-K-ATPase (proton pump)
Secretin stimulus	Acid in duodenum
Secretin action	Pancreatic HCO_3^- secretion
CCK stimulus	Fat + protein in duodenum
CCK action	Pancreatic enzymes + gallbladder contraction
Incretins	GIP + GLP-1: augment insulin release
Terminal ileum absorbs	B12 + bile salts
SGLT1	Na^+/glucose cotransporter. Basis of ORS
Iron absorption site	Duodenum. Via DMT1. Regulated by hepcidin
Hepcidin	Degrades ferroportin → reduces iron absorption
Fat-soluble vitamins	A, D, E, K. Deficient in fat malabsorption
Fat absorption route	Chylomicrons → lacteals → lymph (bypass liver)
Auerbach's plexus	Motility (between muscle layers)
Meissner's plexus	Secretion (submucosa)
NSAIDs → gastropathy	COX inhibition → ↓ prostaglandins → ↓ mucosal protection

2.5 RENAL PHYSIOLOGY

Nephron & GFR

Nephron: Glomerulus → PCT → Loop of Henle (descending thin, ascending thin, TAL) → DCT → Collecting duct.

GFR: Normal ~125 mL/min (~180 L/day). Measured by creatinine clearance (slight overestimate). Gold standard = inulin clearance.

Autoregulation: MAP 80–180 mmHg. Below = GFR falls. Myogenic response + tubuloglomerular feedback (macula densa).

Triple whammy: ACE-i (dilates efferent) + NSAID (constricts afferent) + diuretic (volume depletion) = AKI.

⚡ **EXAM TIP: ACE-i/ARBs dilate efferent arteriole → ↓GFR. NSAIDs constrict afferent → ↓GFR. "Triple whammy" (ACE-i + NSAID + diuretic) = common exam AKI scenario.**

Tubular Function & Diuretic Sites

Tubular Segments

Segment	Reabsorbs	Key Transporter	Diuretic	Side Effects
PCT (~65%)	Na^+, K^+, Cl^-, glucose, amino acids, HCO_3^-, H_2O, PO_4	Na-H exchanger (NHE3), SGLT2, Na-K ATPase (basolateral)	Acetazolamide (CA inhibitor)	Metabolic acidosis, alkaline diuresis
TAL (Loop of Henle)	Na^+, K^+, $2Cl^-$ (no water)	NKCC2 cotransporter	Loop diuretics (furosemide)	HypoK^+, hypoCa^{2+}, hypoMg^{2+}, alkalosis
DCT	Na^+, Cl^-	NCC cotransporter	Thiazides (bendroflumethiazide)	HypoK^+, hypoNa^+, HYPERcalcaemia
Collecting duct	Na^+ (via ENaC), H_2O (via AQP2)	ENaC (Na^+ channel), AQP2	Spironolactone, amiloride	HYPERkalaemia

💡 **HIGH YIELD: NKCC2 = TAL = furosemide. NCC = DCT = thiazides. ENaC = collecting duct = amiloride/spironolactone. Diuretic site identification is tested in EVERY sitting. Loop diuretics cause hypoCa; thiazides cause hyperCa (opposite effects on calcium).**

⚡ **EXAM TIP: Thiazides cause HYPERcalcaemia (enhance DCT Ca^{2+} reabsorption) — OPPOSITE to loop diuretics which waste calcium. Thiazides used for calcium stone prevention. Past paper: "Diuretic that raises calcium?" → Thiazide.**

Water Balance: ADH & SIADH vs DI

ADH (vasopressin): From posterior pituitary. Stimulus: ↑ osmolality (detected by hypothalamic osmoreceptors) or ↓ blood volume/pressure. V2 receptors in collecting duct → AQP2 insertion → water reabsorption.

Desmopressin (DDAVP): Synthetic V2-selective analogue. Used for cranial DI, nocturnal enuresis, von Willebrand disease.

SIADH vs Diabetes Insipidus

Feature	SIADH	Cranial DI	Nephrogenic DI
Serum Na^+	LOW (dilutional)	HIGH	HIGH
Serum osmolality	LOW (<275)	HIGH (>295)	HIGH (>295)
Urine osmolality	Inappropriately HIGH (>100)	LOW (<300, dilute)	LOW (<300, dilute)
Urine volume	LOW (concentrated)	HIGH (polyuria)	HIGH (polyuria)
ADH level	Inappropriately HIGH	LOW	Normal/HIGH (but kidney unresponsive)
Cause	Lung Ca, CNS disease, drugs	Head injury, surgery, tumour	Lithium, hypercalcaemia, CKD
Response to DDAVP	N/A	Urine concentrates (↑ osmolality)	No response

Treatment	Fluid restriction, demeclocycline, tolvaptan	Desmopressin (DDAVP)	Treat cause; thiazides (paradoxically)

HIGH YIELD: SIADH: hypoNa^+ + low serum osmolality + concentrated urine + euvolaemic. Cranial DI: responds to DDAVP. Nephrogenic DI: does NOT respond (lithium, hypercalcaemia). Correct Na^+ slowly (<10 mmol/24h) to avoid osmotic demyelination. This is tested in EVERY sitting.

Acid–Base Balance

Henderson–Hasselbalch: pH = pKa + log([HCO_3^-] / [0.03 × $PaCO_2$]). pH determined by HCO_3^-:CO_2 ratio (~20:1 = pH 7.4).

Anion gap: = Na^+ – (Cl^- + HCO_3^-). Normal 8–12. Raised = unmeasured anions.

Raised AG acidosis: KULT: Ketones, Uraemia, Lactic acid, Toxins. Or MUDPILES.

Disturbance	Primary Change	Compensation	Example
Metabolic acidosis	↓ HCO_3^-	↓ CO_2 (hyperventilation, fast)	DKA, lactic acidosis, renal failure
Metabolic alkalosis	↑ HCO_3^-	↑ CO_2 (hypoventilation, fast)	Vomiting, diuretics
Respiratory acidosis	↑ CO_2	↑ HCO_3^- (renal, slow: days)	COPD, hypoventilation
Respiratory alkalosis	↓ CO_2	↓ HCO_3^- (renal, slow: days)	Hyperventilation, anxiety, PE

EXAM TIP: Compensation NEVER fully corrects pH. If pH is normal with abnormal CO_2 + HCO_3^- = mixed disorder. Respiratory compensation = fast (minutes). Renal compensation = slow (days). HypoK^+ causes metabolic alkalosis (and vice versa).

Potassium Balance

Normal: 3.5–5.0 mmol/L. 98% intracellular. Tightly regulated.

HyperK^+ ECG (in order): Tall peaked T waves → P wave loss → wide QRS → sine wave → VF/asystole.

HyperK^+ treatment: 1. IV calcium gluconate (cardioprotection FIRST). 2. Insulin + glucose (shift K^+ into cells). 3. Salbutamol nebuliser. 4. Calcium resonium / Na zirconium cyclosilicate. 5. Dialysis.

HIGH YIELD: HyperK^+ ECG: peaked T → lost P → wide QRS → sine wave → arrest. Treatment: calcium gluconate FIRST (cardioprotection), then insulin+glucose to shift K^+. Insulin drives K^+ INTO cells.

Rapid Recall — Renal

Topic / Prompt	Key Fact / Answer
Normal GFR	~125 mL/min (~180 L/day)
PCT reabsorbs	~65% of everything (bulk reabsorption)
NKCC2	TAL. Blocked by loop diuretics (furosemide)
NCC	DCT. Blocked by thiazides
ENaC	Collecting duct. Blocked by amiloride
Aldosterone target	ENaC in collecting duct (↑Na^+ reabsorption, ↑K^+ secretion)
Spironolactone	Aldosterone antagonist. K^+-sparing. Risk: hyperK^+
Loop diuretics: Ca^{2+}	WASTE calcium (hypocalcaemia)
Thiazides: Ca^{2+}	RETAIN calcium (hypercalcaemia). Used for Ca stones
ADH receptor	V2 in collecting duct → AQP2 insertion
SIADH	HypoNa^+ + low serum osm + concentrated urine + euvolaemic
Cranial DI	Responds to DDAVP (low ADH)
Nephrogenic DI	Does NOT respond to DDAVP (lithium, hypercalcaemia)
Correct Na^+ slowly	<10 mmol/L per 24h (osmotic demyelination risk)
Anion gap formula	Na^+ – (Cl^- + HCO_3^-). Normal 8–12
Raised AG acidosis (KULT)	Ketones, Uraemia, Lactic acid, Toxins
HyperK^+ ECG	Peaked T → lost P → wide QRS → sine wave

HyperK^+ Rx first	IV calcium gluconate (cardioprotection)
HypoK^+ causes	Metabolic alkalosis (H^+/K^+ exchange)
Triple whammy	ACE-i + NSAID + diuretic → AKI

2.6 ENDOCRINE PHYSIOLOGY

Pituitary & Hypothalamus

Anterior pituitary: ACTH, TSH, LH, FSH, GH, Prolactin. Controlled by hypothalamic releasing/inhibiting hormones via portal system.

Posterior pituitary: ADH (vasopressin) + Oxytocin. Synthesised in hypothalamus, stored and released from posterior pituitary.

Dopamine inhibits prolactin: Dopamine antagonists (metoclopramide, antipsychotics) → hyperprolactinaemia → galactorrhoea, amenorrhoea.

> ⚡ **EXAM TIP: Dopamine INHIBITS prolactin. Dopamine antagonists → ↑ prolactin. Pituitary stalk transection also raises prolactin (loss of dopamine inhibition). Past paper: "Metoclopramide side effect?" → Galactorrhoea.**

Adrenal Function

Adrenal Cortex

Zones: Glomerulosa = aldosterone (mineralocorticoid). Fasciculata = cortisol (glucocorticoid). Reticularis = androgens (DHEA).

Mnemonic: "GFR" = Glomerulosa, Fasciculata, Reticularis. "Salt, Sugar, Sex" = mineralocorticoid, glucocorticoid, androgen.

Cortisol regulation: CRH → ACTH → Cortisol. Negative feedback. Diurnal rhythm: peak 6–8 AM, nadir midnight.

Cushing's syndrome: Glucocorticoid excess. Commonest cause = exogenous steroids. Central obesity, striae, proximal myopathy, hyperglycaemia, osteoporosis.

Addisonian crisis: Acute adrenal insufficiency. Shock, hypotension, hypoglycaemia, hyperK$^+$, hypoNa$^+$. Treatment: IV hydrocortisone 100 mg STAT + fluids. Give steroids BEFORE blood results.

> 💡 **HIGH YIELD: Addisonian crisis: hypotension + hypoNa$^+$ + hyperK$^+$ + hypoglycaemia. Treat with IV hydrocortisone immediately. Do NOT wait for results. Primary Addison's: ↑ACTH (drives pigmentation). Secondary: ↓ACTH (no pigmentation).**

Adrenal Medulla

Catecholamines: Adrenaline (~80%) + noradrenaline (~20%). Degraded by MAO + COMT → VMA (urinary metabolite).

Phaeochromocytoma: Catecholamine-secreting tumour. Triad: headache, sweating, palpitations + hypertension. Diagnose: plasma/urine metanephrines.

> ⚡ **EXAM TIP: Phaeochromocytoma: alpha-blocker FIRST (phenoxybenzamine), then beta-blocker. Beta-blocker alone → unopposed alpha → hypertensive crisis. Rule of 10s: 10% bilateral, malignant, extra-adrenal, familial.**

Thyroid

T4 = main product (~90%). T3 = most active (~10% secreted, rest from peripheral T4→T3 conversion). Only FREE hormone is active.

Pregnancy: ↑TBG → ↑total T4, but FREE T4 is normal.

Hypothyroidism: ↑TSH, ↓FT4. Fatigue, weight gain, cold intolerance, constipation, bradycardia, dry skin.

Hyperthyroidism: ↓TSH, ↑FT4/FT3. Weight loss, heat intolerance, tremor, tachycardia/AF, diarrhoea, anxiety.

Thyroid storm Rx: 1. Beta-blocker (propranolol — also inhibits T4→T3). 2. Thionamide (PTU/carbimazole). 3. Lugol's iodine (AFTER thionamide). 4. Hydrocortisone (prevents adrenal crisis + inhibits T4→T3). 5. Supportive.

> 💡 **HIGH YIELD: Thyroid storm: propranolol FIRST, then thionamide, then Lugol's iodine (after thionamide). Propranolol also inhibits T4→T3 conversion. Thyroid is the most commonly tested endocrine topic in past papers.**

Insulin, Glucagon & Diabetes

Insulin: Only hormone that LOWERS glucose. ↑GLUT4 insertion (muscle, adipose), ↑glycogen synthesis, ↑lipogenesis, ↓gluconeogenesis. Also drives K^+ INTO cells.

Insulin receptor: Tyrosine kinase. Brain (GLUT1) and liver (GLUT2) = insulin-INDEPENDENT uptake.

C-peptide: Released equimolarly with insulin. High = endogenous (insulinoma). Low = exogenous insulin.

DKA: Type 1 typically. Triad: hyperglycaemia + ketosis + acidosis. Rx: IV fluids FIRST, then insulin + K^+ replacement (insulin shifts K^+ into cells).

HHS: Type 2. Severe hyperglycaemia (>30 mmol/L) + dehydration + hyperosmolality. Minimal ketosis.

⚡ **EXAM TIP: DKA treatment: fluids FIRST, then insulin. Monitor K^+ closely (insulin drives K^+ into cells → hypoK^+ risk). Renal threshold for glucose ~10–11 mmol/L → glycosuria above this. SGLT2 inhibitors deliberately lower threshold.**

Calcium & PTH

PTH: From parathyroid chief cells. Stimulus = ↓ ionised Ca^{2+}. Effects: ↑ Ca^{2+} (bone resorption + renal reabsorption + gut via vitamin D), ↓ PO_4 (renal excretion).

Vitamin D activation: Skin (UV → D3) → Liver (25-hydroxylation) → Kidney (1α-hydroxylation → active calcitriol). PTH stimulates renal 1α-hydroxylase.

Primary hyperparathyroidism: ↑Ca^{2+}, ↓PO_4, ↑PTH, ↑ALP.

Corrected calcium: = Measured Ca + 0.02 × (40 – albumin g/L). Hypoalbuminaemia falsely lowers total Ca.

Chvostek's sign: Tap facial nerve → twitch. Trousseau's sign: BP cuff inflated → carpopedal spasm. Both = hypocalcaemia.

💡 **HIGH YIELD: PTH: ↑Ca^{2+}, ↓PO_4. Vitamin D activation: skin → liver (25-OH) → kidney (1,25-OH, active). PTH stimulates final step. Hyperventilation → alkalosis → ↑ Ca binding to albumin → ↓ ionised Ca^{2+} → tetany.**

Rapid Recall — Endocrine

Topic / Prompt	Key Fact / Answer
Dopamine's effect on prolactin	Inhibits. Antagonists → hyperprolactinaemia
Adrenal cortex zones (GFR)	Glomerulosa (aldosterone), Fasciculata (cortisol), Reticularis (androgens)
Addisonian crisis	HypoNa^+ + hyperK^+ + hypoglycaemia + shock. IV hydrocortisone STAT
Primary Addison's ACTH	HIGH (→ pigmentation)
Secondary adrenal insufficiency ACTH	LOW (no pigmentation)
Phaeochromocytoma Rx	Alpha-blocker FIRST, then beta-blocker
Thyroid: T4 vs T3	T4 = main product. T3 = most active (peripheral conversion)
Thyroid storm Rx order	Propranolol → thionamide → Lugol's iodine → hydrocortisone
Insulin receptor type	Tyrosine kinase
Insulin-independent glucose uptake	Brain (GLUT1), liver (GLUT2)
C-peptide: high	Endogenous insulin (insulinoma)
C-peptide: low	Exogenous insulin administration
DKA treatment order	IV fluids FIRST, then insulin + K^+ replacement
HHS vs DKA	HHS: minimal ketosis, more dehydrated, higher glucose (>30)
PTH effect	Raises Ca^{2+}, lowers PO_4
Vitamin D activation	Skin → liver (25-OH) → kidney (1,25-OH active)
1α-hydroxylase stimulated by	PTH + hypophosphataemia
Corrected calcium formula	Measured Ca + 0.02 × (40 – albumin)
Chvostek's sign	Tap facial nerve → facial twitch (hypoCa)
Trousseau's sign	BP cuff → carpopedal spasm (hypoCa)

Chapter 3

PHARMACOLOGY

~25% of exam | ~45 questions

MRCEM Primary Exam Night Revision Notes

Chapter Contents

3.1 GI Pharmacology

Proton-Pump Inhibitors (Omeprazole)

- **MOA:** Irreversibly inhibit H^+/K^+ ATPase (proton pump) on parietal cell apical surface
- Prodrugs activated in the acidic parietal cell secretory canaliculus
- Block the final common pathway of acid secretion regardless of stimulus
- Maximal effect takes 2–3 days; duration up to 72 hours (irreversible binding)
- **Dosing:** PO: 20–40 mg OD; IV: 40 mg (upper GI haemorrhage)
- **Cautions:** Mask gastric malignancy; long-term risks: hypomagnesaemia, B12 deficiency, fractures, C. difficile, iron deficiency
- Omeprazole inhibits CYP2C19 → may reduce clopidogrel activation

⚡ **EXAM TIP:** PPIs are prodrugs activated in acidic canaliculus. They irreversibly inhibit the proton pump (final common pathway). Superior to H2RAs for NSAID gastroprotection. Omeprazole inhibits CYP2C19 – avoid with clopidogrel (use lansoprazole).

Gastric Acid Secretion – Pharmacological Targets

Stimulus	Receptor	Drug Class	Example
Histamine	H2 receptor	H2RA	Famotidine
Acetylcholine	M3 muscarinic	Antimuscarinic	Pirenzepine
Gastrin	CCK-2	No specific drug	—
Final pathway	H^+/K^+ ATPase	PPI	Omeprazole
PGE2	EP3 (inhibitory)	PGE1 analogue	Misoprostol

Antacids & Antispasmodics

- Aluminium hydroxide = constipating; Magnesium carbonate = laxative (combination balances effects)
- Reduce absorption of tetracyclines, fluoroquinolones, iron, bisphosphonates
- Hyoscine butylbromide: quaternary ammonium → poorly absorbed orally; antimuscarinic SEs (dry mouth, blurred vision, tachycardia, urinary retention, constipation)

NSAID-Associated Ulcers

- Co-prescribe PPI if NSAID essential; stop NSAID if possible
- Misoprostol (PGE1 analogue): alternative gastroprotection – contraindicated in pregnancy (abortifacient)

💡 **HIGH YIELD:** NSAID ulcers may be painless in the elderly. GI bleeding can be first presentation. NSAIDs inhibit COX-1 → reduced PGE2 → loss of mucosal protection. Asked repeatedly in past papers.

Acute Diarrhoea & IBD

- Primary management = fluid and electrolyte replacement
- Antimotility drugs: avoid in children, bloody diarrhoea, C. difficile (risk of toxic megacolon)
- IBD acute flares: aminosalicylates (topical/oral) + steroids (topical/oral/IV by severity)
- Laxatives: very limited ED role; stimulant laxatives risk hypokalaemia

Rapid Recall – GI Pharmacology

Topic / Prompt	Key Fact / Answer

PPI MOA	Irreversible H^+/K^+ ATPase inhibition; prodrug activated in acidic canaliculus
Omeprazole doses	PO: 20–40 mg OD; IV: 40 mg
$Al(OH)_3$ vs $MgCO_3$	Al = constipation; Mg = diarrhoea
Antacid interactions	Reduce absorption of tetracyclines, quinolones, iron, bisphosphonates
Hyoscine butylbromide	Quaternary ammonium → poor oral absorption
Misoprostol	PGE1 analogue; CI in pregnancy (abortifacient)
Acute diarrhoea	Fluids first; avoid antimotility in children/bloody diarrhoea/C. diff
Long-term PPI risks	HypoMg, B12 deficiency, fractures, C. difficile, Fe deficiency

3.2 Cardiovascular Pharmacology

Digoxin

- **MOA:** Inhibits Na^+/K^+-ATPase → ↑ intracellular Ca^{2+} → positive inotropy; ↑ vagal tone → ↓ AV conduction
- Narrow therapeutic index (0.5–2.0 ng/mL); T½ ~36h; renal excretion; measure level ≥6h post-dose
- Toxicity precipitated by HYPOKALAEMIA (K^+ competes for binding site), hypercalcaemia, hypomagnesaemia
- Toxicity features: any arrhythmia, yellow/green visual halos, nausea; Rx: DigiFab for life-threatening

⚡ **EXAM TIP:** Digoxin toxicity is precipitated by hypokalaemia – always check K^+. Loop/thiazide diuretics cause hypoK → potentiate toxicity. Amiodarone and verapamil increase digoxin levels. Asked in multiple sittings.

Diuretics

Class	Site	Mechanism	Key SEs
Loop (furosemide)	TAL	Blocks NKCC2	HypoK, HypoCa, HypoMg, ototoxicity
Thiazide	DCT	Blocks NCC	HypoK, HypoNa, HYPERCa, HyperGLUC
K^+-sparing	Collecting duct	Aldosterone antagonist / ENaC block	HyperK
Osmotic (mannitol)	PT + loop	Osmotic water retention	Fluid overload (initial)

💡 **HIGH YIELD:** Loops LOSE calcium (hypocalcaemia – used to treat acute hypercalcaemia). Thiazides cause HYPERcalcaemia. Both cause hypoK, hypoNa, hypoMg. Mannitol for raised ICP: IV bolus draws water from brain. CI if renal failure.

Anti-Arrhythmics

- **Adenosine:** Adenosine: 6–12–12 mg rapid IV for SVT; CI in asthma (use verapamil); dipyridamole potentiates, theophylline antagonises
- **Amiodarone:** Amiodarone: broad-spectrum; VF: 300 mg after 3rd shock; T½ 40–100 days; toxicity: thyroid, lung fibrosis, liver, cornea, skin (photosensitivity)
- **Flecainide:** Flecainide: Class IC; AF cardioversion; NEVER in structural/ischaemic heart disease (CAST trial)

⚡ **EXAM TIP:** Adenosine CI in asthma (use verapamil). Amiodarone in cardiac arrest: 300 mg after 3rd shock. Potentiates warfarin (reduce dose by ½). Flecainide in structurally normal hearts only.

Beta-Blockers

Drug	Selectivity	Key Features
Propranolol	Non-selective (β1+β2)	Lipophilic (CNS SEs); CI in asthma; thyrotoxicosis, migraine, tremor, varices
Esmolol	Cardioselective (β1)	Ultra-short T½ ~9 min; IV only; esterase metabolism; acute SVT/aortic dissection
Labetalol	α+β blocker	Safe in PREGNANCY; hypertensive emergency; pre-eclampsia
Sotalol	Non-selective + Class III	QT prolongation → Torsades risk; renally cleared

ACE Inhibitors (Captopril)

- **MOA:** Block ACE → ↓ angiotensin II + ↓ bradykinin breakdown
- SEs: dry cough (10–15%, bradykinin – switch to ARB), hyperkalaemia, first-dose hypotension, angioedema
- CI: pregnancy (teratogenic), bilateral renal artery stenosis, hyperkalaemia
- **Clinical:** "Triple whammy": ACEi + NSAID + diuretic → AKI

Nitrates (GTN)

- **MOA:** Converted to NO → ↑ cGMP → venodilation (↓ preload); arterial dilation at higher doses
- Absolute CI: sildenafil (PDE5 inhibitors) – both increase cGMP → profound hypotension

⚡ **EXAM TIP:** GTN + sildenafil = ABSOLUTE CI. Wait ≥24h after sildenafil, ≥48h after tadalafil. Ask about PDE5 use BEFORE giving GTN in chest pain. Asked repeatedly.

Calcium-Channel Blockers

- **Rate-limiting:** Verapamil: rate-limiting; SVT if asthma (alternative to adenosine); NEVER with β-blockers; CI in HF, WPW+AF
- **Dihydropyridine:** Nifedipine: vasospastic angina, Raynaud's; avoid short-acting in ACS (reflex tachycardia)
- Nimodipine: cerebral vasospasm post-SAH; 60 mg 4-hourly for 21 days

Adrenaline

- Cardiac arrest: 1 mg IV (1:10,000) every 3–5 min; shockable rhythms: after 3rd shock
- Anaphylaxis: 0.5 mg IM (1:1,000) anterolateral thigh; repeat every 5 min

⚡ **EXAM TIP:** Adrenaline doses: Cardiac arrest = 1 mg IV (1:10,000). Anaphylaxis = 0.5 mg IM (1:1,000). NEVER give 1:1,000 IV in non-arrest. IM route for anaphylaxis (not SC). Anterolateral thigh.

Anticoagulants

- UFH: APTT-monitored; fully reversed by protamine. LMWH: no routine monitoring; partially reversed by protamine
- HIT: day 5–10; paradoxically PROTHROMBOTIC; stop all heparin; use argatroban/fondaparinux
- Warfarin: Vit K antagonist (II, VII, IX, X); INR-monitored; reversal: IV vit K + PCC (4-factor)
- Aspirin: irreversible COX-1 → ↓ TXA2; ACS 300 mg load; CI <16y (Reye's)
- Clopidogrel: P2Y12 (ADP) blocker; CYP2C19 prodrug; avoid omeprazole (use lansoprazole)

💡 **HIGH YIELD:** Warfarin reversal: Major bleeding = IV vit K + PCC. PCC works within minutes. Amiodarone commonly causes supratherapeutic INR. Streptokinase: use ONCE only (antigenic). Tenecteplase: single bolus, preferred pre-hospital.

Rapid Recall – CV Pharmacology

Topic / Prompt	Key Fact / Answer
Digoxin toxicity	Precipitated by hypoK; any arrhythmia; yellow halos; Rx: DigiFab
Furosemide	NKCC2 blocker; HypoCa; IV for acute pulmonary oedema
Thiazide	HYPERcalcaemia; HyperGLUC (Glucose, Lipids, Urate, Calcium)
Adenosine	6–12–12 mg rapid IV for SVT; CI: asthma
Amiodarone in arrest	300 mg after 3rd shock; T½ 40–100 days
ACEi	Cough (bradykinin), hyperK, first-dose hypotension, angioedema; CI: pregnancy

GTN	NO donor → cGMP; CI: sildenafil, hypotension, severe AS
Adrenaline (arrest)	1 mg IV (1:10,000); Anaphylaxis: 0.5 mg IM (1:1,000)
Warfarin reversal	IV vit K + PCC for major bleeding

3.3 Respiratory Pharmacology

Salbutamol

- **MOA:** Selective β2-agonist → ↑ cAMP → bronchial smooth muscle relaxation; also drives K^+ intracellularly
- **Dosing:** Neb: 2.5–5 mg; onset 3–5 min; duration 4–6h
- SEs: tremor, tachycardia, hypokalaemia (monitor K^+ with repeated nebs + steroids)
- **Off-label:** Hyperkalaemia: 10–20 mg neb (temporary effect; combine with insulin/dextrose)

⚡ **EXAM TIP:** Salbutamol: Tremor, Tachycardia, hypoKalaemia. Monitor K^+ in acute severe asthma. Also used for hyperkalaemia management. LABA must NEVER be used without ICS in asthma (SMART trial).

Ipratropium Bromide

- **MOA:** M3 antagonist → blocks vagal bronchoconstriction; additive with β2-agonists
- Neb: 500 µg; onset 15–30 min (slower than salbutamol); quaternary ammonium → minimal systemic SEs

Aminophylline / Theophylline

- **MOA:** PDE inhibitor → ↑ cAMP → bronchodilation; also adenosine receptor antagonist
- Narrow therapeutic index: 10–20 mg/L; OMIT loading dose if already on oral theophylline
- Toxicity: nausea → tachycardia → arrhythmias → SEIZURES
- CYP1A2 metabolism: ↑ levels: erythromycin, ciprofloxacin, cimetidine; ↓ levels: SMOKING, rifampicin

Corticosteroids (Respiratory)

- Hydrocortisone: IV 100 mg for acute severe asthma, anaphylaxis adjunct, adrenal crisis
- Prednisolone: 40–50 mg PO for acute exacerbation; ≥5 days (no taper for short course)
- Beclomethasone (ICS): prophylactic only (not rescue); SEs: oral candidiasis (rinse mouth), dysphonia

Antihistamines

Feature	Non-Sedating (2nd gen)	Sedating (1st gen)
Type substance	Cetirizine	Chlorphenamine
BBB penetration	Minimal	Crosses BBB → sedation
Anticholinergic	Minimal	Present (dry mouth, retention)
Key use	Rhinitis, urticaria (daytime)	Anaphylaxis adjunct (10 mg IV)

Anaphylaxis Management

- 1. Adrenaline 0.5 mg IM (1:1,000) anterolateral thigh – FIRST-LINE; repeat every 5 min
- 2. High-flow O_2 (15 L/min) → 3. IV fluid bolus 500 mL–1 L → 4. Chlorphenamine 10 mg IV
- 5. Hydrocortisone 200 mg IV (prevents late-phase) → 6. Nebulised salbutamol if bronchospasm

⚡ **EXAM TIP:** Anaphylaxis: Adrenaline IM is the ONLY first-line. Chlorphenamine and hydrocortisone are ADJUNCTS only – never delay adrenaline. Post-anaphylaxis: observe 6–12h, prescribe auto-injector, check tryptase at 1h/6h/>24h.

Acute Severe Asthma – Treatment Order

- O_2 (target 94–98%) → Salbutamol neb 5 mg → Ipratropium 500 µg → Prednisolone 40–50 mg PO / Hydrocortisone 100 mg IV
- If not responding: $MgSO_4$ 1.2–2 g IV over 20 min → Aminophylline IV (last resort) → ICU

💡 **HIGH YIELD:** A normal or rising $PaCO_2$ in acute asthma is OMINOUS – tiring patient. COPD: target SpO_2 88–92%. High-flow O_2 worsens hypercapnia.

Rapid Recall – Respiratory Pharmacology

Topic / Prompt	Key Fact / Answer
Salbutamol	β2 agonist; tremor, tachycardia, hypoK; also used for hyperK
Ipratropium	M3 antagonist; neb 500 µg; slower onset; additive with salbutamol
Aminophylline	PDE inhibitor; narrow TI (10–20); OMIT loading if on theophylline; toxicity: seizures
Beclomethasone (ICS)	Prophylactic only; oral candidiasis; rinse mouth + spacer
Cetirizine	Non-sedating antihistamine; 10 mg OD; minimal BBB penetration
Anaphylaxis 1st line	Adrenaline 0.5 mg IM (1:1,000); anterolateral thigh
Asthma treatment order	O_2 → salbutamol → ipratropium → steroids → $MgSO_4$ → aminophylline

3.4 CNS Pharmacology

Benzodiazepines

- **MOA:** Enhance GABA-A receptor → increase FREQUENCY of Cl^- channel opening → neuronal hyperpolarisation
- Effects: anxiolytic, sedative, anticonvulsant, muscle relaxant, amnesic (anterograde)
- Withdrawal can cause seizures and be fatal – never stop abruptly in dependent patients

Drug	T½	Active Metabolites	Key Use
Diazepam	20–100h	Yes (long-acting)	Seizures (PR in children), anxiety, spasm
Chlordiazepoxide	5–30h	Yes	Alcohol withdrawal (1st line)
Lorazepam	10–20h	None	Status epilepticus IV (1st line in hospital)
Midazolam	1.5–2.5h	None	Buccal for seizures; procedural sedation

⚡ **EXAM TIP:** BZDs increase FREQUENCY of Cl^- opening; barbiturates increase DURATION – classic MCQ distinction. Lorazepam: no active metabolites = safer in liver disease. Flumazenil: BZD reversal but CAUTION with chronic BZD/TCA co-ingestion (seizure risk).

Antipsychotics & Extrapyramidal Symptoms

- All antipsychotics block D2 receptors in mesolimbic pathway; EPS from D2 blockade in nigrostriatal pathway

EPS Type	Onset	Features	Management
Acute dystonia	Hours–days	Torticollis, oculogyric crisis	IM procyclidine
Akathisia	Days–weeks	Restlessness, inability to sit still	Reduce dose; propranolol
Parkinsonism	Weeks–months	Tremor, rigidity, bradykinesia	Reduce dose; procyclidine
Tardive dyskinesia	Months–years	Lip-smacking, tongue protrusion	May be irreversible; stop drug

- NMS: hyperthermia >40°C, lead-pipe rigidity, autonomic instability, ↑CK; Rx: stop drug, dantrolene

💡 **HIGH YIELD:** NMS vs serotonin syndrome: NMS = lead-pipe rigidity, slow onset (days); serotonin syndrome = clonus/hyperreflexia, rapid onset (hours). Both cause hyperthermia. Metoclopramide = D2 antagonist → EPS risk (past paper HOT topic).

Lithium

- Narrow TI: 0.4–1.0 mmol/L; toxicity >1.5; always 12h post-dose trough level
- SEs at therapeutic levels: fine tremor, polyuria/polydipsia (nephrogenic DI), hypothyroidism
- Toxicity precipitants: NSAIDs, ACEi, thiazides (all reduce renal clearance); dehydration
- Teratogenic: Ebstein's anomaly (tricuspid valve malformation)

⚡ **EXAM TIP:** Classic scenario: patient on lithium started on NSAID or thiazide → toxicity. Also dehydration from intercurrent illness. Toxicity >2.5 mmol/L: haemodialysis.

TCA Overdose (Amitriptyline)

- Na^+ channel blockade → QRS prolongation (>100 ms = significant; >160 ms = high VT/VF risk)
- Toxic triad: seizures + arrhythmias + hypotension
- Antidote: IV sodium bicarbonate 8.4% for QRS >100 ms (Na^+ load overcomes channel blockade)
- Avoid: flumazenil (lowers seizure threshold), phenytoin, class Ia/Ic antiarrhythmics

Antiemetics

Cause of Vomiting	Key Receptor	Best Antiemetic
Motion sickness	H1, M1 (vestibular)	Cyclizine or hyoscine
Drug-induced/metabolic	D2 (CTZ)	Metoclopramide, prochlorperazine
Chemotherapy	5-HT3 (vagal/CTZ)	Ondansetron
Raised ICP	H1	Cyclizine (avoid metoclopramide)

- Metoclopramide: D2 antagonist + 5-HT4 agonist (prokinetic); max 30 mg/24h for max 5 days; EPS risk especially in young females

Opioids

- All act primarily at μ receptors; SEs: respiratory depression, constipation, miosis, N&V
- Tolerance develops to most effects EXCEPT constipation and miosis
- Morphine: M6G active metabolite accumulates in renal failure; codeine: CYP2D6 prodrug → morphine (CI <12y)
- Tramadol: weak μ + monoamine reuptake inhibitor; KEY risks: seizures + serotonin syndrome
- Naloxone: μ antagonist; 400 μg IV; short T½ – repeat/infuse as needed

Antiepileptics & Status Epilepticus

Drug	Mechanism	Key SE/Feature
Carbamazepine	Na^+ channel blocker	Auto-induction; hypoNa (SIADH); enzyme INDUCER; NOT for absence
Phenytoin	Na^+ channel blocker	Zero-order kinetics; gingival hyperplasia; IV needs cardiac monitoring
Valproate	GABA + Na^+ + Ca^{2+}	MOST teratogenic AED; hepatotoxicity; enzyme INHIBITOR; broad-spectrum

- Status epilepticus protocol: 1st line: IV lorazepam 4 mg (repeat once at 10–15 min) / buccal midazolam 10 mg
- 2nd line: IV phenytoin 20 mg/kg OR levetiracetam 40–60 mg/kg
- Refractory: RSI + ICU (thiopental/propofol/midazolam infusion)

Enzyme Inducers & Inhibitors

- Inducers (PC BRAGS): Phenytoin, Carbamazepine, Barbiturates, Rifampicin, Alcohol (chronic), Griseofulvin, St John's Wort
- Inhibitors (ODEVICES): Omeprazole, Disulfiram, Erythromycin, Valproate, Isoniazid, Ciprofloxacin/Cimetidine, Ethanol (acute), SSRIs

💡 **HIGH YIELD:** Carbamazepine = enzyme inducer (reduces OCP efficacy – past paper HOT topic). Zero-order kinetics = phenytoin, alcohol, aspirin (high-dose). Narrow TI drugs: phenytoin, lithium, digoxin, warfarin, theophylline, gentamicin.

Rapid Recall – CNS Pharmacology

Topic / Prompt	Key Fact / Answer
BZD vs barbiturate	BZD = frequency of Cl^- opening; barbiturate = duration
Lorazepam	1st-line IV BZD for status; no active metabolites; liver-safe
Metoclopramide	D2 antagonist + 5-HT4 prokinetic; EPS risk; max 5 days

TCA overdose	QRS >100 ms → IV $NaHCO_3$ 8.4%; toxic triad: seizures + arrhythmias + hypotension
Lithium toxicity	Precipitated by NSAIDs/thiazides/ACEi; haemodialysis if >2.5
Naloxone	μ antagonist; 400 μg IV; short T½ – may need repeat doses
Status protocol	Lorazepam IV → repeat → phenytoin/levetiracetam → RSI + ICU
NAC in paracetamol OD	Most effective <8h; replenishes glutathione; King's: pH <7.3

3.5 Antimicrobials

Mechanisms of Antibacterial Action

Mechanism	Drug Classes	Kill Type
Cell wall synthesis	Penicillins, Cephalosporins, Carbapenems, Vancomycin	Bactericidal
Protein synthesis (30S)	Aminoglycosides, Tetracyclines	Aminoglyc: cidal; Tet: static
Protein synthesis (50S)	Macrolides, Chloramphenicol	Mainly bacteriostatic
DNA synthesis	Quinolones (fluoroquinolones)	Bactericidal
Folate synthesis	Trimethoprim, Sulfonamides	Bacteriostatic
DNA damage	Metronidazole	Bactericidal (anaerobes)

💡 **HIGH YIELD:** 30S = aminoglycosides + tetracyclines (doxycycline). 50S = macrolides. This distinction is asked in EVERY sitting. MRSA: altered PBP2a (mecA gene) → resistance to ALL beta-lactams; treat with vancomycin or linezolid.

Key Antibiotics

- Benzylpenicillin: IV/IM only (acid labile); pre-hospital meningococcal disease; narrow spectrum
- Flucloxacillin: penicillinase-resistant; 1st-line S. aureus (NOT MRSA); hepatotoxicity risk >14 days
- Amoxicillin: rash in EBV infection; co-amoxiclav: + clavulanic acid for bite wounds, complicated UTI
- Ceftriaxone: long T½ (OD dosing); 1st-line meningitis; IM for gonorrhoea; avoid in neonates (kernicterus)
- Doxycycline: 30S inhibitor; 1st-line Chlamydia and early Lyme; CI <12y and pregnancy (teeth/bone)
- Gentamicin: 30S (irreversible); TDM essential; nephrotoxicity (usually reversible), ototoxicity (may be irreversible)
- Erythromycin: 50S inhibitor; CYP3A4 inhibitor (many interactions); QT prolongation; pertussis treatment

Other Key Antimicrobials

- Metronidazole: anaerobes + protozoa; disulfiram-like reaction with alcohol; 1st-line anaerobic infections
- Vancomycin: MRSA; oral for moderate–severe C. difficile; Red Man Syndrome (rate-related, NOT allergy)
- Quinolones (ciprofloxacin): tendon rupture (Achilles; risk ↑ age >60, steroids); lowers seizure threshold
- Trimethoprim: folate antagonist; 1st-line uncomplicated UTI; hyperkalaemia (blocks ENaC)

⚡ **EXAM TIP:** Quinolones → tendon rupture: stop immediately at first sign of tendon pain. Clindamycin → C. difficile. Co-amoxiclav → cholestatic jaundice. Amoxicillin rash in EBV. All asked repeatedly in past papers.

TB Treatment (RIPE)

- Initial phase (2 months): Rifampicin + Isoniazid + Pyrazinamide + Ethambutol
- Continuation (4 months): Rifampicin + Isoniazid
- Rifampicin: orange body fluids + potent CYP inducer; Isoniazid: peripheral neuropathy (give B6)
- Pyrazinamide: most hepatotoxic; Ethambutol: optic neuritis (check visual acuity)

Antivirals & Antifungals

- Aciclovir: nucleoside analogue; activated by viral thymidine kinase; inhibits viral DNA polymerase
- Herpes encephalitis: IV aciclovir 10 mg/kg TDS for 14–21 days – start empirically, do NOT delay
- Nystatin: topical antifungal for Candida (not absorbed – no systemic effect)

Rapid Recall – Antimicrobials

Topic / Prompt	Key Fact / Answer
30S inhibitors	Aminoglycosides (gentamicin), Tetracyclines (doxycycline)
50S inhibitors	Macrolides (erythromycin), Chloramphenicol
Quinolones	DNA gyrase inhibitors; tendon rupture; CI: children, pregnancy
C. difficile	Caused by: cephalosporins, clindamycin, co-amoxiclav; Rx: oral vancomycin
Gentamicin	TDM essential; nephro + ototoxicity; once-daily dosing preferred
TB (RIPE)	Rifampicin (inducer) + Isoniazid (neuropathy/B6) + Pyrazinamide (hepatotoxic) + Ethambutol (optic neuritis)
Aciclovir	Viral TK activation; herpes encephalitis = emergency – start immediately
Meningitis 1st line	Ceftriaxone (± amoxicillin for Listeria cover if >50y)

3.6 Endocrine Pharmacology

Insulin Types

Type	Example	Onset	Duration	Key Note
Rapid-acting	Lispro, Aspart	10–20 min	3–5h	Before meals; used in pumps
Short-acting (soluble)	Actrapid	30–60 min	6–8h	ONLY insulin given IV (DKA)
Intermediate (NPH)	Insulatard	1–2h	16–24h	Cloudy; needs mixing
Long-acting (basal)	Glargine, Detemir	1–2h	20–42h	Peakless; clear; cannot mix

⚡ **EXAM TIP:** Only SOLUBLE (short-acting) insulin can be given IV – this is the insulin used in DKA (fixed-rate IV infusion 0.1 units/kg/h). Do NOT stop insulin when glucose normalises – add 10% dextrose and continue until ketones clear.

DKA Management – Key Pharmacological Points

- FRII: 0.1 units/kg/h of soluble insulin (e.g. Actrapid)
- IV fluids: aggressive 0.9% NaCl resuscitation (4–6 L in first 12h)
- K^+ replacement: insulin drives K^+ intracellularly; monitor hourly; do NOT give insulin if K^+ <3.5 until corrected
- Add 10% glucose when BG ≤14 mmol/L – continue insulin to clear ketones
- Continue long-acting SC insulin alongside FRII

Oral Antidiabetics (Principles)

- Metformin: 1st-line T2DM; reduces hepatic glucose output; NO hypoglycaemia; risk of lactic acidosis (CI: eGFR <30, tissue hypoxia)
- Sulphonylureas (gliclazide): stimulate insulin secretion; HIGH hypoglycaemia risk (especially elderly/renal impairment)
- Patients on insulin or sulphonylureas must inform DVLA

Thyroid & Corticosteroids

- Propranolol for thyrotoxicosis symptom control (also blocks peripheral T4→T3 conversion)
- Corticosteroid long-term SEs: Cushing's, osteoporosis, adrenal suppression, immunosuppression, diabetes, cataracts
- Never stop long-term steroids abruptly – adrenal crisis risk; carry steroid card

Rapid Recall – Endocrine Pharmacology

Topic / Prompt	Key Fact / Answer
IV insulin type	Soluble (short-acting) ONLY; e.g. Actrapid
DKA insulin rate	0.1 units/kg/h FRII; continue until ketones clear
DKA K^+	Do NOT give insulin if K^+ <3.5; monitor hourly
Metformin	1st-line T2DM; lactic acidosis risk; CI: eGFR <30
Sulphonylurea	Stimulates insulin release; HIGH hypo risk; inform DVLA
Steroid withdrawal	Never stop abruptly; adrenal crisis risk

3.7 Fluids & Electrolytes

IV Crystalloids – Composition

Fluid	Na^+ (mmol/L)	K^+	Cl^-	Other	Tonicity
0.9% NaCl	154	0	154	—	Isotonic
Hartmann's	131	5	111	Lactate 29, Ca^{2+} 2	Isotonic
5% Dextrose	0	0	0	Glucose 50 g/L	Hypotonic in vivo

- 0.9% NaCl: large volumes → hyperchloraemic metabolic acidosis (supraphysiological Cl^-)
- Hartmann's: more physiological; lactate → bicarbonate; NEVER co-infuse with blood (Ca^{2+} chelates citrate)
- 5% Dextrose: glucose metabolised → free water → distributes across TBW; NOT for resuscitation

⚡ **EXAM TIP:** 5% dextrose is isotonic in the bag but hypotonic in vivo. Poor plasma expander – only ~80 mL/L stays in plasma. Hartmann's contains lactate (metabolised to bicarbonate). Both Hartmann's and its bicarbonate content are repeated past paper topics.

Colloids

- Albumin: 4.5% (isotonic expander) and 20% (hyper-oncotic); for large-volume paracentesis, burns
- Gelofusine: synthetic colloid; anaphylaxis risk; stays intravascular ~3–4h

Potassium Replacement

- IV KCl: NEVER as bolus push (fatal cardiac arrest); max peripheral rate 10 mmol/h; max concentration 40 mmol/L
- Severe hypoK: up to 40 mmol/h via central line with cardiac monitoring

Hyperkalaemia Management

- Cardiac protection: 10 mL 10% calcium gluconate IV (stabilises myocardium; does NOT lower K^+)
- Shift K^+ into cells: insulin 10 units + 25 g glucose; salbutamol 10–20 mg neb; $NaHCO_3$
- Remove K^+: calcium resonium PO/PR; loop diuretics; haemodialysis

Rapid Recall – Fluids & Electrolytes

Topic / Prompt	Key Fact / Answer
0.9% NaCl	Isotonic; ECF replacement; large volumes → hyperchloraemic acidosis
Hartmann's	More physiological; lactate → HCO_3^-; NEVER with blood products
5% Dextrose	Hypotonic in vivo; NOT for resuscitation; distributes across TBW
IV KCl	Never bolus; max 10 mmol/h peripheral; cardiac monitoring if faster
HyperK 1st step	10 mL 10% calcium gluconate IV (cardiac protection)
$NaHCO_3$ in TCA OD	8.4% for QRS >100 ms; Na^+ load overcomes channel blockade

3.8 MSK Pharmacology

COX Pathway

- Arachidonic acid → COX pathway: prostaglandins, prostacyclin, TXA2
- COX-1: constitutive (housekeeping – gastric protection, renal blood flow, platelet TXA2)
- COX-2: inducible at sites of inflammation
- NSAIDs inhibit COX; Corticosteroids inhibit phospholipase A2 → block BOTH pathways

NSAIDs – Comparison

Feature	Ibuprofen	Naproxen	Diclofenac	Mefenamic Acid
GI risk	LOWEST	Intermediate	Intermediate	Intermediate
CV risk	Lowest (low dose)	LOWEST of NSAIDs	HIGHEST CV risk	Moderate
Special	1st choice; safe >3m; OTC	Long T½ (BD); gout	Strong anti-inflam; MHRA CV warning	Haemolytic anaemia (past paper!)

- All NSAIDs: GI ulceration, renal impairment, bronchospasm, hypertension, bleeding
- CI: active peptic ulcer, severe HF, severe renal/hepatic impairment, 3rd trimester pregnancy
- Triple whammy: NSAID + ACEi + diuretic → AKI

⚡ **EXAM TIP:** Ibuprofen = lowest GI risk. Diclofenac = highest CV risk (MI – past paper topic). Mefenamic acid = haemolytic anaemia (asked in EVERY sitting). NSAIDs in 3rd trimester: premature closure of ductus arteriosus.

Gout Pharmacology

- Colchicine: inhibits microtubule polymerisation → prevents neutrophil migration; used when NSAIDs/steroids CI (e.g. HF)
- Allopurinol: xanthine oxidase inhibitor; prophylaxis only (never start in acute attack)

Rapid Recall – MSK Pharmacology

Topic / Prompt	Key Fact / Answer
COX-1 vs COX-2	COX-1 constitutive (GI/renal/platelet); COX-2 inducible (inflammation)
Ibuprofen	Lowest GI risk; 1st-choice NSAID; safe >3 months age
Diclofenac	Highest CV risk (MI); strong anti-inflammatory
Mefenamic acid	Causes haemolytic anaemia – repeated exam topic
Colchicine	Microtubule inhibitor; acute gout when NSAIDs CI (e.g. HF)
Triple whammy	NSAID + ACEi + diuretic → AKI

3.9 Immunological Products & Vaccines

Vaccine Types

Type	Examples	Key Points
Live attenuated	MMR, BCG, rotavirus, varicella, oral polio, nasal flu	CI: pregnancy, immunocompromised, <6 months
Inactivated	IPV, hepatitis A, rabies, influenza (injected)	Safe in immunosuppressed; may need boosters
Toxoid	Tetanus, diphtheria	Inactivated toxin; requires boosters
Conjugate	Hib, MenC, PCV	Polysaccharide linked to protein carrier

- Live vaccines CI in pregnancy and severe immunodeficiency (low CD4 in AIDS – BCG most dangerous)
- Immunoglobulin = passive adaptive immunity (pre-formed antibodies; temporary protection)

Tetanus Management

- Clean wound, fully vaccinated (<10y since last dose): no vaccine needed
- Tetanus-prone wound (puncture, contaminated, burns, bites): consider booster ± tetanus immunoglobulin

Rapid Recall – Vaccines

Topic / Prompt	Key Fact / Answer
Live vaccines	MMR, BCG, rotavirus, varicella, oral polio; CI: pregnancy, immunosuppressed
Immunoglobulin	Passive adaptive immunity; pre-formed antibodies
Chickenpox in pregnancy	Non-immune: give VZIG within 10 days of exposure
Rabies post-exposure	5 doses (days 0,3,7,14,28) + immunoglobulin at wound site on day 0

3.10 Anaesthesia

IV Induction Agents – Comparison

Property	Thiopental	Etomidate	Propofol	Ketamine
Mechanism	GABA-A agonist	GABA-A agonist	GABA-A agonist	NMDA antagonist
BP effect	↓↓	Minimal change	↓↓↓	↑↑ (only one that ↑BP)
ICP	↓↓	↓	↓↓	↑
Analgesia	None	None	None	Excellent
Resp depression	Marked	Moderate	Marked	Minimal (bronchodilator)
Porphyria-safe?	NO	NO	YES	NO
Key SE	Tissue necrosis if extravasated	Adrenal suppression (11β-hydroxylase)	PRIS; most hypotension	Emergence phenomena; ↑ICP

⚡ **EXAM TIP:** Haemodynamic instability → etomidate or ketamine. Head injury (stable) → thiopental or propofol. Asthma → ketamine (bronchodilator). Status epilepticus → thiopental or propofol. Etomidate: adrenal suppression via 11β-hydroxylase = very commonly tested.

Nitrous Oxide (N_2O)

- 50% N_2O + 50% O_2 (Entonox); analgesic via opioid system + NMDA antagonism; rapid onset/offset
- Expands gas-filled spaces (34× more soluble than N_2): CI in pneumothorax, bowel obstruction, pneumocephalus
- Inactivates vitamin B12 → megaloblastic anaemia with prolonged/repeated use
- Diffusion hypoxia on discontinuation – give 100% O_2 for several minutes after stopping

💡 **HIGH YIELD:** N_2O: expands closed gas spaces (CI: pneumothorax); inactivates B12 (megaloblastic anaemia); diffusion hypoxia. Cannot produce anaesthesia alone (MAC >100%). All frequently tested.

Neuromuscular Blocking Agents

- Suxamethonium: depolarising NMBA; 1–1.5 mg/kg IV; onset 30–60s; duration 3–5 min
- Key risk: HYPERKALAEMIA (CI: burns >24h, denervation, crush injury, muscular dystrophy)
- Malignant hyperthermia: suxamethonium + volatile agents trigger; RYR1 mutation; Rx: dantrolene IV
- Rocuronium: non-depolarising; 1.2 mg/kg for RSI; reversed by sugammadex

Local Anaesthetics

- Block voltage-gated Na^+ channels → prevent depolarisation; work poorly in infected (acidic) tissue
- Amides (2 'i's): lidocaine, bupivacaine, prilocaine; Esters (1 'i'): procaine, cocaine

Agent	Max Dose (plain)	Max Dose (+ adrenaline)	Key Note
Lidocaine	3 mg/kg	7 mg/kg	Fastest onset; most common in ED
Bupivacaine	2 mg/kg	2.5 mg/kg	MOST CARDIOTOXIC; longest acting
Prilocaine	6 mg/kg	9 mg/kg	Highest max dose; methaemoglobinaemia; Bier's block

LA Systemic Toxicity (LAST)

- CNS signs first: perioral tingling, metallic taste, tinnitus → seizures → then cardiovascular collapse
- Treatment: stop injection; ABC; benzodiazepines for seizures; 20% Intralipid 1.5 mL/kg IV bolus
- Bupivacaine causes refractory cardiac arrest – standard ALS may fail; prolonged resuscitation needed

⚡ **EXAM TIP:** Suxamethonium → hyperkalaemia (CI: burns >24h, crush, denervation, dystrophy). Bupivacaine = MOST cardiotoxic LA; Rx: 20% Intralipid. LAST: CNS signs before CVS collapse (tingling, tinnitus, seizures). All are past paper HOT topics.

Rapid Recall – Anaesthesia

Topic / Prompt	Key Fact / Answer
Etomidate	Most haemodynamically stable; adrenal suppression (11β-hydroxylase)
Ketamine	Only IV agent with ↑BP + analgesia; NMDA antagonist; bronchodilator; emergence phenomena
Propofol	Most hypotension; antiemetic; PRIS with prolonged infusion
Suxamethonium	Depolarising NMBA; hyperK risk; malignant hyperthermia trigger
N_2O	Expands gas spaces (CI: pneumothorax); B12 inactivation; diffusion hypoxia
Lidocaine max dose	3 mg/kg plain; 7 mg/kg with adrenaline
Bupivacaine	Most cardiotoxic LA; Rx: 20% Intralipid 1.5 mL/kg bolus
LAST progression	Tingling → metallic taste → tinnitus → seizures → CVS collapse
Malignant hyperthermia	Suxamethonium + volatiles; RYR1; ↑temp, rigidity; Rx: dantrolene

Chapter 4: Microbiology

~10% of exam | ~18 questions

- 4A. Principles of Microbiology — Innate Immunity, Mechanisms of Disease, Infection Control, Investigation, Immunisation
- 4B. Bacterial Pathogens — Streptococci & Staphylococci, TB, Clostridia, Neisseria, Pertussis, Enterobacteriaceae, H. pylori, Campylobacter, Legionella, Pseudomonas, Chlamydia
- 4C. Viral Pathogens — Herpes Viruses, HIV, Hepatitis, Measles, Mumps, Rubella, Respiratory Viruses, GI Viruses
- 4D. Fungi, Parasites & Malaria — Candida, Cryptococcus, Dermatophytes, Helminths, Malaria

4A. Principles of Microbiology

Barriers to Infection

Barrier	Location	Mechanism	Impairment
Skin	Body surface	Physical (keratin) + chemical (sebum, fatty acids, acidic pH ~5.5)	Burns, eczema, cannulation
Mucociliary clearance	Respiratory tract	Ciliated epithelium + mucus trapping ("escalator")	Smoking, CF, intubation, GA
Lysozyme	Tears, saliva, nasal secretions	Cleaves peptidoglycan (more effective vs Gram-positives)	Rare — redundant sources
Gastric acid	Stomach	pH 1–2 kills ingested organisms	PPIs, achlorhydria, gastrectomy
Urinary flushing	Urinary tract	Unidirectional urine flow washes organisms	Catheterisation, obstruction
Normal flora	Skin, gut, vagina	Competitive exclusion + bacteriocin production	Antibiotics → C. difficile

⚡ **EXAM TIP:** PPI use increases risk of C. difficile and other GI infections — asked repeatedly. Also know: burns → Pseudomonas + S. aureus; cannulae → S. aureus + S. epidermidis.

Normal Flora by Body Site

Body Site	Normal Flora	Clinical Note
Skin	S. epidermidis, Corynebacterium, P. acnes	S. epidermidis = commonest line infection organism
Mouth	Viridans streptococci, Neisseria spp.	Viridans strep → subacute endocarditis after dental procedures
Upper respiratory tract	S. pneumoniae, H. influenzae, Moraxella	Normal carriage — pathogenic if defences breached
Gut	Bacteroides, E. coli, Enterococcus, Clostridia	Disruption → C. difficile; E. coli = commonest UTI organism
Vagina	Lactobacillus spp.	Maintains acidic pH; disruption → bacterial vaginosis

Phagocytes and Opsonisation

- **Neutrophils:** Most abundant WBC (60–70%). First responders. Short-lived (6–12h in tissues). Pus = dead neutrophils
- **Macrophages:** Derived from monocytes. Tissue names: Kupffer cells (liver), alveolar macrophages (lung), microglia (CNS), osteoclasts (bone)
- **Key opsonins:** IgG antibody (most effective) and C3b (complement). Opsonisation enhances phagocytosis
- **Encapsulated bacteria** resist phagocytosis — capsule prevents opsonin binding. Mnemonic "SHiNE": **S. pneumoniae, H. influenzae, N. meningitidis, E. coli** (neonates)

⚡ **EXAM TIP:** Past paper: Splenectomy patient susceptible to infection — defect in macrophage function (impaired opsonisation of encapsulated bacteria). S. pneumoniae is the COMMONEST cause of OPSI (~60%).

Post-Splenectomy Management

- **Vaccination:** Pneumococcal + Meningococcal ACWY + B + Hib + annual influenza
- **Lifelong prophylactic antibiotics:** Phenoxymethylpenicillin (penicillin V) 250–500 mg BD
- **Patient education:** MedicAlert bracelet; urgent medical attention for any febrile illness

Complement System

- Three pathways converge at **C3 convertase**: Classical (IgG/IgM), Alternative (spontaneous), Lectin (MBL)
- **C3b** = opsonisation. **C5a** = most potent chemotaxis. **C3a, C4a, C5a** = anaphylatoxins. **C5b–C9** = membrane attack complex (MAC)

Deficiency	Clinical Association
C1, C2, C4 (classical)	SLE-like syndrome; recurrent pyogenic infections
C3	Severe recurrent pyogenic infections (convergence point)
C5–C9 (terminal/MAC)	Recurrent **Neisserial** infections (N. meningitidis, N. gonorrhoeae)
C1 esterase inhibitor	Hereditary angioedema (NOT immunodeficiency)

💡 **HIGH YIELD:** C5–9 deficiency → recurrent NEISSERIAL infections. This is asked in multiple past paper sittings. Also remember: complement activation by S. pneumoniae → C3b opsonisation.

Classification of Pathogens

Category	Definition	Examples
Obligate pathogen	ALWAYS causes disease when present	HIV, M. tuberculosis, rabies, P. falciparum
Conditional pathogen	Normal flora; causes disease if barriers breached	S. aureus, E. coli, S. pneumoniae
Opportunistic pathogen	Only in immunocompromised hosts	Pneumocystis jirovecii, Candida, Aspergillus, CMV

⚡ **EXAM TIP:** Past paper asked pathogen type for cellulitis organism: S. aureus = CONDITIONAL pathogen. S. pneumoniae asked as commensal organism example.

Exotoxins vs Endotoxins

Feature	Exotoxins	Endotoxins
Source	Secreted by living bacteria (mostly Gram+)	Gram-negative outer membrane (LPS/lipid A)
Composition	Polypeptides	Lipopolysaccharide
Heat stability	Heat-LABILE	Heat-STABLE
Toxoid formation	YES (e.g. tetanus, diphtheria vaccines)	NO
Specificity	Highly specific tissue effects	Non-specific systemic inflammation
Potency	Very potent (small amounts)	Less potent (large amounts needed)

- **Cholera toxin:** ↑cAMP → massive Cl^-/water secretion → rice-water diarrhoea
- **Tetanospasmin (C. tetani):** Blocks glycine + GABA release → spastic paralysis
- **Botulinum toxin (C. botulinum):** Blocks ACh release at NMJ → flaccid paralysis

Hospital-Acquired Infection (HAI)

- Definition: infection NOT present at admission; typically develops ≥48h after admission
- **Cannulation** = COMMONEST cause of hospital bacteraemia. Replace peripheral cannulae at 48–72h. Organisms: S. aureus, S. epidermidis
- **Urinary catheters:** ~5% per day bacteriuria risk. Organisms: E. coli, Klebsiella, Enterococcus, Pseudomonas, Proteus
- **Hand hygiene** = single most important measure. Alcohol gel does NOT kill C. difficile spores or norovirus → soap and water MANDATORY

💡 **HIGH YIELD:** Cannula = commonest cause of hospital bacteraemia has been tested multiple times. S. epidermidis (coagulase-negative staph) forms biofilm on prosthetic devices — asked as organism in line infections.

Sterilisation vs Disinfection

- **Disinfection:** REDUCES organisms to non-infectious level. Does NOT eliminate spores
- **Sterilisation:** ELIMINATES ALL organisms including spores. Gold standard: autoclaving (134°C for 3 min or 121°C for 15 min)
- **C. difficile spores:** Resistant to alcohol and heat. Use sodium hypochlorite (bleach) for environmental decontamination

Key Microbiology Investigations

Technique	Principle	Key Applications
Gram stain	Crystal violet → iodine → alcohol → safranin	CSF (meningitis), sputum, wounds. Gram+ = purple; Gram– = pink
Ziehl–Neelsen (ZN)	Acid-fast stain (carbol fuchsin)	Sputum for **M. tuberculosis** (acid-fast bacilli)
Giemsa stain	Romanowsky stain of blood films	**Malaria** parasites (ring forms in RBCs)
India ink	Negative staining of CSF	**Cryptococcus neoformans** (capsule halo)
KOH preparation	Dissolves keratin, shows fungal elements	**Dermatophytes** (skin scrapings)
NAAT/PCR	Nucleic acid amplification	TB (GeneXpert), Chlamydia, HSV encephalitis, N. meningitidis

⚡ **EXAM TIP:** Malaria stain = Giemsa and TB stain = Ziehl–Neelsen are asked in EVERY sitting. Also: NAAT/PCR = gold standard for Chlamydia trachomatis diagnosis.

Serology Principles

- **Antibody detection** = INDIRECT (detects immune response). IgM = acute infection; IgG = past/immunity
- **Antigen detection** = DIRECT (detects organism). CSF capsular antigen useful when antibiotics given before LP
- **Blood cultures:** Take BEFORE antibiotics. Volume of blood is the single most important factor for yield

Vaccine Types

Type	Description	Key Examples	Properties
Live attenuated	Weakened live organism	MMR, BCG, oral polio, varicella, rotavirus, yellow fever, nasal flu	Strong immunity; CONTRAINDICATED in immunosuppressed / pregnancy
Inactivated	Killed organism or component	Inactivated polio (Salk), Hep A, rabies, injected flu	Safer; weaker response; needs boosters; SAFE in immunosuppressed
Toxoid	Detoxified exotoxin	Tetanus toxoid, diphtheria toxoid	Stimulates antitoxin antibodies; very safe
Conjugate/subunit	Capsular polysaccharide ± protein carrier	Hib, PCV13, MenACWY, HBV (recombinant), HPV	Effective in <2 years; T-dependent response

⚡ **EXAM TIP:** Past paper asked: which is a live vaccine? Answer: BCG (also MMR, oral polio, varicella, rotavirus, nasal flu). Know that live vaccines are CONTRAINDICATED in pregnancy and immunosuppression.

Passive Immunity

- **Anti-D immunoglobulin:** Within 72h of sensitising event in Rh-negative mothers
- **HBIG:** Given WITH HBV vaccine after needlestick from HBV+ source
- **TIG (tetanus immunoglobulin):** For tetanus-prone wounds in incompletely immunised patients
- **VZIG:** For susceptible immunosuppressed/pregnant contacts of varicella

Tetanus Wound Management

Immunisation Status	Clean Minor Wound	Tetanus-Prone Wound
Fully immunised (5 doses)	Nothing required	Nothing required (consider booster if very high risk)
Primary course complete, boosters incomplete	Vaccine booster	Vaccine booster + consider TIG
Not immunised / unknown	Full vaccine course	Full vaccine course + TIG

- **Tetanus-prone wounds:** Puncture wounds, ≥6h old, soil/faecal contamination, devitalised tissue, open fractures, burns

> 💡 **HIGH YIELD:** Rabies management in endemic area (bat bite): 5-dose vaccine + rabies immunoglobulin regardless of prior vaccination. This has been recalled.

Rapid Recall — Principles of Microbiology

Topic / Prompt	Key Fact / Answer
Key opsonins	IgG (most effective) and C3b
Splenectomy → risk from	Encapsulated organisms: S. pneumoniae (#1), H. influenzae, N. meningitidis
C5–9 deficiency	Recurrent Neisserial infections
Commonest cause of hospital bacteraemia	Cannulation (S. aureus + S. epidermidis)
Alcohol gel does NOT kill	C. difficile spores and norovirus
Gold standard sterilisation	Autoclaving (134°C / 3 min)
Malaria stain	Giemsa
TB stain	Ziehl–Neelsen (acid-fast bacilli)
Gold standard for Chlamydia diagnosis	NAAT / PCR
Live vaccines (know these)	MMR, BCG, oral polio, varicella, rotavirus, yellow fever, nasal flu
Anti-D timing	Within 72 hours of sensitising event
IgM indicates	Acute / recent infection

4B. Bacterial Pathogens

Streptococcus pyogenes (Group A Strep — GAS)

- **Gram+ cocci in chains.** β-haemolytic. Key virulence factor: **M protein** (anti-phagocytic)
- **Infections:** Pharyngitis/tonsillitis, scarlet fever (erythrogenic toxin → sandpaper rash + strawberry tongue), impetigo, erysipelas, cellulitis, **necrotising fasciitis** (Type II), streptococcal TSS
- **Post-infectious:** Rheumatic fever (2–4 weeks post-PHARYNGITIS only — molecular mimicry). Post-streptococcal glomerulonephritis (1–3 weeks post-pharyngitis OR skin infection)
- **Treatment:** Penicillin V (pharyngitis), benzylpenicillin IV (severe). ASO titre for post-infectious complications

⚡ **EXAM TIP:** Multiorgan failure + TSS in child = S. pyogenes (GAS). Rheumatic fever follows PHARYNGITIS only, not skin infection. GN can follow either.

Streptococcus pneumoniae (Pneumococcus)

- **Gram+ diplococci (lancet-shaped).** α-haemolytic. **Optochin-sensitive** + bile-soluble. Key virulence factor: polysaccharide capsule
- **Commonest cause of:** Community-acquired pneumonia (CAP), adult bacterial meningitis, OPSI, otitis media
- **Diagnosis:** Sputum/blood culture, urinary pneumococcal antigen (useful even after antibiotics). CSF: Gram+ diplococci, low glucose, high protein
- **Treatment:** Amoxicillin (CAP), ceftriaxone (meningitis). Prevention: PCV13 + PPV23 vaccines

💡 **HIGH YIELD:** S. pneumoniae = commonest cause of CAP and adult meningitis. Asked as the organism causing consolidation pneumonia in multiple sittings. Urinary antigen useful even after antibiotics started.

Staphylococcus aureus

- **Gram+ cocci in clusters.** Coagulase-POSITIVE. Catalase-positive. Golden colonies on agar. Ferments mannitol (yellow on MSA)
- **Virulence:** Protein A (binds IgG Fc → prevents opsonisation), coagulase, catalase, β-lactamase (>90% penicillin-resistant)
- **Toxins:** TSST-1 (superantigen → TSS), exfoliative toxins (scalded skin syndrome), PVL (necrotising pneumonia), **heat-stable enterotoxins** (food poisoning: preformed toxin → rapid onset 1–6h)
- **Infections:** Skin/soft tissue (#1), osteomyelitis (commonest cause all ages), **acute endocarditis** (esp. IVDU → tricuspid valve), post-influenza pneumonia, bacteraemia
- **MRSA:** mecA gene → altered PBP2a → resistant to ALL β-lactams. Treatment: **vancomycin** (IV). Decolonisation: nasal mupirocin + chlorhexidine wash
- **Treatment (MSSA):** Flucloxacillin (first-line — β-lactamase stable)

⚡ **EXAM TIP:** Food poisoning with vomiting 1–6h after eating = S. aureus PREFORMED heat-stable toxin (asked directly). IVDU + endocarditis = S. aureus. S. aureus virulence factor = Protein A.

Staphylococcus epidermidis

- **Gram+ cocci in clusters.** Coagulase-NEGATIVE. Most abundant skin commensal
- **Key feature:** Biofilm formation on plastic/metal → prosthetic device infections, IV line infections, CSF shunt infections, prosthetic valve endocarditis (commonest cause)
- Single positive blood culture may = contamination. Multiple positives needed for confidence

💡 **HIGH YIELD:** S. epidermidis = coagulase-NEGATIVE = line/prosthetic infections. Asked directly in past papers as the organism in lower limb cellulitis with IV access.

Staphylococci vs Streptococci

Feature	Staphylococci	Streptococci
Arrangement	Clusters	Chains or pairs

Catalase	POSITIVE	NEGATIVE
Key species	S. aureus (coagulase+), S. epidermidis (coagulase–)	S. pyogenes (β, Group A), S. pneumoniae (α, diplococci)
Key differentiating test	Coagulase test	Haemolysis pattern + Lancefield grouping

Tuberculosis (M. tuberculosis)

- **Acid-fast bacillus (AFB).** ZN stain. Mycolic acid-rich waxy cell wall. Extremely slow-growing. Obligate aerobe → lung apices
- **Transmission:** Aerosol (droplet nuclei). Resistance depends on **T-cell (cell-mediated) immunity** — NOT antibodies
- **Granuloma formation:** Macrophages engulf bacilli → cannot kill → granuloma with caseous necrosis. Ghon focus + hilar nodes = Ghon complex
- **Latent TB:** ~5–10% lifetime reactivation risk. HIV = greatest risk factor for reactivation
- **Clinical:** Pulmonary (cough >3 weeks, haemoptysis, night sweats, upper lobe cavitation). Renal (sterile pyuria). Spinal (Pott disease). Miliary (millet seed CXR)
- **Diagnosis:** ZN stain (sputum), GeneXpert PCR (rapid, detects rifampicin resistance), LJ culture (gold standard, 2–8 weeks), IGRA (not affected by BCG)
- **Treatment RIPE:** Rifampicin + Isoniazid + Pyrazinamide + Ethambutol (2 months) then RI (4 months). Side effects mnemonic: **R**ed (orange secretions), **I**nflamed nerves (neuropathy → give B6), **P**ainful joints (gout), **E**yes (optic neuritis)

⚡ **EXAM TIP:** TB stain = Ziehl–Neelsen (asked every sitting). Rifampicin = potent CYP450 inducer (drug interactions with OCP, warfarin). Isoniazid → peripheral neuropathy → give pyridoxine (B6).

Clostridial Infections

- All Clostridia: **Gram+ anaerobic spore-forming bacilli.** Spores resist heat, desiccation, disinfectants

Species	Disease	Key Toxin/Mechanism	Treatment
C. difficile	Pseudomembranous colitis	**Toxin B** (cytotoxin) = primary virulence factor. High-risk ABx: clindamycin, fluoroquinolones, cephalosporins	Stop offending ABx + oral vancomycin (1st line). Alcohol gel does NOT kill spores
C. perfringens	Gas gangrene	α-toxin (lecithinase) → cell membrane destruction. Crepitus. Gas on X-ray	Surgical debridement + benzylpenicillin + clindamycin
C. tetani	Tetanus (spastic paralysis)	**Tetanospasmin** blocks glycine + GABA → unopposed motor firing. Trismus = earliest sign	TIG + metronidazole + wound debridement + vaccine

💡 **HIGH YIELD:** C. difficile + associated antibiotic = clindamycin (and fluoroquinolones, cephalosporins, co-amoxiclav). Prevention of spread = soap and water hand washing (NOT alcohol gel). Both are hot topics.

Neisseria

- Both Neisseria species: **Gram– diplococci** ("kidney bean" shaped pairs)

Feature	N. meningitidis	N. gonorrhoeae
Transmission	**Respiratory droplets** (close contact)	Sexually transmitted; vertical (neonate)
Key virulence	Polysaccharide capsule; IgA protease	Pili (attachment); IgA protease; antigenic variation
Key disease	Meningitis, meningococcal septicaemia (non-blanching rash, DIC, Waterhouse–Friderichsen)	Urethritis (purulent discharge), PID, ophthalmia neonatorum (2–5 days), disseminated → septic arthritis

Diagnosis	Blood/CSF culture, PCR, latex agglutination	Gram stain (intracellular diplococci), NAAT, chocolate agar culture
Treatment	IV ceftriaxone. Pre-hospital: IM benzylpenicillin	IM ceftriaxone (single dose). Contact tracing essential
Contacts	Ciprofloxacin (single dose) for household contacts	Trace and treat all partners within 2–4 weeks

⚡ **EXAM TIP:** N. meningitidis transmission = respiratory DROPLETS (not airborne). Non-blanching rash + fever = give IM benzylpenicillin IMMEDIATELY. Group B commonest in UK. Complement C5–9 deficiency predisposes.

Bordetella pertussis (Whooping Cough)

- **Gram– coccobacillus.** Highly infectious (attack rate ~90% in household). Pertussis toxin = AB exotoxin
- **Three phases:** Catarrhal (1–2 weeks, most infectious) → Paroxysmal (2–8 weeks, whooping cough) → Convalescent (weeks–months, "100-day cough")
- **Diagnosis:** Pernasal swab (culture/PCR). Marked **lymphocytosis** on FBC. Antibiotics of LIMITED benefit once paroxysmal phase established
- **Infants:** May present with apnoea rather than classical whoop. Maternal vaccination in pregnancy protects neonates

Enterobacteriaceae & GI Gram-Negatives

Organism	Gram/Features	Key Infections	Key Facts
Klebsiella	Gram– rod, mucoid capsule	HAP/VAP, UTI, liver abscess	"Currant jelly" sputum, ESBL-producing strains increasing
Salmonella	Gram– rod, non-lactose fermenter (pale on MacConkey)	Gastroenteritis (self-limiting), typhoid (stepladder fever, rose spots), **osteomyelitis in sickle cell**	ABx NOT routinely indicated for uncomplicated GE. Typhoid: intestinal perforation in 3rd week
E. coli	Gram– rod, LACTOSE fermenter (pink on MacConkey)	UTI (#1 cause all ages), neonatal meningitis (K1 capsule = 2nd commonest after GBS), O157:H7 → HUS	Avoid ABx in EHEC/HUS (may increase Shiga toxin release)
H. pylori	Gram– spiral rod, urease+	Chronic gastritis, peptic ulcer (90–95% DU), gastric carcinoma (WHO Group 1), MALT lymphoma	Urease → ammonia → raises pH. Dx: urea breath test. Rx: PPI + 2 ABx (triple therapy)
Campylobacter jejuni	Gram– curved rod ("gull-wing")	Commonest bacterial GE in UK. **Guillain–Barré syndrome** (commonest trigger)	Undercooked poultry. ABx of limited benefit. Reactive arthritis (HLA-B27)

⚡ **EXAM TIP:** Salmonella = commonest cause of osteomyelitis in SICKLE CELL disease (asked in 3+ sittings). Campylobacter + ascending paralysis = GBS (asked directly). E. coli cholecystitis also recalled.

Legionella pneumophila

- **Gram– rod.** Thrives in warm water (20–45°C): cooling towers, air conditioning, showers. NOT person-to-person
- **Legionnaires' disease:** Atypical pneumonia + **confusion** + **diarrhoea** + **hyponatraemia** + deranged LFTs. "Relative bradycardia + confusion" is classic exam clue
- **Diagnosis:** Urinary antigen test (first-line, detects serogroup 1 only). Culture on BCYE agar
- **Treatment:** Macrolide (clarithromycin) or fluoroquinolone (levofloxacin). Notifiable disease

💡 **HIGH YIELD:** Nursing home pneumonia organism = Legionella (recalled in multiple sittings). Hyponatraemia is a key distinguishing clue in atypical pneumonia.

Pseudomonas aeruginosa

- **Gram– rod.** Obligate aerobe. Oxidase-POSITIVE. Blue-green pigment (pyocyanin), sweet/grape-like odour. Lives in MOIST hospital environments
- **Key infections:** Burns wounds, CF lung colonisation, contact lens **keratitis**, malignant otitis externa (diabetics), ecthyma gangrenosum (neutropenia)
- **Highly antibiotic-resistant.** Anti-pseudomonal agents: piperacillin-tazobactam, ceftazidime, meropenem, ciprofloxacin, gentamicin, colistin (last resort)

Chlamydia

- **Obligate intracellular bacteria** (cannot make own ATP). Biphasic life cycle: **EB** (infectious) → **RB** (replicating)

Species	Key Disease	Notes
C. trachomatis	Commonest bacterial STI. Urethritis, PID, ophthalmia neonatorum (5–14 days), reactive arthritis	Often asymptomatic (~70% women). Dx: NAAT/PCR (gold standard). Rx: doxycycline 7 days
C. psittaci	Psittacosis (atypical pneumonia)	From infected birds (parrots, pigeons). Rx: doxycycline
C. pneumoniae	Mild atypical pneumonia, pharyngitis	Person-to-person. Usually self-limiting

⚡ **EXAM TIP:** Neonatal eye discharge: onset 5–14 days = Chlamydia. Onset 2–5 days = Gonococcal. Chlamydial ophthalmia needs ORAL erythromycin (topical alone insufficient due to nasopharyngeal colonisation).

Rapid Recall — Bacterial Pathogens

Topic / Prompt	Key Fact / Answer
Staphylococci vs Streptococci differentiator	Catalase test (Staph = +, Strep = –)
S. aureus coagulase	POSITIVE (S. epidermidis = negative)
S. aureus food poisoning	Preformed heat-stable enterotoxin; onset 1–6 hours
MRSA mechanism	mecA gene → altered PBP2a → resistant to ALL β-lactams
S. pneumoniae differentiator	Optochin-sensitive + bile-soluble (α-haemolytic)
Subacute endocarditis organism	Viridans streptococci (α-haemolytic, optochin-resistant)
Acute endocarditis (IVDU)	S. aureus (tricuspid valve)
Osteomyelitis in sickle cell	Salmonella (S. aureus in all other patients)
Commonest bacterial GE (UK)	Campylobacter jejuni
Campylobacter key complication	Guillain–Barré syndrome (commonest trigger)
C. difficile first-line treatment	Oral vancomycin
Tetanospasmin mechanism	Blocks glycine + GABA → spastic paralysis
N. meningitidis transmission	Respiratory droplets (NOT airborne)
Legionella clue	Atypical pneumonia + confusion + hyponatraemia + diarrhoea
Chlamydia gold standard diagnosis	NAAT / PCR

4C. Viral Pathogens

Herpes Simplex Virus (HSV)

Feature	HSV-1	HSV-2
Primary site	Orolabial (cold sores)	Genital herpes
Latent site	Trigeminal ganglion	Sacral dorsal root ganglia (S2–S4)
Transmission	Direct contact (saliva)	Sexual; vertical (neonatal)

- **HSV encephalitis:** Most common sporadic viral encephalitis. HSV-1 → TEMPORAL lobe predilection. MRI = imaging of choice. CSF PCR = gold standard. **Start IV aciclovir IMMEDIATELY** — do NOT wait for results. Mortality >70% untreated
- **Eczema herpeticum:** Disseminated HSV in atopic eczema — dermatological emergency → urgent IV aciclovir
- **Aciclovir:** Guanosine analogue. Requires viral thymidine kinase for activation → selective. Side effect: crystal nephropathy (ensure hydration)
- **Erythema multiforme:** HSV is the commonest trigger (target lesions on palms/soles)

Varicella-Zoster Virus (VZV)

- **Chickenpox:** Incubation 10–21 days. Infectious from 48h BEFORE rash until ALL vesicles crusted. Crops at DIFFERENT stages (cf. smallpox = same stage). Centripetal distribution
- **VZV pneumonia:** Commonest serious ADULT complication (especially smokers, pregnant, immunocompromised)
- **Pregnancy:** <20 weeks → fetal varicella syndrome (1–2%). Around delivery (−5 to +2 days) → neonatal varicella → give VZIG
- **Shingles (herpes zoster):** VZV reactivation from dorsal root ganglia. Dermatomal, unilateral, does NOT cross midline
- **Hutchinson's sign:** Nose tip involvement = V1 (nasociliary nerve) → HIGH risk corneal involvement → urgent ophthalmology
- **Ramsay Hunt syndrome:** VZV in geniculate ganglion. Triad: CN VII palsy + ear vesicles + sensorineural hearing loss
- **Post-herpetic neuralgia:** Commonest shingles complication. Risk increases with age. Treat: amitriptyline, gabapentin

HIV

- **RNA retrovirus.** gp120 binds CD4 + co-receptor (CCR5/CXCR4). Reverse transcriptase → integrase → provirus
- **Seroconversion (2–6 weeks):** Glandular fever-like illness. Antibody tests may be NEGATIVE (window period)
- **CD4 <200 = AIDS.** PCP = commonest AIDS-defining illness (dry cough, bilateral ground-glass CXR, raised LDH, Rx: co-trimoxazole)
- **4th-generation test:** Detects both HIV Ag (p24) + Ab. Window ~4 weeks. First-line screening
- **ART:** ≥3 drugs from ≥2 classes. Treat ALL patients regardless of CD4. PEP within 72h of exposure
- **Needlestick risk:** HIV ~0.3%, HCV ~3%, HBV ~30%. Vertical transmission: ~25% → <1% with ART + C-section

AIDS-Defining Infection	Organism	CD4 Threshold	Key Feature
PCP	Pneumocystis jirovecii	<200	Bilateral ground-glass, raised LDH. Rx: co-trimoxazole
Cerebral toxoplasmosis	T. gondii	<100	Ring-enhancing lesions on CT/MRI
CMV retinitis	CMV	<50	"Pizza pie" fundus. Rx: ganciclovir
Cryptococcal meningitis	C. neoformans	<100	India ink +, raised CSF pressure. Rx: amphotericin B

Oesophageal candidiasis	Candida albicans	<200	Dysphagia. Rx: fluconazole

> 💡 **HIGH YIELD:** HIV patient with respiratory symptoms = PCP (Pneumocystis jirovecii). Past paper asks the predominant cell in PCP pneumonia = plasma cells/macrophages (foamy exudate).

Hepatitis

Feature	Hep A	Hep B	Hep C
Virus	RNA picornavirus	DNA hepadnavirus	RNA flavivirus
Transmission	Faecal–oral	Blood, sexual, vertical	Blood-borne (IVDU commonest UK)
Incubation	2–6 weeks	6 wk–6 months	2 wk–6 months
Chronicity	**NEVER**	5–10% adults; **90% neonates**	**75–85%** (highest)
Diagnosis	Anti-HAV IgM (acute)	HBsAg (infection); anti-HBc IgM (acute); HBeAg (high infectivity)	Anti-HCV + HCV RNA (active)
Vaccine	Yes (inactivated)	Yes (recombinant HBsAg)	**NO vaccine**
Cirrhosis / HCC	No	Yes	Yes
Treatment	Supportive	Interferon / antivirals	DAAs (>95% cure)

- **Hep B serology key:** HBsAg = infection. Anti-HBs = immunity. **Vaccinated = anti-HBs ONLY** (no anti-HBc). HBeAg = HIGH infectivity
- **Hep D (delta virus):** Requires HBsAg to replicate — only infects HBV+ patients. Superinfection accelerates cirrhosis

> ⚡ **EXAM TIP:** Hepatitis B diagnostic marker = HBsAg (recalled). Vaccinated patients have anti-HBs ONLY. Key distinction: Hep A = NEVER chronic; Hep C = 75–85% chronic (highest rate).

Measles, Mumps, Rubella

Feature	Measles	Mumps	Rubella
Virus family	Paramyxovirus	Paramyxovirus	Togavirus
Incubation	10–14 days	14–21 days	14–21 days
Key sign	**Koplik spots** + 3 C's (cough, coryza, conjunctivitis)	**Parotid swelling**	**Post-auricular + suboccipital LNs**
Rash	Maculopapular, craniocaudal	Usually none	Faint maculopapular, 3 days
Key complication	**Pneumonia** (commonest cause of death). SSPE (7–10 yrs later, fatal)	**Orchitis** (post-pubertal, usually unilateral). **Deafness** (commonest acquired SN deafness in children)	**Congenital rubella syndrome:** deafness + PDA + cataracts. 1st trimester = up to 90% risk
Vaccine	MMR (live)	MMR (live)	MMR (live) — contraindicated in pregnancy

> ⚡ **EXAM TIP:** Measles: Koplik spots are PATHOGNOMONIC. Rubella in pregnancy: triad = deafness + cardiac (PDA) + cataracts. SSPE occurs 7–10 years post-measles — fatal progressive neurodegeneration.

Respiratory Viruses

Virus	Type	Key Association	Treatment

Rhinovirus	Picornavirus (>100 serotypes)	Common cold. No vaccine possible	Supportive
Influenza	Orthomyxovirus	Seasonal flu. **Drift** = epidemics; **Shift** = pandemics (A only)	Oseltamivir (within 48h). Annual vaccine
Parainfluenza	Paramyxovirus	Commonest cause of **croup** (children 6mo–3yr). Steeple sign on X-ray	Oral dexamethasone
RSV	Paramyxovirus	Commonest cause of **bronchiolitis** (<1 yr). Winter epidemics	Supportive ONLY (bronchodilators/steroids do NOT work). Palivizumab for prophylaxis

HIGH YIELD: Influenza: DRIFT = minor = epidemics. SHIFT = major = pandemics (A ONLY). This is the most frequently tested microbiology concept. Shift = reassortment between subtypes.

- **Influenza attachment:** Haemagglutinin (HA) binds sialic acid on respiratory epithelium. Neuraminidase (NA) aids virion release. Oseltamivir = neuraminidase inhibitor
- **Coxsackievirus B** = commonest cause of viral myocarditis (recalled in past papers)

GI Viruses

Feature	Rotavirus	Norovirus
Virus type	Reovirus (dsRNA)	Calicivirus (ssRNA)
Peak age	6 months–2 years	ALL ages
Key symptom	**Profuse watery diarrhoea**	**Projectile vomiting**
Duration	3–8 days	12–72 hours
Setting	Community (childhood)	**Outbreaks** (hospitals, cruise ships)
Vaccine	Yes (oral, live — 8+12 weeks)	NO vaccine
Alcohol gel effective?	Probably not	**NO** (non-enveloped virus)

Rapid Recall — Viral Pathogens

Topic / Prompt	Key Fact / Answer
HSV encephalitis imaging	MRI (temporal lobe). CSF PCR = gold standard. Start aciclovir IMMEDIATELY
Chickenpox incubation	10–21 days. Infectious 48h before rash until all crusted
Shingles key feature	Dermatomal, unilateral, does NOT cross midline
Hutchinson's sign	Nose tip = V1 involvement → ophthalmology emergency
HIV CD4 <200	AIDS. PCP = commonest AIDS-defining illness
Needlestick risk (HIV:HCV:HBV)	0.3% : 3% : 30%
Hep A chronicity	NEVER chronic
Hep C chronicity	75–85% (highest of all)
Hep B vaccinated serology	Anti-HBs ONLY (no anti-HBc)
Influenza drift vs shift	Drift = epidemics. Shift = pandemics (A only)
Influenza attachment molecule	Haemagglutinin (HA)
Commonest cause of croup	Parainfluenza

Commonest cause of bronchiolitis	RSV (<1 year). Bronchodilators/steroids DON’T work
Myocarditis organism	Coxsackievirus B
Rotavirus vaccine schedule	Oral, live, at 8 and 12 weeks

4D. Fungi, Parasites & Malaria

Candida

- **Candida albicans:** Most common pathogenic yeast. Normal flora (mouth, GI, vagina). Dimorphic (yeasts + pseudohyphae)
- **Predisposing factors:** Immunosuppression (HIV, chemo), antibiotics (disrupt flora), diabetes, indwelling devices, pregnancy, extremes of age
- **Clinical:** Oral thrush (white patches), oesophageal candidiasis (AIDS-defining), vulvovaginal candidiasis, intertrigo, candidaemia (line-related)
- **Diagnosis:** Clinical + KOH (pseudohyphae). Germ tube test differentiates C. albicans. Culture on Sabouraud agar
- **Treatment:** Nystatin (topical only). Fluconazole (systemic). Echinocandin (caspofungin) for candidaemia

Cryptococcus neoformans

- **Encapsulated yeast.** Found in soil contaminated with **pigeon droppings**. Transmission: inhalation
- **Strongly associated with HIV/AIDS (CD4 <100).** Causes subacute/chronic meningitis: headache, confusion, raised ICP
- **Diagnosis:** India ink (capsule halo), CrAg (highly sensitive), CSF analysis (lymphocytic, low glucose)
- **Treatment:** Amphotericin B + flucytosine (induction) → fluconazole (consolidation/maintenance). Serial LP for raised ICP

⚡ **EXAM TIP:** Pigeon fancier + immunocompromised + meningitis = Cryptococcus. India ink shows capsule halo. CrAg has largely replaced India ink.

Dermatophytes

- Three genera: **Trichophyton, Microsporum, Epidermophyton.** Infect keratinised tissue (skin, hair, nails). Produce keratinases
- **Tinea pedis** (athlete's foot) = commonest dermatophyte infection. Tinea corporis (ringworm) = annular plaque with raised scaly border + central clearing
- **Diagnosis:** Skin scraping from **active advancing edge** + KOH → branching hyphae. Culture on Sabouraud agar
- **Treatment:** Topical azoles/terbinafine for localised. **Systemic required** for tinea capitis (always) and onychomycosis

Helminths (Worms)

Worm	Transmission	Cardinal Feature	Diagnosis	Treatment
Threadworm (Enterobius)	Faecal–oral (eggs). Itch-scratch-oral cycle	**Perianal itch** (nocturnal). Commonest UK helminth	**Sellotape/Scotch tape test** (NOT stool)	Mebendazole + treat WHOLE family + hygiene
Roundworm (Ascaris)	Faecal–oral (eggs from soil)	Gut → liver → lungs → gut. **Löffler syndrome** (eosinophilic pneumonitis). Intestinal obstruction	Stool microscopy (eggs)	Albendazole (single dose)
Hookworm (Ancylostoma/Necator)	Skin penetration (larvae from soil)	**Iron-deficiency anaemia** (commonest cause worldwide). Ground itch at entry	Stool microscopy (eggs)	Albendazole + iron supplementation
Pork tapeworm (T. solium)	Ingestion of undercooked pork (larvae) OR eggs (cysticercosis)	**Neurocysticercosis** = commonest cause of acquired epilepsy worldwide. Seizures	Stool (eggs/proglottids); CT/MRI brain for NCC	Praziquantel (intestinal). Albendazole + steroids (NCC)

Beef tapeworm (T. saginata)	Ingestion of undercooked beef	Usually mild. Motile proglottids in stool	Stool (eggs/proglottids)	Praziquantel

⚡ **EXAM TIP:** Giardia lamblia attachment = suckling disc (recalled directly). Hookworm = iron-deficiency anaemia worldwide. Threadworm diagnosis = Sellotape test (NOT routine stool sample).

Malaria

- **Plasmodium species** transmitted by female **Anopheles** mosquitoes. **P. falciparum** = most dangerous, most deaths

Species	Key Features	Recurrence
P. falciparum	Most severe. Cerebral malaria. Multi-organ failure. Infects ALL RBC ages → high parasitaemia. PfEMP-1 → sequestration	No hypnozoites (recrudescence from incomplete Rx)
P. vivax / P. ovale	Benign tertian (48h cycle). Enlarged RBCs, Schüffner's dots	YES — dormant **hypnozoites** in liver → relapses months–years later
P. malariae	Quartan (72h cycle). Mild	No hypnozoites but very low-level persistence possible

- **Diagnosis: Thick and thin blood films** (gold standard). Thick = detection. Thin = species ID + parasitaemia %. **Giemsa stain.** Serial films needed (single negative does NOT exclude). RDTs available
- **P. falciparum blood film:** Ring forms predominate, multiple rings per RBC, **banana/crescent-shaped gametocytes** (pathognomonic)
- **Severe falciparum features:** Cerebral malaria, severe anaemia (Hb <5), renal failure, ARDS, hypoglycaemia, acidosis, DIC, hyperparasitaemia
- **Treatment principles:** If species unknown → treat as P. falciparum. Severe: **IV artesunate** (first-line). P. vivax/ovale: chloroquine + **primaquine** (kills hypnozoites — check G6PD first, causes haemolysis in deficiency)
- **Returning traveller rule:** ANY fever within 1 year of travel to endemic area → investigate for malaria. Prophylaxis does NOT fully prevent infection

💡 **HIGH YIELD:** Malaria stain = GIEMSA (asked every sitting). P. falciparum: renal failure + fever + Nigeria travel = asked directly. Primaquine kills hypnozoites but causes haemolysis in G6PD deficiency.

The Immunocompromised Patient

Immune Defect	Examples	Associated Infections
Neutropenia	Chemotherapy, aplastic anaemia	Gram-negatives (E. coli, Pseudomonas, Klebsiella), S. aureus, Candida, Aspergillus
T-cell deficiency	HIV/AIDS, transplant immunosuppression	PCP, CMV, Cryptococcus, Toxoplasma, TB, Candida
B-cell / antibody deficiency	Hypogammaglobulinaemia, CLL, myeloma	Encapsulated bacteria (S. pneumoniae, H. influenzae, N. meningitidis)
Complement deficiency	Inherited complement disorders	N. meningitidis (terminal C5–9), S. pneumoniae
Splenectomy / asplenia	Post-splenectomy, sickle cell	Encapsulated: S. pneumoniae, H. influenzae, N. meningitidis, severe malaria

Rapid Recall — Fungi, Parasites & Malaria

Topic / Prompt	Key Fact / Answer

Candida risk factors	Antibiotics (flora disruption), immunosuppression, diabetes, devices
Cryptococcus association	Pigeon droppings + HIV (CD4 <100) + meningitis
India ink shows	Encapsulated yeast with clear capsule halo (Cryptococcus)
Tinea pedis	Commonest dermatophyte infection (athlete's foot)
Threadworm diagnosis	Sellotape (Scotch tape) test — NOT routine stool sample
Hookworm hallmark	Iron-deficiency anaemia (commonest cause worldwide)
Neurocysticercosis	Commonest cause of acquired epilepsy worldwide (T. solium)
Giardia attachment	Suckling disc
Malaria stain	GIEMSA stain on thick/thin blood films
P. falciparum gametocyte shape	Banana / crescent-shaped (pathognomonic)
Hypnozoites (liver dormancy)	P. vivax and P. ovale → primaquine for radical cure
Primaquine contraindication	G6PD deficiency (causes haemolysis)
Fever in returning traveller	Investigate for malaria if within 1 year of endemic travel
Severe malaria first-line	IV artesunate

Chapter 5

PATHOLOGY

~10% of exam | ~18 questions

5.1 The Inflammatory Response

Acute Inflammation

Acute inflammation is the immediate, short-lived (hours to days) response of vascularised tissue to injury. It aims to eliminate the cause of injury, clear damaged tissue, and initiate repair.

Five Cardinal Signs

Sign	Latin	Mechanism
Redness	Rubor	Vasodilation → increased blood flow
Heat	Calor	Vasodilation + increased metabolic activity
Swelling	Tumor	Increased vascular permeability → exudation of fluid (oedema)
Pain	Dolor	Bradykinin, prostaglandins stimulate nerve endings; pressure from swelling
Loss of function	Functio laesa	Combination of pain, swelling, and tissue destruction

Vascular Changes & Cellular Events

- Transient vasoconstriction (seconds) → sustained vasodilation (histamine, NO-mediated)
- Increased vascular permeability: endothelial cell contraction → protein-rich exudate leaks into interstitium
- Stasis: slowed blood flow → leucocyte margination

Leucocyte Recruitment (Multi-Step Process)

Step	Process	Key Molecules
1	Margination	Leucocytes move to vessel periphery as flow slows
2	Rolling	Loose adhesion via selectins (E-selectin, P-selectin, L-selectin)
3	Adhesion	Firm attachment via integrins binding ICAM-1 / VCAM-1
4	Transmigration	Diapedesis through endothelial gaps (postcapillary venules)
5	Chemotaxis	Directed migration along gradient (C5a, LTB4, IL-8, bacterial peptides)

> ⚡ **EXAM TIP:** Selectins = Rolling; Integrins = Adhesion. "Selectins Select where to roll; Integrins Integrate (firmly attach)." Frequently tested.

Phagocytosis

- Recognition & attachment: opsonins (IgG, C3b) coat microbes → bind Fc and C3b receptors
- Engulfment: pseudopods form phagosome
- **Killing:** Oxygen-dependent (respiratory burst → superoxide, H_2O_2, myeloperoxidase system) and Oxygen-independent (lysozyme, defensins, lactoferrin)

Chemical Mediators of Acute Inflammation

Mediator	Source	Key Actions
Histamine	Mast cells, basophils, platelets	Vasodilation; ↑ vascular permeability; bronchoconstriction; immediate (minutes)
Bradykinin	Kinin system (plasma)	Pain; vasodilation; ↑ permeability; smooth muscle contraction
Prostaglandins (PGE_2, PGI_2)	Arachidonic acid via COX	Pain; fever (PGE_2 on hypothalamus); vasodilation; potentiate oedema

Leukotrienes (LTB_4, $LTC_4/D_4/E_4$)	Arachidonic acid via lipoxygenase	LTB_4: chemotaxis; $LTC_4/D_4/E_4$: bronchoconstriction, vasoconstriction, ↑ permeability (SRS-A)
Thromboxane A_2	Platelets via COX	Platelet aggregation; vasoconstriction
Complement (C3a, C5a)	Complement cascade	C3a/C5a: anaphylatoxins; C5a: chemotaxis; C3b: opsonisation; C5b-9 MAC → lysis
Cytokines (TNF-α, IL-1, IL-6)	Macrophages, T cells	Fever; acute phase proteins; leucocyte & endothelial activation
Nitric oxide (NO)	Endothelium, macrophages	Vasodilation; microbicidal

💡 **HIGH YIELD:** Arachidonic acid metabolism: NSAIDs inhibit COX → reduce prostaglandins (pain, fever). Corticosteroids inhibit phospholipase A_2 → block entire pathway. Montelukast = leukotriene receptor antagonist (asthma). Tested repeatedly.

Outcomes of Acute Inflammation

- Resolution: complete restoration if injury limited and tissue can regenerate
- Abscess formation: walled-off pus (dead neutrophils, liquefied tissue)
- Chronic inflammation: if cause persists or acute response inadequate
- Fibrosis / scarring: if regeneration not possible

Exudate vs Transudate

Feature	Exudate	Transudate
Mechanism	↑ vascular permeability (inflammation)	↑ hydrostatic pressure OR ↓ oncotic pressure
Protein	>30 g/L	<30 g/L
Specific gravity	>1.020	<1.012
Cells	Many inflammatory cells	Few cells
LDH	High	Low
Causes	Infection, inflammation, malignancy	Heart failure, cirrhosis, nephrotic syndrome

⚡ **EXAM TIP:** Light's criteria for pleural exudate (ANY one met): (1) Pleural protein / serum protein >0.5; (2) Pleural LDH / serum LDH >0.6; (3) Pleural LDH > 2/3 upper limit of normal serum LDH.

Chronic Inflammation

Prolonged process (weeks to years) where tissue destruction, inflammation, and attempted repair occur simultaneously. Macrophages are the DOMINANT cell.

- Causes: persistent infection (TB, fungi), toxic agents (silica, asbestos), autoimmune disease (RA, SLE, Crohn's)

Key Cells of Chronic Inflammation

Cell Type	Role
Macrophages	Dominant cell; activated by IFN-γ; phagocytosis; antigen presentation; secrete TNF, IL-1
Lymphocytes	T cells activate macrophages (IFN-γ); B cells → antibody production
Plasma cells	Antibody-secreting B cells; prominent in chronic infections
Eosinophils	Parasites and allergic reactions; release major basic protein
Fibroblasts	Produce collagen and ECM → fibrosis and scarring
Giant cells	Fused macrophages: Langhans (TB), foreign body type, Touton (fat necrosis)

Granulomatous Inflammation

Granulomas = organised collections of activated macrophages (epithelioid cells) ± multinucleated giant cells, surrounded by lymphocytes.

Type	Histology	Examples
Caseating	Central caseous necrosis; Langhans giant cells (nuclei in horseshoe)	TB (classic); fungal infections
Non-caseating	No central necrosis; well-formed	Sarcoidosis; Crohn's; berylliosis
Foreign body	Giant cells with scattered nuclei; foreign material	Suture, talc, silicone, splinters
Suppurative	Central neutrophilic abscess	Cat-scratch disease

⚡ **EXAM TIP:** Caseating granuloma = TB until proven otherwise. Non-caseating = broader differential (sarcoidosis, Crohn's, berylliosis). Classic distinction question.

Inflammatory Markers: CRP, RF, ANF/ANA

Marker	Key Facts
CRP	Acute phase protein; liver produces in response to IL-6. Rises 6–12h, peaks 48h, t½ ~19h. Non-specific. Bacterial infection often >100 mg/L. Binds phosphocholine → activates complement → opsonisation.
ESR	Rate RBCs settle in 1h. Elevated by fibrinogen/Ig (rouleaux). Slower than CRP. Markedly raised: temporal arteritis, myeloma (often >100).
Rheumatoid Factor	IgM antibody against Fc of IgG. Positive ~70% RA. NOT specific: also SLE, Sjögren's, Hep C, endocarditis, elderly. ~30% RA is RF-negative.
ANA (ANF)	Antibodies against nuclear components. >95% SLE positive (sensitive). NOT specific. Reported as titre + pattern.

Specific Autoantibodies

Antibody	Disease Association
Anti-dsDNA	SLE (highly specific); correlates with disease activity and lupus nephritis
Anti-Smith	SLE (very specific, less sensitive)
Anti-Ro (SSA) / Anti-La (SSB)	Sjögren's syndrome; neonatal lupus
Anti-centromere	Limited cutaneous systemic sclerosis (CREST)
Anti-Scl-70	Diffuse systemic sclerosis
Anti-Jo-1	Polymyositis / dermatomyositis
Anti-histone	Drug-induced lupus
Anti-CCP	RA (more specific than RF; ~95% specificity)
c-ANCA (anti-PR3)	GPA (Wegener's granulomatosis)
p-ANCA (anti-MPO)	MPA; EGPA (Churg–Strauss)

💡 **HIGH YIELD:** ANA is SENSITIVE but not specific for SLE. Anti-dsDNA is SPECIFIC for SLE. Use ANA for screening; specific antibodies for confirmation.

Rapid Recall — Inflammatory Response

Topic / Prompt	Key Fact / Answer
Five cardinal signs	Rubor, calor, tumor, dolor, functio laesa

Selectins vs integrins	Selectins = rolling; integrins = firm adhesion
Opsonins	IgG and C3b
Oxygen-dependent killing	Respiratory burst: superoxide, H_2O_2, myeloperoxidase
NSAIDs mechanism	COX inhibition → ↓ prostaglandins
Corticosteroids mechanism	Phospholipase A_2 inhibition → blocks PGs AND leukotrienes
Exudate vs transudate protein	Exudate >30 g/L; transudate <30 g/L
Dominant cell — chronic inflammation	Macrophage
Caseating granuloma	TB (until proven otherwise)
CRP trigger cytokine	IL-6
RF definition	IgM against Fc portion of IgG
Most specific antibody for SLE	Anti-dsDNA
Anti-CCP	RA (more specific than RF)
c-ANCA (anti-PR3)	GPA (Wegener's)

5.2 The Immune Response

Innate (Non-Specific) Immunity

First line of defence; rapid (minutes–hours); no memory; present from birth.

Component	Details
Physical barriers	Skin; mucous membranes; mucociliary escalator; urinary flushing
Chemical barriers	Gastric acid; lysozyme (tears, saliva); defensins; sebum
Cellular	Neutrophils (first responders); macrophages; NK cells; dendritic cells; mast cells
Humoral	Complement system; acute phase proteins (CRP); interferons (antiviral)
Pattern recognition	TLRs on macrophages/DCs recognise PAMPs

Adaptive (Specific) Immunity

Slower onset (days–weeks); highly specific; generates immunological memory.

- Cell-mediated: T lymphocytes (CD4+ helper, CD8+ cytotoxic) → intracellular pathogens, transplant rejection, tumour surveillance
- Humoral: B lymphocytes → plasma cells → antibodies → extracellular pathogens, complement activation, opsonisation

Immunoglobulin Classes

Class	Key Features
IgG	Most abundant (75%); crosses placenta; secondary response; opsonisation; complement activation (classical)
IgM	Largest (pentamer); first produced (primary response); strong complement activator; does NOT cross placenta; isoagglutinins
IgA	Mucosal immunity (secretory IgA: saliva, tears, breast milk, gut); dimer with J-chain + secretory component
IgE	Allergic reactions; binds mast cells (FcεRI); parasites; Type I hypersensitivity; lowest serum level
IgD	B cell surface receptor; role in B cell activation; very low serum levels

> **HIGH YIELD:** Mnemonic: GAMED — IgG (crosses placenta), IgA (mucosal), IgM (first response, pentamer), IgE (allergy/parasites), IgD (B cell surface).

T-Cell Subsets

Subset	Marker	Function
Th1	CD4+	Activate macrophages (IFN-γ); cell-mediated immunity; intracellular pathogens
Th2	CD4+	Activate B cells & eosinophils (IL-4, IL-5, IL-13); humoral immunity; parasites; allergy
Cytotoxic	CD8+	Directly kill virus-infected/tumour cells via perforin/granzymes
Treg	CD4+ CD25+ FoxP3+	Suppress immune responses; self-tolerance; prevent autoimmunity
Th17	CD4+	Neutrophil recruitment (IL-17); mucosal defence; implicated in autoimmune disease

Hypersensitivity Reactions — Gell & Coombs Classification

	Type I	Type II	Type III	Type IV

Name	Immediate / Anaphylactic	Cytotoxic / Antibody-mediated	Immune complex	Delayed (cell-mediated)
Timing	Minutes	Hours–days	Hours–days (4–10h)	24–72 hours
Mediator	IgE	IgG or IgM	Ag-Ab complexes (IgG/IgM)	T cells (CD4+ Th1, CD8+)
Examples	Anaphylaxis, hay fever, asthma, urticaria, food allergy	AIHA, Goodpasture's, transfusion, Graves', MG, HDN, ITP	SLE, post-strep GN, serum sickness, PAN, farmer's lung	Contact dermatitis, Mantoux, TB, sarcoidosis, Crohn's, transplant rejection

Type I: Anaphylaxis (Detail)

- Sensitisation: allergen → Th2 → IL-4 → B cell class-switch to IgE → IgE binds FcεRI on mast cells/basophils
- Re-exposure: allergen cross-links IgE → mast cell degranulation
- Immediate phase (min): histamine → vasodilation, bronchoconstriction, ↑ permeability
- Late phase (4–8h): leukotrienes, prostaglandins, cytokines → eosinophil recruitment

Feature	Details
Triggers	Foods (peanuts, shellfish), insect stings, drugs (penicillin, NSAIDs), latex, contrast media
Pathophysiology	Massive mast cell degranulation → histamine + leukotrienes → vasodilation, bronchoconstriction, shock
Diagnosis	Clinical; serum mast cell tryptase (take at 1h, 6h, and >24h baseline)
First-line Rx	IM ADRENALINE 1:1000 — Adult 0.5 mg (500 mcg) IM anterolateral thigh; repeat every 5 min
Adjuncts	High-flow O_2; IV fluids; chlorphenamine 10 mg IV; hydrocortisone 200 mg IV; neb salbutamol

Anaphylaxis vs Anaphylactoid Reactions

Feature	Anaphylaxis (True)	Anaphylactoid
Mechanism	IgE-mediated (Type I)	Direct mast cell degranulation; NOT IgE
Prior sensitisation	Required	NOT required (first exposure)
Clinical presentation	Identical	Identical (indistinguishable)
Common triggers	Penicillin, foods, stings	Radiocontrast, NSAIDs, opioids, vancomycin
Treatment	Same: IM adrenaline	Same: IM adrenaline

> ⚡ **EXAM TIP:** Anaphylaxis and anaphylactoid reactions are clinically indistinguishable — both treated with IM adrenaline. Key difference: IgE-mediated vs direct mast cell degranulation. Specific curriculum requirement.

Type II: Cytotoxic / Antibody-Mediated

- IgG/IgM bind cell surface or ECM antigens → 3 mechanisms: complement-dependent cytotoxicity, ADCC, or antibody-mediated cellular dysfunction

Condition	Mechanism
AIHA	IgG/IgM vs RBC antigens → complement + phagocytosis
HDN	Maternal anti-D IgG crosses placenta → attacks fetal Rh+ RBCs
Goodpasture's	Anti-GBM antibodies → GN + pulmonary haemorrhage

Graves' disease	Stimulatory TSI antibodies to TSH receptor → hyperthyroidism
Myasthenia gravis	Anti-AChR antibodies → block neuromuscular transmission
ITP	Anti-platelet antibodies → splenic destruction
Rheumatic fever	Cross-reactive anti-strep M protein Abs → valve damage (molecular mimicry)

Type III: Immune Complex

- Ag–Ab complexes deposit in tissues → complement activation (C3a, C5a) → neutrophil recruitment → tissue damage
- SLE (DNA–anti-DNA complexes), post-strep GN, serum sickness (7–14 days), PAN (Hep B), farmer's lung

Type IV: Delayed-Type Hypersensitivity

- T-cell mediated; NO antibodies; takes 24–72 hours
- CD4+ Th1 → IFN-γ → macrophage activation → granulomatous inflammation
- Examples: contact dermatitis, Mantoux test, TB, sarcoidosis, Crohn's, chronic transplant rejection, Type 1 DM

> ⚡ **EXAM TIP:** Type III hypersensitivity → low C3 and C4 (complement consumed by immune complex deposition). Past paper tested.

Rapid Recall — Immune Response

Topic / Prompt	Key Fact / Answer
IgG	Most abundant; crosses placenta; secondary response
IgM	Pentamer; first response; strong complement activator
IgA	Mucosal immunity (secretory IgA)
IgE	Allergy; mast cell binding; parasites
Type I hypersensitivity	IgE-mediated; minutes; anaphylaxis, asthma, urticaria
Type II hypersensitivity	IgG/IgM vs cell surface; AIHA, Goodpasture's, Graves', MG
Type III hypersensitivity	Immune complexes; SLE, post-strep GN, serum sickness
Type IV hypersensitivity	T-cell mediated; 24–72h; contact dermatitis, Mantoux, TB
Anaphylaxis first-line Rx	IM adrenaline 0.5 mg (1:1000) anterolateral thigh
Anaphylactoid — key difference	Direct mast cell degranulation; NOT IgE; same treatment
Tryptase timing	Take at 1h, 6h, and >24h (baseline)
Mast cell responsible for anaphylaxis	Mast cell (past paper: nut allergy → which cell?)
Type III → complement	Low C3 and C4 (consumed)
Organ accepted by immune system	Cornea (avascular → immune privilege)

5.3 Infection

The curriculum requires knowledge of typical causes, pathological processes, and investigation of common ED infections. Detailed microbiology is in Chapter 4; this section focuses on pathological principles.

Infective Pathology by System (Summary)

Infection	Common Pathogens	Pathological Process	Key Investigations
URTI	Rhinovirus, coronavirus; S. pyogenes	Mucosal inflammation; lymphoid hyperplasia	Clinical; Centor/FeverPAIN
Pneumonia	S. pneumoniae, H. influenzae, Mycoplasma, Legionella	Alveolar consolidation; neutrophilic infiltrate	CXR, sputum, blood cultures, urinary antigens
Meningitis	N. meningitidis, S. pneumoniae; neonates: GBS, E. coli	Purulent exudate in subarachnoid space (bacterial)	LP (CSF analysis), blood cultures, PCR
Encephalitis	HSV-1 (commonest)	Inflammatory infiltrate; haemorrhagic necrosis (temporal lobes)	CSF PCR (HSV DNA); MRI
Endocarditis	S. aureus (acute), S. viridans (subacute)	Vegetations on valves; emboli	Serial blood cultures ×3; echo; Duke criteria
Cellulitis	S. pyogenes (GAS), S. aureus	Spreading dermal/subcutaneous infection	Clinical; blood cultures if septic
UTI	E. coli (>80%), Proteus, Klebsiella	Bacterial urothelial colonisation; neutrophilic inflammation	Dipstick, MSU MC&S
Bone/joint	S. aureus (commonest); Salmonella (sickle cell)	Osteomyelitis: vascular compromise → necrosis; septic arthritis: purulent effusion	Blood cultures, joint aspirate, MRI

Sepsis (Sepsis-3 Definition)

- **Sepsis:** life-threatening organ dysfunction caused by dysregulated host response to infection
- **Septic shock:** sepsis + persistent hypotension requiring vasopressors (MAP ≥65) AND lactate >2 mmol/L despite adequate fluids

Pathophysiology of Sepsis

- Pro-inflammatory cytokines (TNF-α, IL-1, IL-6) → endothelial activation/damage
- NO-mediated vasodilation → distributive shock → hypotension
- Increased capillary permeability → third-spacing → oedema + hypovolaemia
- Microvascular thrombosis (DIC) → organ ischaemia
- Mitochondrial dysfunction → cytopathic hypoxia
- End result: MODS (kidney, liver, lung/ARDS, brain, coagulation)

SIRS Criteria (Reference)

Parameter	Criterion
Temperature	>38°C or <36°C
Heart rate	>90 bpm
Respiratory rate	>20/min or $PaCO_2$ <4.3 kPa
WCC	>12 or <4 ×10^9/L or >10% bands

SIRS = ≥2 criteria. Old definition: SIRS + infection = sepsis. Now superseded by Sepsis-3 / SOFA-based definition but remains useful conceptually.

Rapid Recall — Infection

Topic / Prompt	Key Fact / Answer
Commonest pneumonia organism	S. pneumoniae
Commonest UTI organism	E. coli (>80%)
Endocarditis in IVDU	S. aureus (past paper tested)
HSV encephalitis location	Temporal lobes
Osteomyelitis in sickle cell	Salmonella
Sepsis-3 definition	Life-threatening organ dysfunction from dysregulated host response to infection
Septic shock lactate threshold	>2 mmol/L despite adequate fluid resuscitation

5.4 Wound Healing

Regeneration vs Repair

Process	Definition	Outcome
Regeneration	Replacement by identical cells	Normal structure/function restored; requires proliferative capacity
Repair (fibrosis)	Replacement with connective tissue (scar)	Loss of specialised function; occurs when regeneration not possible

Cell Types by Proliferative Capacity

Category	Definition	Examples
Labile	Continuously dividing	Skin epidermis, GI epithelium, bone marrow, respiratory epithelium
Stable (quiescent)	Normally in G_0; re-enter cycle if stimulated	Hepatocytes, renal tubular cells, fibroblasts, smooth muscle
Permanent	Cannot re-enter cell cycle; replaced by scar	CNS neurones, cardiac myocytes, skeletal muscle (limited)

⚡ **EXAM TIP:** Permanent cells (neurones, cardiac myocytes) cannot regenerate. This explains why stroke and MI cause permanent functional loss → heal by fibrosis/gliosis, not regeneration.

Phases of Wound Healing

Phase	Timing	Key Events
1. Haemostasis	Seconds–minutes	Vasoconstriction; platelet plug; coagulation cascade → fibrin clot (scaffold)
2. Inflammation	Hours–days (peak 24–72h)	Neutrophils (24–48h) then macrophages (48–96h); debridement; macrophages = KEY orchestrators
3. Proliferation	Days–weeks (3–21 days)	Angiogenesis; granulation tissue; collagen synthesis (type III first); epithelialisation; wound contraction (myofibroblasts)
4. Remodelling	Weeks–months/years	Type III collagen → type I; cross-linking ↑ tensile strength; max ~80% original (never 100%)

💡 **HIGH YIELD:** Past paper: First phase of wound healing = haemostasis. First cell in inflammatory phase = neutrophil. First cell in proliferation = macrophage (orchestrator). Maturation phase = type III collagen replaced by type I. All repeatedly tested.

Primary vs Secondary Intention

Feature	Primary Intention	Secondary Intention
Description	Clean, apposed edges (sutures)	Open wound; edges not apposed; heals from base
Granulation tissue	Minimal	Extensive
Contraction	Minimal	Significant (myofibroblasts)
Scarring	Narrow, linear	Wider, irregular
Time	Faster	Slower
Infection risk	Lower	Higher
Examples	Surgical wound, laceration repair	Abscess cavity, burns, ulcers

Tertiary intention (delayed primary closure): wound left open 3–5 days (contaminated), then closed surgically once infection risk passed.

Factors Affecting Wound Healing

Factor	Effect
Infection (most important local)	Bacteria compete for nutrients, release toxins, prolong inflammation
Blood supply	Ischaemia impairs oxygen/nutrient delivery
Foreign bodies	Prolong inflammation; nidus for infection
Nutrition — Vitamin C	Essential for collagen cross-linking (proline/lysine hydroxylation). Deficiency = scurvy → poor healing, bleeding gums, old scar breakdown
Nutrition — Protein, zinc	Protein for collagen synthesis; zinc for cell proliferation
Diabetes	Microangiopathy; impaired neutrophils; neuropathy; hyperglycaemia inhibits healing
Steroids	Inhibit inflammation and collagen synthesis
Smoking	Vasoconstriction (nicotine); CO → reduced O_2; impaired fibroblast function
Age	Elderly: reduced cell proliferation, impaired immunity

⚡ **EXAM TIP:** Vitamin C is essential for collagen cross-linking. Scurvy → poor wound healing, bleeding gums, petechiae, old scar breakdown. Favourite exam question.

💡 **HIGH YIELD:** Past paper: Delayed wound healing after Caesarean section → infection (most important local factor). Also tested: steroids, diabetes, malnutrition.

Wound Healing in Specific Tissues

Tissue	Key Points
Skin	Standard phases. Scar reaches ~80% tensile strength by 3 months, never 100%. Hypertrophic scar: within wound boundaries. Keloid: extends BEYOND wound margins, does not regress, common in dark skin (ears, sternum, shoulders).
Tendon	Poor blood supply → slow healing. Intrinsic (tenocytes) + extrinsic (fibroblasts → adhesions). ~80% strength at 6 months. Early controlled mobilisation reduces adhesions.
Peripheral nerve	Wallerian degeneration: distal segment degenerates (3–7 days). Schwann cells form bands of Büngner. Regeneration ~1 mm/day (~1 inch/month). Neurotmesis requires surgical repair.
Bone	Unique: heals by REGENERATION (new bone), not scar. Stages: haematoma (0–5d) → inflammation (1–7d) → soft callus (1–3wk) → hard callus (3–12wk) → remodelling (months–years, Wolff's law).
Myocardium	Permanent cells → heals by FIBROSIS (scar), not regeneration. 3–7 days post-MI = highest rupture risk (macrophage debridement). Mature scar by ~6 weeks.
Brain	Permanent cells (CNS neurones). Heals by GLIOSIS (astrocytes), not fibrosis. Liquefactive necrosis → cystic cavity. Microglia = CNS macrophages. No collagen scar.

⚡ **EXAM TIP:** 3–7 days post-MI = highest risk of myocardial rupture (wall weakest during macrophage debridement). Rupture → tamponade (free wall), VSD (septum), acute MR (papillary muscle).

⚡ **EXAM TIP:** Nerve regeneration rate = ~1 mm/day (1 inch/month). Allows prediction of recovery time from injury to target muscle.

Bone Healing — Factors

Promotes Healing	Impairs Healing
Good blood supply	Poor blood supply (scaphoid waist, femoral neck)

Immobilisation / stability	Excessive movement / inadequate fixation
Good nutrition (Ca^{2+}, vitamin D, protein)	Malnutrition; vitamin D deficiency
Young age	Old age; osteoporosis
Appropriate weight-bearing	Infection (osteomyelitis); smoking; interposed soft tissue

Rapid Recall — Wound Healing

Topic / Prompt	Key Fact / Answer
First phase of wound healing	Haemostasis (past paper ×3+)
First cell in inflammation	Neutrophil (24–48h)
Key orchestrator of repair	Macrophage
Remodelling phase collagen change	Type III → type I (past paper ×3+)
Max tensile strength of scar	~80% of original (never 100%)
Vitamin C role	Collagen cross-linking (hydroxylation of proline/lysine)
Keloid vs hypertrophic scar	Keloid extends BEYOND wound; hypertrophic stays within
Nerve regeneration rate	~1 mm/day (~1 inch/month)
Wallerian degeneration	Distal nerve segment degenerates; Schwann cells form bands of Büngner
Bone healing — unique feature	Regeneration (new bone), NOT scar tissue
Myocardium healing	Fibrosis (permanent cells); highest rupture risk 3–7 days
Brain healing	Gliosis (astrocytes); liquefactive necrosis → cystic cavity
Delayed wound healing — C-section	Infection (most important local factor)

5.5 Haematology

Anaemia — Definition & Classification by MCV

Anaemia = reduced Hb below normal for age/sex. Males <130 g/L; females <120 g/L; pregnancy <110 g/L.

Type	MCV	Common Causes
Microcytic	<80 fL	Iron deficiency (commonest overall); thalassaemia; chronic disease (sometimes); sideroblastic; lead poisoning. Mnemonic: TAILS
Normocytic	80–100 fL	Acute blood loss; chronic disease (commonest); renal failure (↓ EPO); marrow failure/infiltration; haemolysis; mixed deficiency
Macrocytic	>100 fL	B_{12} deficiency (megaloblastic); folate deficiency; alcohol; liver disease; hypothyroidism; myelodysplasia; reticulocytosis; drugs (methotrexate, phenytoin)

> 💡 **HIGH YIELD:** Microcytic mnemonic TAILS: Thalassaemia, Anaemia of chronic disease, Iron deficiency, Lead poisoning, Sideroblastic. Macrocytic: B_{12}/folate, alcohol, liver, hypothyroid, reticulocytosis.

Iron Deficiency Anaemia

Feature	Details
Causes	Chronic blood loss (menorrhagia, GI bleed — malignancy in >50s); poor intake; malabsorption (coeliac); ↑ demand (pregnancy)
Blood film	Microcytic hypochromic RBCs; pencil cells; target cells; anisocytosis
Iron studies	Low ferritin (best single test); low serum iron; high TIBC; low transferrin saturation
Clinical	Fatigue, pallor, dyspnoea; koilonychia (spoon nails); angular stomatitis; glossitis; pica
Management	Treat cause; oral ferrous sulphate 200 mg TDS; IV iron if intolerant/malabsorption

Vitamin B_{12} Deficiency

- Causes: pernicious anaemia (anti-intrinsic factor Abs, commonest UK cause), veganism, gastrectomy, terminal ileal disease (Crohn's)
- Features: megaloblastic anaemia + neurological (subacute combined degeneration: peripheral neuropathy, dorsal column loss, corticospinal tract)
- Film: oval macrocytes, hypersegmented neutrophils (≥5 lobes)
- Rx: IM hydroxocobalamin

> ⚡ **EXAM TIP:** Always check B_{12} before giving folate. Folate alone in B_{12} deficiency can precipitate/worsen subacute combined degeneration of the cord. Classic exam point.

> 💡 **HIGH YIELD:** Past paper: Pernicious anaemia → parietal cells destroyed (produce intrinsic factor). Site = body/fundus of stomach. Tested ×3+ sittings.

Haemolytic Anaemia

- Features: ↑ reticulocytes, ↑ unconjugated bilirubin, ↑ LDH, ↓ haptoglobin, ↑ urinary urobilinogen
- Intravascular: haemoglobinuria, schistocytes (DIC, TTP/HUS, mechanical valve)
- Extravascular: splenomegaly; spherocytes (hereditary spherocytosis, AIHA)
- Direct Coombs test (DAT) positive in AIHA

> 💡 **HIGH YIELD:** Past paper: Sickle cell + anaemia + high reticulocytes → haemolytic crisis. Mefenamic acid → haemolytic anaemia (NSAID, tested ×3+). Nitrous oxide → megaloblastic anaemia (inhibits B_{12}).

Leukaemia — The Four Main Types

Type	Age	Key Features	Key Investigations
ALL	Children (peak 2–5y)	Commonest childhood cancer; bone pain, hepatosplenomegaly, CNS involvement	FBC; lymphoblasts on film; marrow biopsy; Philadelphia chr t(9;22) in ~25% adult ALL
AML	Adults (median ~65y)	Auer rods (pathognomonic); gum infiltration (M4/M5); DIC in M3 (treat with ATRA)	FBC; myeloblasts + Auer rods; cytogenetics — t(15;17) in M3
CLL	Elderly (>60y)	Commonest adult leukaemia (West); often incidental lymphocytosis; smudge cells	Lymphocytosis >5×10⁹/L; smudge cells; immunophenotyping
CML	Adults (40–60y)	Massive splenomegaly; very high WCC (often >100); basophilia; may transform to blast crisis	Philadelphia chromosome t(9;22) BCR-ABL → imatinib

⚡ **EXAM TIP:** Philadelphia chromosome t(9;22) = BCR-ABL = CML (>95%) and ~25% adult ALL. Treatment = imatinib. Auer rods = AML (pathognomonic). Both are top exam questions.

💡 **HIGH YIELD:** Past paper: Commonest childhood cancer = ALL. Commonest leukaemia in adults (West) = CLL. Both tested repeatedly.

Lymphoma

Feature	Hodgkin Lymphoma	Non-Hodgkin Lymphoma
Diagnostic cell	Reed-Sternberg (“owl-eye” binucleate)	Various subtypes
Age	Bimodal: 20–30 + >50	Any; increases with age
Spread	Contiguous nodal	Non-contiguous; extranodal more common
B symptoms	Fever, night sweats, >10% weight loss	Present in some
Associations	EBV	HIV, EBV (Burkitt), H. pylori (MALT), coeliac
Key subtypes	Mixed cellularity, nodular sclerosis	DLBCL (commonest NHL); follicular (commonest indolent); Burkitt t(8;14) c-MYC
Prognosis	Good (80–90% cure)	Variable by subtype

Multiple Myeloma

Malignant plasma cell proliferation producing monoclonal immunoglobulin (paraprotein). Clinical features = CRAB:

	Feature	Mechanism
C	Calcium (elevated)	Osteoclast activation → bone destruction → hypercalcaemia
R	Renal impairment	Light chain deposition; hypercalcaemia; dehydration; amyloidosis
A	Anaemia	Marrow infiltration → reduced erythropoiesis
B	Bone disease	Lytic lesions (punched-out); NO osteoblastic activity → bone scan may be NORMAL; fractures

- Other: recurrent infections (immunoparesis); hyperviscosity; amyloidosis; peripheral neuropathy
- Investigations: serum protein electrophoresis (M-band, usually IgG >50%); urine Bence Jones protein; serum free light chains; marrow biopsy (>10% plasma cells); skeletal survey / low-dose CT

⚡ **EXAM TIP:** Myeloma lesions are purely LYTIC. Isotope bone scan may be NORMAL (detects osteoblastic activity only). Use skeletal survey or CT. Classic exam pitfall.

> 💡 **HIGH YIELD:** Past paper: Humerus fracture in myeloma → commonest Ig = IgG. Myeloma gives NORMAL or LOW ALP (no osteoblastic activity). Tested ×2+ sittings.

Coagulation Tests

Test	Pathway	Normal	Prolonged In
PT	Extrinsic + common (VII, X, V, II, fibrinogen)	10–14s	Warfarin; liver disease; DIC; vit K deficiency; factor VII def
INR	Standardised PT	1.0	Warfarin target 2–3 (2.5–3.5 mechanical valves)
APTT	Intrinsic + common (XII, XI, IX, VIII, X, V, II, fibrinogen)	25–40s	Heparin; haemophilia A (VIII) / B (IX); DIC; lupus anticoagulant; vWD
D-dimer	Fibrin degradation	<500 ng/mL	DVT, PE, DIC, infection, malignancy (sensitive, NOT specific)

Inherited Coagulation Disorders

Disorder	Deficient Factor	Features	APTT	PT
Haemophilia A	Factor VIII (X-linked)	Haemarthroses, deep muscle haematomas	Prolonged	Normal
Haemophilia B	Factor IX (X-linked)	Clinically identical to Haemophilia A	Prolonged	Normal
von Willebrand disease	vWF (AD, usually)	Commonest inherited bleeding disorder; mucocutaneous bleeding; nosebleeds, menorrhagia	Prolonged (or normal)	Normal

> ⚡ **EXAM TIP:** Haemophilia = deep bleeding (joints, muscles). vWD / platelet disorders = mucocutaneous bleeding (nosebleeds, gums, menorrhagia). This distinction is frequently tested.

> 💡 **HIGH YIELD:** Past paper: Girl with epistaxis → coagulation test = APTT (intrinsic pathway; prolonged in haemophilia, vWD). Tested repeatedly.

DIC (Disseminated Intravascular Coagulation)

- **Pathophysiology:** widespread coagulation activation → simultaneous THROMBOSIS (microthrombi) AND HAEMORRHAGE (consumption of factors/platelets)
- Causes: sepsis (commonest), massive trauma, obstetric emergencies (abruption, amniotic fluid embolism), malignancy (AML-M3), burns, transfusion reactions
- **Lab:** ↓ platelets; prolonged PT & APTT; ↓ fibrinogen; ↑ D-dimers & FDPs; ↑ LDH; schistocytes on film
- **Management:** Treat UNDERLYING CAUSE. Supportive: platelets if <50 + bleeding; FFP; cryoprecipitate (fibrinogen); red cells

> 💡 **HIGH YIELD:** Past paper: DIC lab findings = low platelets + prolonged PT/APTT + low fibrinogen + raised D-dimers + schistocytes. Tested ×3+ sittings.

Vitamin K Deficiency

- Vitamin K required for factors II, VII, IX, X and proteins C & S. Mnemonic: "1972" = 10, 9, 7, 2
- Causes: warfarin, liver disease, malabsorption, neonatal (haemorrhagic disease of newborn), prolonged antibiotics
- Lab: prolonged PT first (factor VII has shortest half-life); APTT prolonged if severe

> ⚡ **EXAM TIP:** Past paper: Prolonged PT — which factor deficiency? Factor VII (shortest half-life; first to be depleted in vitamin K deficiency/warfarin).

Thrombophilia

Type	Condition	Details
Inherited	Factor V Leiden	Commonest inherited (~5% Caucasians); FV resistant to activated protein C; ~5× VTE risk
Inherited	Prothrombin G20210A	2nd commonest; ↑ prothrombin levels; ~3× VTE risk
Inherited	Protein C / S deficiency	Protein C inactivates Va/VIIIa; S is cofactor
Inherited	AT-III deficiency	Most thrombogenic inherited thrombophilia; heparin resistance
Acquired	Antiphospholipid syndrome	Arterial AND venous thrombosis; recurrent miscarriage; paradoxically prolongs APTT in vitro
Acquired	Malignancy	Trousseau's syndrome; mucin-secreting tumours
Acquired	OCP / pregnancy	Oestrogen ↑ clotting factors (fibrinogen, VII, X)
Acquired	Nephrotic syndrome	Loss of AT-III in urine

⚡ **EXAM TIP:** Virchow's triad: (1) Stasis; (2) Endothelial injury; (3) Hypercoagulability. Antiphospholipid syndrome causes THROMBOSIS in vivo but prolongs APTT in vitro (paradox). Classic exam question.

Bleeding Pattern Recognition

Feature	Platelet / vWD Disorder	Coagulation Factor Disorder
Bleeding type	Mucocutaneous: petechiae, purpura, gum, nosebleeds	Deep: haemarthroses, muscle haematomas
Onset after trauma	Immediate	Delayed (hours)
Petechiae	Yes	No
Haemarthroses	Rare	Characteristic
PT / APTT	Usually normal	Prolonged
Bleeding time	Prolonged	Normal

Rapid Recall — Haematology

Topic / Prompt	Key Fact / Answer
Iron deficiency — best single test	Ferritin (low)
Microcytic anaemia mnemonic	TAILS: Thalassaemia, ACD, Iron, Lead, Sideroblastic
B_{12} deficiency neurological	Subacute combined degeneration of cord
Check B_{12} before giving…	Folate (to avoid precipitating cord degeneration)
Pernicious anaemia — cells destroyed	Parietal cells (body/fundus of stomach)
Sickle cell osteomyelitis organism	Salmonella
Mefenamic acid haemolytic anaemia	Yes (NSAID; tested ×3+)
ALL — age group	Children (peak 2–5y); commonest childhood cancer
Auer rods	AML (pathognomonic)
Philadelphia chromosome	t(9;22) BCR-ABL = CML; also ~25% adult ALL → imatinib
Myeloma — CRAB	Calcium, Renal, Anaemia, Bone (lytic lesions)
Myeloma — bone scan	May be NORMAL (no osteoblastic activity)
Myeloma — commonest Ig	IgG (>50%)
Haemophilia — bleeding pattern	Deep (haemarthroses, muscles); prolonged APTT, normal PT
vWD — bleeding pattern	Mucocutaneous; commonest inherited bleeding disorder

DIC — commonest cause	Sepsis
DIC — lab findings	↓ platelets, ↑ PT/APTT, ↓ fibrinogen, ↑ D-dimers, schistocytes
Vitamin K — factors	II, VII, IX, X (“1972”)
Factor V Leiden	Commonest inherited thrombophilia; FV resistant to APC
Antiphospholipid — paradox	Thrombosis in vivo; prolongs APTT in vitro
Virchow’s triad	Stasis, endothelial injury, hypercoagulability
Girl with epistaxis — test	APTT (vWD / haemophilia screen)

Chapter 6

Evidence-Based Medicine

~5% of exam | ~9 questions

Statistics • Study Design • Critical Appraisal

Chapter Contents:

6.1 Definition & Principles of EBM

What Is Evidence-Based Medicine?

Evidence-Based Medicine (EBM) is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients (Sackett, 1996).

Three Pillars of EBM:

Pillar	Description
1. Best available research evidence	Findings from clinically relevant research — especially systematic reviews and RCTs
2. Clinical expertise	The clinician's accumulated experience, education, and clinical skills
3. Patient values and preferences	The unique preferences, concerns, and expectations each patient brings

⚡ **EXAM TIP:** EBM is NOT "cookbook medicine." It does not replace clinical judgement — it integrates best evidence with clinical expertise and patient wishes.

The Five Steps of Practising EBM

Step	Action	Detail
1	ASK	Formulate a clear clinical question using PICO format
2	ACQUIRE	Search for best evidence (Cochrane, PubMed, NICE)
3	APPRAISE	Critically evaluate validity, impact, and applicability
4	APPLY	Integrate evidence with clinical expertise and patient values
5	ASSESS	Evaluate the outcome and audit performance

The PICO Framework

Letter	Component	Example
P	Patient / Population / Problem	Adult ED patients with suspected PE
I	Intervention / Exposure	D-dimer testing
C	Comparison / Control	No D-dimer (clinical assessment alone)
O	Outcome	Sensitivity and specificity for PE diagnosis

💡 **HIGH YIELD:** PICO is a frequently tested framework. Be able to construct a PICO question from a clinical scenario. The comparison group is often omitted in simple diagnostic questions.

Hierarchy of Evidence

Level	Study Type	Strength
I (highest)	Systematic reviews & meta-analyses of RCTs	Strongest; synthesises multiple RCTs; reduces random error
II	Randomised controlled trials (RCTs)	Gold standard for interventions; controls for confounders
III	Cohort studies (prospective / retrospective)	Good for prognosis & aetiology; cannot prove causation
IV	Case-control studies	Efficient for rare diseases; retrospective; recall bias
V	Cross-sectional studies / Surveys	Prevalence data; snapshot; cannot determine causation
VI	Case reports / Case series	Lowest level; descriptive; no control group
—	Expert opinion / Narrative reviews	Not based on systematic evidence appraisal

> ⚡ **EXAM TIP:** The exam frequently asks you to rank study types. Remember: Systematic review > RCT > Cohort > Case-control > Cross-sectional > Case report > Expert opinion.

6.2 Study Methodologies

Experimental vs Observational Studies

Feature	Experimental	Observational
Definition	Investigator assigns the intervention	Investigator observes without intervening
Key types	RCT; quasi-experimental	Cohort; case-control; cross-sectional; case report
Causation	Can establish causation (RCT)	Demonstrates association only (not causation)
Ethics	Requires equipoise; some exposures cannot be randomised	Ethical for exposures that cannot be randomised (e.g. smoking)

Randomised Controlled Trials (RCTs)

- Participants randomly allocated to intervention or control group and followed prospectively
- Randomisation minimises confounding by distributing known AND unknown confounders equally
- Control group: may receive placebo, standard care, or an alternative intervention
- Gold standard for assessing interventions (highest internal validity)

Key RCT Terminology:

Feature	Definition	Purpose
Randomisation	Allocation by chance (e.g. computer-generated)	Eliminates selection bias; balances confounders
Allocation concealment	Enrolling person does not know next allocation	Prevents selection bias at recruitment (≠ blinding)
Single-blind	Participant does not know allocation	Reduces placebo effect
Double-blind	Participant AND clinician unaware	Gold standard — reduces performance + detection bias
Triple-blind	Participant, clinician, AND analyst blinded	Also reduces analysis bias
Placebo	Inert substance / sham procedure	Controls for the placebo effect
ITT analysis	All analysed in ORIGINALLY randomised group	Preserves randomisation; reflects real-world effectiveness
Per-protocol	Only compliant completers analysed	Assesses efficacy under ideal conditions; subject to bias
Crossover design	Participants receive both treatments (with washout)	Each participant = own control; fewer participants needed
Cluster randomisation	Groups (hospitals) randomised, not individuals	Used when individual randomisation is impractical
Equipoise	Genuine uncertainty about which treatment is better	Ethical prerequisite for randomisation

> ⚡ **EXAM TIP:** Allocation concealment ≠ Blinding. Allocation concealment occurs BEFORE randomisation (prevents selection bias). Blinding occurs AFTER randomisation (prevents performance/detection bias). A favourite exam distinction.

RCT Advantages: Gold standard for interventions; randomisation controls known + unknown confounders; can establish causation; blinding reduces bias; prospective design reduces recall bias.

RCT Disadvantages: Expensive and time-consuming; ethical constraints (cannot randomise harmful exposures); strict criteria may limit generalisability; attrition reduces power; Hawthorne effect; not suitable for rare outcomes.

Cohort Studies

- Group classified by EXPOSURE status → followed over time to compare outcomes

- Can be prospective (present → future) or retrospective (existing records)
- **Can calculate relative risk (RR)** and incidence rates directly
- Good for rare exposures; can study multiple outcomes from a single exposure
- Cannot prove causation — confounders may remain despite matching/adjustment

Key distinction: Prospective cohort = higher quality data but expensive/slow. Retrospective cohort = uses existing records, faster but dependent on data quality.

Case-Control Studies

- Start with OUTCOME: identify cases (with disease) and controls (without disease)
- Look BACKWARDS to compare previous exposure rates — always retrospective
- **Calculate odds ratio (OR)** — cannot calculate incidence or RR
- **Ideal for rare diseases** — most efficient design when outcomes are uncommon
- Main limitations: recall bias, selection bias, cannot establish temporal relationship

> 💡 **HIGH YIELD:** Cohort = start with EXPOSURE, follow to OUTCOME → calculate RELATIVE RISK. Case-control = start with OUTCOME, look back at EXPOSURE → calculate ODDS RATIO. This is one of the most commonly tested distinctions.

Cross-Sectional Studies (Surveys)

- Snapshot of a population at a single point in time
- **Measures prevalence** (not incidence) — good for disease burden and health planning
- Cannot establish temporal relationship (exposure and outcome measured simultaneously)
- Subject to prevalence-incidence (Neyman) bias: may miss rapidly fatal or resolving conditions

Case Reports and Case Series

- Case report = single patient; case series = group of patients with similar condition
- No control group — cannot test hypotheses; lowest level of evidence
- Useful for rare presentations; generate hypotheses; educational value

Systematic Reviews and Meta-Analyses

- **Systematic review:** Structured, comprehensive review of ALL literature on a specific question using predefined protocol
- **Meta-analysis:** Statistical technique combining results from multiple studies to produce a pooled estimate of effect
- **Forest plot:** Graphical display — each line = one study (length = 95% CI, square = point estimate, diamond = pooled result)
- **Funnel plot:** Detects publication bias — asymmetry suggests small negative studies are missing
- **Heterogeneity (I^2):** Measures how much studies differ; 0% = none; >75% = substantial

> ⚡ **EXAM TIP:** In a forest plot, if the diamond CROSSES the line of no effect (OR=1 or RR=1), the result is NOT statistically significant. Funnel plot asymmetry = suspect publication bias.

Advantages: Highest level of evidence; increases power and precision; resolves conflicting results; explicit methodology.

Limitations: Publication bias; heterogeneity ("apples and oranges"); "garbage in, garbage out"; depends on inclusion criteria chosen.

Study Design Comparison Summary

Study Design	Direction	Key Measure	Best For	Main Limitation
RCT	Prospective	RR, ARR, NNT	Testing interventions	Expensive; ethical limits

Systematic review	Retro (of studies)	Pooled estimate	Summarising evidence	Publication bias; heterogeneity
Prospective cohort	Prospective	RR, Incidence	Prognosis; rare exposures	Expensive; attrition; confounding
Retrospective cohort	Retrospective	RR (records)	As above but faster	Data quality; confounding
Case-control	Retrospective	OR	Rare diseases	Recall bias; selection bias
Cross-sectional	Snapshot	Prevalence, OR	Prevalence; planning	No temporal sequence
Case report/series	Retrospective	Descriptive	Rare presentations	No control; no hypothesis testing

6.3 Statistics in Medical Practice

Types of Data

Type	Subtype	Definition	Examples
Qualitative	Nominal	Categories with no order	Blood group (A, B, AB, O); sex; alive/dead
Qualitative	Ordinal	Categories with order but unequal intervals	Pain score (mild/mod/severe); ASA grade; GCS
Quantitative	Discrete	Countable whole numbers	Number of fractures; ED attendances
Quantitative	Continuous	Any value within a range	Height; weight; BP; temperature

⚡ **EXAM TIP:** Data type determines which statistical test to use. Parametric tests (t-test, ANOVA) require continuous, normally distributed data. Non-parametric tests are for ordinal data or non-normal distributions. Past papers ask: "Number of patients" = discrete data.

Descriptive Statistics

Measures of Central Tendency:

Measure	Definition	When to Use	Outlier Sensitivity
Mean	Sum of values ÷ number of values	Normally distributed continuous data	Highly affected
Median	Middle value when data ordered	Skewed data; ordinal data	Resistant
Mode	Most frequently occurring value	Categorical/nominal; bimodal distributions	Not affected

Measures of Spread:

Measure	Definition	Use
Range	Maximum − minimum	Simple; affected by outliers
IQR	Q3 − Q1 (middle 50% of data)	Used with median; resistant to outliers
Variance	Average of squared deviations from mean	Mathematical basis for SD
Standard deviation (SD)	Square root of variance	Used with mean; ~68% within ±1 SD, ~95% within ±2 SD, ~99.7% within ±3 SD

💡 **HIGH YIELD:** The 68–95–99.7 rule is repeatedly tested. For normally distributed data: 68% within ±1 SD, 95% within ±2 SD, 99.7% within ±3 SD. If skewed, use median + IQR (not mean + SD).

Normal (Gaussian) Distribution

- Bell-shaped, symmetrical curve: mean = median = mode
- Positively skewed = tail to right, mean > median. Negatively skewed = tail to left, mean < median

Measures of Risk and Association

The 2×2 Table (foundation of epidemiological calculations):

	Disease +	Disease −	Total
Exposure +	a (TP)	b (FP)	a + b
Exposure −	c (FN)	d (TN)	c + d
Total	a + c	b + d	N

Key Risk Measures:

Measure	Formula	Interpretation

Relative Risk (RR)	[a/(a+b)] ÷ [c/(c+d)]	Times more likely exposed group develops outcome vs unexposed. Used in cohort studies/RCTs. RR=1 = no difference
Odds Ratio (OR)	(a×d) ÷ (b×c)	Ratio of odds of exposure in cases vs controls. Used in case-control studies. Approximates RR when disease <10%
ARR	CER − EER	Absolute difference in event rates between control and intervention groups
NNT	1 / ARR	Patients to treat to prevent one additional adverse outcome. Lower = more effective
NNH	1 / ARI	Patients exposed before one additional patient is harmed
RRR	ARR / CER	Proportional reduction in risk. Can overstate benefit if baseline risk is low

⚡ **EXAM TIP:** Drug ads often quote RRR because it sounds impressive. Always convert to ARR and NNT. A 50% RRR with baseline risk 2% means ARR = 1% and NNT = 100 — not very impressive at all.

Interpreting RR and OR

Value	Interpretation
RR or OR = 1	No association between exposure and outcome
RR or OR > 1	Exposure INCREASES risk (risk factor)
RR or OR < 1	Exposure DECREASES risk (protective factor)
95% CI includes 1	NOT statistically significant (p > 0.05)
95% CI does NOT include 1	IS statistically significant (p < 0.05)

Inferential Statistics

Hypothesis Testing:

Concept	Definition
Null hypothesis (H_0)	No difference / association between groups (default assumption)
Alternative hypothesis (H_1)	There IS a difference / association
p-value	Probability of results this extreme IF H_0 were true
$p < 0.05$	Statistically significant — reject H_0
$p \geq 0.05$	Not significant — fail to reject H_0
Significance level (α)	Pre-set threshold for rejecting H_0; usually 0.05

Type I and Type II Errors:

	H_0 Actually TRUE	H_0 Actually FALSE
Reject H_0	TYPE I ERROR (α) = False positive ("crying wolf")	CORRECT: True positive (Power = 1 − β)
Fail to reject H_0	CORRECT: True negative	TYPE II ERROR (β) = False negative ("missing the wolf")

💡 **HIGH YIELD:** Type I (α) = false positive. Type II (β) = false negative. Power = 1 − β (probability of detecting a true difference). Convention: power ≥ 80%. Increased by: LARGER SAMPLE SIZE, larger effect size, higher α. Past papers ask: "How to increase power?" → Increase sample size.

Confidence Intervals:

- 95% CI = range within which we are 95% confident the true population value lies
- Wider CI = less precision (small sample). Narrower CI = more precision (large sample)

- For RR/OR: CI crossing 1 = NOT significant. For mean difference: CI crossing 0 = NOT significant
- CIs provide MORE information than p-values alone (show magnitude + precision)

Choosing the Right Statistical Test

Data Type	Comparing 2 Groups	Comparing >2 Groups	Correlation
Continuous (normal)	Unpaired t-test; Paired t-test	ANOVA	Pearson's r
Continuous (non-normal / ordinal)	Mann-Whitney U; Wilcoxon signed-rank	Kruskal-Wallis	Spearman's rank
Categorical / Nominal	Chi-squared; Fisher's exact (small n)	Chi-squared	—

> ⚡ **EXAM TIP:** Parametric tests (t-test, ANOVA, Pearson) assume normally distributed continuous data. Non-parametric tests (Mann-Whitney, Wilcoxon, Kruskal-Wallis, Spearman) make no such assumption — use for ordinal or skewed data.

6.4 Diagnostic Test Statistics

The Diagnostic 2×2 Table

	Disease Present (D+)	Disease Absent (D−)
Test Positive (T+)	a = True Positive (TP)	b = False Positive (FP)
Test Negative (T−)	c = False Negative (FN)	d = True Negative (TN)

Key Diagnostic Measures

Measure	Formula	Definition	Key Point
Sensitivity	TP / (TP + FN)	Proportion WITH disease who test POSITIVE	High = good at RULING OUT (SnNOut)
Specificity	TN / (FP + TN)	Proportion WITHOUT disease who test NEGATIVE	High = good at RULING IN (SpPIn)
PPV	TP / (TP + FP)	Probability +ve test = true disease	Affected by prevalence: ↑prevalence → ↑PPV
NPV	TN / (FN + TN)	Probability −ve test = no disease	Affected by prevalence: ↑prevalence → ↓NPV
LR+	Sens / (1 − Spec)	How much more likely a +ve result in disease	LR+ >10 = strong rule-in
LR−	(1 − Sens) / Spec	How much more likely a −ve result in disease	LR− <0.1 = strong rule-out
Accuracy	(TP+TN) / (TP+FP+FN+TN)	Overall proportion correctly classified	Misleading if prevalence very high or low

> 💡 **HIGH YIELD:** SnNOut = Sensitive test + Negative result → Rules OUT disease. SpPIn = Specific test + Positive result → Rules IN disease. These are the SINGLE MOST TESTED concepts in EBM for MRCEM.

Effect of Prevalence on PPV and NPV

- **Sensitivity and specificity** are properties of the TEST — NOT affected by prevalence
- **PPV and NPV ARE affected by prevalence:**
  - ↑ Prevalence → ↑ PPV (more true positives) but ↓ NPV
  - ↓ Prevalence → ↓ PPV (more false positives) but ↑ NPV

> ⚡ **EXAM TIP:** Clinical implication: D-dimer has high sensitivity for PE (good for ruling out). But in low-risk populations, a positive D-dimer has poor PPV (many false positives). This is why pre-test probability (Wells score) matters.

Pre-Test and Post-Test Probability

- Pre-test probability: estimated probability BEFORE the test (clinical assessment, prevalence, risk factors)
- Post-test probability: probability AFTER the test result (incorporates likelihood ratio)
- Calculation: pre-test odds × LR = post-test odds (Bayesian approach)
- A test is MOST useful when pre-test probability is intermediate (~20–80%)

ROC Curves

- ROC curve: plots sensitivity (y-axis) vs 1−specificity (x-axis) for all cut-off values
- AUC (area under curve) = overall test accuracy. AUC = 1.0: perfect; AUC = 0.5: useless
- AUC > 0.8 = generally a good test. Optimal cut-off = point closest to top-left corner
- Increasing sensitivity always decreases specificity (trade-off)

6.5 Bias, Confounding & Validity

Types of Bias

Bias	Definition	Occurs In	Prevention
Selection bias	Error in how participants are selected/allocated	Case-control; cohort; RCT	Random sampling; allocation concealment
Recall bias	Cases recall exposures differently from controls	Case-control (retrospective)	Objective records; prospective design
Observer / Detection bias	Assessor knowledge of allocation influences measurement	Unblinded studies	Blinding of outcome assessors
Performance bias	Differences in care due to knowledge of allocation	Unblinded RCTs	Double-blinding
Attrition bias	Systematic differences between completers and dropouts	Cohort; RCTs	ITT analysis; minimise dropout
Publication bias	Positive results more likely published	Systematic reviews	Funnel plot; trial registration
Lead-time bias	Screening detects earlier → appears to ↑ survival	Screening studies	Measure mortality, not survival
Length-time bias	Screening catches slow-growing disease → overestimates benefit	Screening studies	RCTs of screening vs no screening
Hawthorne effect	Behaviour changes from being observed	All study types	Blinding; long study duration
Berkson's bias	Hospital controls differ from general population	Hospital case-control	Use community controls
Neyman bias	Cross-sectional misses fatal/resolving conditions	Cross-sectional	Use cohort (incidence) studies

⚡ **EXAM TIP:** Lead-time bias and length-time bias are commonly tested in screening questions. Lead-time = earlier detection makes survival APPEAR longer. Length-time = screening catches slower diseases. Only RCTs can prove screening truly improves outcomes.

Confounding

- **Confounder** = variable independently associated with BOTH exposure AND outcome, NOT on the causal pathway
- Example: coffee drinking and lung cancer — confounded by smoking (smokers drink more coffee AND smoking causes cancer)

Methods to Control Confounding:

Method	Stage	How It Works
Randomisation	Study design	Distributes ALL confounders (known + unknown) equally — ONLY method for unknown confounders
Restriction	Study design	Limit participants to one level (e.g. only non-smokers)
Matching	Study design	Select controls matched on key confounders (age, sex)
Stratification	Analysis	Analyse within separate strata (smokers vs non-smokers)
Multivariate analysis	Analysis	Statistical models adjusting for multiple confounders simultaneously

💡 **HIGH YIELD:** Randomisation is the ONLY method that controls for UNKNOWN confounders. Past papers: "Researcher not considering a third variable" = confounding.

Internal and External Validity

Concept	Definition	Threats
Internal validity	Results are TRUE for the study population (freedom from bias/confounding)	Bias; confounding; poor methodology
External validity (generalisability)	Results can be APPLIED to other populations/settings	Strict criteria; unrepresentative sample; single-centre

⚡ **EXAM TIP:** Internal validity must be established FIRST. If a study is biased, its results cannot be applied anywhere. External validity can then be assessed for your patient population.

6.6 Principles of Critical Appraisal

The Three Questions of Critical Appraisal

Question	What to Ask
1. Are the results VALID?	Appropriate design? Proper randomisation? Adequate blinding? Complete follow-up? ITT used? Confounders controlled?
2. What are the RESULTS?	Size of effect (RR, OR, ARR, NNT)? Precision (CIs)? Statistical significance (p-value)?
3. Are results APPLICABLE?	Patient similar to study population? All important outcomes measured? Benefits outweigh harms? Patient values considered?

Appraising an RCT (CONSORT Essentials)

Element	Questions to Ask
Question	Clear, focused question (PICO)?
Randomisation	Truly random? Allocation concealment adequate?
Blinding	Who was blinded? Was it appropriate?
Baseline comparability	Groups similar at baseline?
Follow-up	Adequate length and completeness? Dropout rates similar?
Analysis	ITT used? CIs reported? Adequate sample size/power?
Outcomes	Clearly defined and clinically relevant? Surrogate endpoints?
Applicability	Population similar to yours? Intervention replicable?

Appraising a Diagnostic Study

- Was there an appropriate gold standard applied to ALL patients?
- Spectrum bias: did the study include mild to severe cases?
- Were index test and reference test interpreted independently (blinded)?
- Verification (work-up) bias: were test-negative patients also verified?

Appraising a Systematic Review

- Clear, focused question? Comprehensive search (multiple databases, grey literature)?
- Explicit selection criteria? Two independent reviewers? Quality assessment done?
- Heterogeneity assessed (I^2, chi-squared)? Forest plot and funnel plot provided?

6.7 Additional High-Yield Topics

Screening

Definition: Systematic application of a test to identify individuals at sufficient risk to benefit from further investigation or preventive action.

Wilson & Jungner Criteria for a Screening Programme:

- Important health problem with known natural history
- Acceptable treatment available; facilities for diagnosis and treatment exist
- Recognisable latent or early symptomatic stage
- Suitable test: simple, safe, precise, validated, and acceptable to the population
- Cost-effective; continuous process (not "one-off")

Screening Biases:

Bias	Explanation
Lead-time bias	Earlier detection → survival from diagnosis appears longer even if death at same time
Length-time bias	Screening preferentially detects slow-growing (indolent) cancers
Selection (volunteer) bias	Health-conscious people more likely to attend screening
Overdiagnosis bias	Screening detects conditions that would never have caused symptoms → unnecessary treatment

Incidence and Prevalence

Measure	Definition	Formula	Uses
Incidence (rate)	NEW cases in a population over a specific time period	New cases / person-time at risk	Risk; aetiology; prognosis
Prevalence (point)	EXISTING cases (new + old) at a point in time	All cases / total population	Disease burden; health planning
Period prevalence	All cases during a defined time period	All cases / average population	When point prevalence impractical

- **Prevalence = Incidence × Duration** — chronic diseases increase prevalence even with stable incidence
- Incidence measured in cohort studies; prevalence in cross-sectional studies

Statistical vs Clinical Significance

- **Statistical significance** ($p < 0.05$) = result unlikely due to chance alone
- **Clinical significance** = result large enough to be meaningful in practice
- Large sample sizes can detect statistically significant but clinically trivial differences
- Example: antihypertensive lowers BP by 1 mmHg ($p = 0.001$) — significant but meaningless

> ⚡ **EXAM TIP:** Always assess the SIZE of the effect (RR, ARR, NNT) and its confidence interval, not just the p-value. Statistical significance ≠ clinical significance.

Intention-to-Treat vs Per-Protocol Analysis

Feature	Intention-to-Treat (ITT)	Per-Protocol (PP)
Definition	ALL analysed in originally randomised group	Only compliant completers analysed
Preserves randomisation	YES	NO (introduces bias)
Measures	Effectiveness (real-world benefit)	Efficacy (ideal conditions)
Bias direction	Conservative (towards null)	May overestimate treatment effect
Preferred for	Primary analysis of RCTs	Supportive / secondary analysis

> 💡 **HIGH YIELD:** ITT is the gold standard for RCT analysis because it preserves randomisation and reflects real-world effectiveness. Per-protocol can introduce bias by excluding non-compliers.

NNT — Worked Example

Drug X vs placebo for preventing stroke:

- Control event rate (CER) = 20/100 = 0.20
- Experimental event rate (EER) = 12/100 = 0.12
- **ARR = CER − EER = 0.20 − 0.12 = 0.08**
- **NNT = 1/ARR = 1/0.08 = 12.5 ≈ 13**
- Interpretation: treat 13 patients to prevent one additional stroke
- **RRR = ARR/CER = 0.08/0.20 = 0.40 = 40%** — sounds impressive but ARR is only 8%

> ⚡ **EXAM TIP:** Past paper: "A drug reduces mortality from 4% to 3%. What is the NNT?" → ARR = 0.04 − 0.03 = 0.01 → NNT = 1/0.01 = 100.

6.8 Rapid Revision Summary

Key Formulae at a Glance

Measure	Formula
Sensitivity	TP / (TP + FN)
Specificity	TN / (FP + TN)
PPV	TP / (TP + FP)
NPV	TN / (FN + TN)
LR+	Sensitivity / (1 − Specificity)
LR−	(1 − Sensitivity) / Specificity
Relative Risk	[a/(a+b)] / [c/(c+d)]
Odds Ratio	(a×d) / (b×c)
ARR	CER − EER
NNT	1 / ARR
RRR	ARR / CER
Prevalence	Existing cases / Total population
Incidence	New cases / Person-time at risk
Power	1 − β

Rapid Recall — Study Design & Statistics

Topic / Prompt	Key Fact / Answer
EBM definition (Sackett)	Conscientious use of best evidence + clinical expertise + patient values
Highest level of evidence	Systematic review / meta-analysis of RCTs
Gold standard for interventions	Randomised controlled trial (RCT)
Cohort study → measures	Relative risk (RR) and incidence
Case-control study → measures	Odds ratio (OR); ideal for rare diseases
Cross-sectional → measures	Prevalence (snapshot); cannot determine causation
SnNOut	Sensitive test + Negative result = Rules OUT disease
SpPIn	Specific test + Positive result = Rules IN disease
PPV/NPV affected by	Disease prevalence (sensitivity/specificity are NOT)
Type I error (α)	False positive — "crying wolf" (usually 0.05)
Type II error (β)	False negative — "missing the wolf" (usually 0.20)
Power = 1 − β	Probability of detecting a true difference (≥80%)
Increase study power	Increase sample size (most important)
Allocation concealment vs blinding	Concealment = BEFORE randomisation; Blinding = AFTER
ITT vs per-protocol	ITT = gold standard; preserves randomisation; real-world
NNT	1/ARR — lower NNT = more effective treatment
Forest plot: diamond crosses line	Result NOT statistically significant
Funnel plot asymmetry	Suggests publication bias
Confounding controlled by	Randomisation (only method for UNKNOWN confounders)
Lead-time bias	Screening detects earlier → survival APPEARS longer
Length-time bias	Screening catches slow-growing disease

Prevalence = Incidence × Duration	Chronic diseases ↑ prevalence even with stable incidence
68–95–99.7 rule	% within ±1, ±2, ±3 SD of mean (normal distribution)
Statistical ≠ clinical significance	Always look at effect SIZE (NNT, ARR) not just p-value

Common Exam Scenarios

Topic / Prompt	Key Fact / Answer
Best design for rare disease?	Case-control study
Which design establishes causation?	RCT (randomisation controls confounders)
99% sensitive test, patient tests −ve?	SnNOut → very unlikely to have disease
95% CI for OR = 0.85–1.32. Significant?	NO — CI crosses 1 (includes no effect)
Error: finding difference that doesn't exist?	Type I error (α / false positive)
How to increase power?	Increase sample size
ITT vs per-protocol advantage?	Preserves randomisation; avoids attrition bias
Asymmetrical funnel plot?	Suspect publication bias
Drug reduces mortality 4% → 3%. NNT?	ARR = 0.01; NNT = 100
Count data (number of patients) type?	Discrete data (quantitative)
Study where researcher ignores 3rd variable?	Confounding
5-year cancer survival bias in screening?	Lead-time bias