SIDE 1/2 PATHOPHYSIOLOGY · Exam blueprint · Immunity · Antibodies · Hypersensitivity I–IV · HIV · Autoimmunity · Cancer · MSK & pain

EXAM REVISION · MODULES 3–7

Compiled by **AskSia** · mapped to the 2804NRS syllabus · asksia.ai/cheatsheet/griffith-2804nrs

0 · Exam Blueprint

READ FIRST

★ Two assessments drive the marks: the **A2 concept map (40%)** and the **End-of-Trimester Exam (40%)** (the in-class quiz, ~20%, covers Modules 1–2 only). The EOTE = 50 MCQ (half the marks) + 12 short-answer (half) and examines **Modules 3–7**: immunity → cancer → MSK/pain → genetics & ageing → neuro/autonomic + the pharmacology woven through.

Train both reflexes: MCQ recall = the tables & trap-facts here; SAQ = *explain a mechanism in prose* — walk a pathophysiological cascade or a drug's mechanism of action in 3–5 linked steps.

SIA → ***For every SAQ "explain…", answer as a chain: trigger → mechanism step → mechanism step → clinical sign. Markers reward the links, not a list of facts.***

0b · The A2 Cascade Template

CONCEPT-MAP SPINE

The A2 concept map (and every "explain the pathophysiology" SAQ) follows ONE colour-coded chain. Learn the shape and slot any disease in:

RF → AETIOLOGY → PATHOPHYSIOLOGY → MANIFESTATIONS

`Risk factor → aetiology/trigger → pathophysiology (step-by-step) → clinical manifestations → +1 diagnostic test +1 management`

Worked (cervical cancer, the A2 case): RF = smoking, immunosuppression, multiple partners → aetiology = persistent high-risk **HPV** infection → pathophys = viral oncoproteins inactivate **p53/Rb** tumour suppressors → dysplasia (CIN) → carcinoma in situ → invasive squamous-cell carcinoma → local + lymphatic spread → manifestations = abnormal/post-coital bleeding, discharge, pelvic pain. Dx = Pap/HPV test + biopsy; Mx = surgery/radiotherapy ± chemo. *(HIV co-infection accelerates it via CD4 loss.)* Reuse this exact skeleton for stroke, MS, arthritis or any disease the exam throws at you.

0c · Assessment Shape

WHERE THE MARKS ARE

ITEM	WT	FORM & SCOPE
A1 quiz	~20%	20 MCQ/20 min in class · Mod 1–2
A2 map	40%	concept map + 500 words
A3 EOTE	**40%**	50 MCQ + 12 SAQ · Mod 3–7

The MCQ half rewards **breadth** (recognise the trap); the SAQ half rewards **depth** (explain a cascade or a mechanism of action in prose). Weight prep on immunology → cancer → MSK/pain → genetics/ageing → neuro/autonomic. *(Modules 1–2 are A1 scaffolding, not on the EOTE.)*

0d · Foundations (scaffold)

MOD 1–2 UNDERPIN

Cell adaptation: hypertrophy = bigger cells; hyperplasia = more cells; metaplasia = reversible cell-type switch; **dysplasia = disordered, pre-malignant.**

Necrosis = swelling + lysis + inflammation, not ATP-needing; **apoptosis** = shrinkage + apoptotic bodies, no inflammation, ATP-dependent.

Healing: resolution / regeneration (same tissue, needs mitosis) / repair-fibrosis (scar, loses function). 1st intention (edges approximated) vs 2nd (open gap, bigger scar). Healing needs age, nutrition (protein, vit C, zinc), oxygenation; corticosteroids impair it.

1 · Immunity · Innate vs Adaptive

3.1 ☆

Innate — non-specific, immediate, no memory. *1st line* = barriers (skin, mucosa, cilia, stomach acid, lysozyme, flora); *2nd line* = inflammation, fever, phagocytes, NK cells, complement, interferons.

Adaptive — specific, slower, has memory; recognises antigens. Two arms:

- **Humoral** = **B cells** → plasma cells → antibodies; hits *extracellular* pathogens/toxins.
- **Cell-mediated** = **T cells**; hits *intracellular* (viruses), cancer, transplants.

Inflammation & fever are INNATE (2nd line) — a classic MCQ trap.

1b · Immune Cells

WHO DOES WHAT

CELL	ROLE
Neutrophil	1st responder, **acute** bacterial, phagocytosis
Macrophage	phagocytosis, APC, **chronic**, cytokines
T-helper (CD4)	coordinate both arms (cytokines)
Cytotoxic T (CD8)	kill infected/cancer cells
B cell	→ plasma cell (antibody) + memory
NK cell	**innate**; kill virus/tumour, no sensitisation

T cells mature in the **thymus**; B cells in **bone marrow**.

1c · Primary vs Secondary Response

BASIS OF VACCINES

Primary — 1st exposure; 1–2 week lag, mainly **IgM**, low titre. **Secondary** — re-exposure; faster, stronger, higher titre (mainly **IgG**) via **memory cells**. Vaccination exploits this.

1d · Complement & Mediators

INNATE EFFECTORS

Complement = plasma protein cascade: **opsonisation** (tag for phagocytosis), **chemotaxis** (C5a), anaphylatoxins (C3a/C5a → mast-cell degranulation), and the **membrane attack complex (MAC)** that lyses pathogens.

Interferons = antiviral; **cytokines** (TNF, IL-1, IL-6) drive fever & acute-phase response. Markers: **CRP**, **ESR**, WBC (neutrophils ↑ acute, lymphocytes ↑ viral/chronic).

1e · How Humoral Immunity Works

SAQ CASCADE

Antigen enters → **APC (macrophage/dendritic)** presents it → activates **helper T (CD4)** → cytokines stimulate the matching **B cell** → clonal expansion → plasma cells secrete antibody + memory B cells form. Antibodies then **neutralise**, **opsonise** and **activate complement**. This is the chain a "describe the immune response" SAQ wants.

Antibody functions: neutralisation, opsonisation (tag for phagocytes), complement activation (→ MAC), agglutination, and ADCC (flag cells for NK killing).

1f · Cell-Mediated Immunity

THE T-CELL ARM

Intracellular antigen (virus, tumour) on the cell surface → **cytotoxic T (CD8)** → perforin/granzymes → apoptosis of the infected/abnormal cell. Helper T amplify; regulatory T enforce tolerance. This arm drives **Type IV** hypersensitivity and transplant rejection.

2 · The 5 Antibody Classes

3.1 ☆ MCQ GOLD

Y-shaped: 2 **heavy** + 2 **light** chains; variable region (Fab) binds antigen, constant region (Fc) = class/effector.

IG	KEY FACT
IgM	**First** & **largest** (pentamer); primary response; complement
IgG	**Most abundant**; only Ig to cross placenta; secondary response
IgA	**Secretions** — saliva, tears, mucus, breast milk
IgE	Mast cells/basophils; **allergy**/anaphylaxis, parasites
IgD	B-cell surface receptor; role least understood

Mnemonic: *M* first, *G* placenta, *A* area-secretions, *E* allergy.

3 · Types of Immunity

3.3 ☆

TYPE	SOURCE	MEMORY
Natural active	infection → own Ab	**Yes**
Artificial active	**vaccine** → own Ab	**Yes**
Natural passive	placenta / breast milk	No
Artificial passive	Ab **injected** (antivenom)	No

Active = you make it (slow, lasting, memory); passive = given (immediate, temporary, no memory). "Natural/artificial" = how acquired; "active/passive" = who makes the antibody. Passive's lack of memory is a common MCQ.

3b · Vaccination

3.3.3

= **artificial active** immunity: a harmless form of the antigen (live-attenuated, inactivated, toxoid, subunit, mRNA) primes a **primary response** + memory cells, so the real exposure triggers a fast, strong **secondary response**. Boosters top up waning memory. **Herd immunity** protects the unvaccinated by cutting transmission.

Newborns get **natural passive** cover from maternal **IgG** (placenta) and **IgA** (breast milk) until their own active immunity matures — immediate but no memory, so it fades. Antivenom and post-exposure rabies immunoglobulin are the *artificial* passive equivalents.

3c · Immune Drugs

3.2.3 / 3.3

- **Immunosuppressants** — transplant/autoimmune. **Calcineurin inhibitors** (cyclosporine) block IL-2 → ↓T-cell proliferation; AEs: nephro/hepatotoxicity, infection.
- **Monoclonal antibodies ("-mab")** — single clone, highly specific; e.g. anti-TNF **infliximab**, trastuzumab. Target cytokines or cancer antigens.
- **Corticosteroids** — broad immunosuppression for all 4 hypersensitivity types, anaphylaxis, autoimmune disease.

Corticosteroids preferentially suppress **cell-mediated** immunity (humoral less affected) and shrink lymphoid tissue. Prolonged use → infection risk, hyperglycaemia, osteoporosis, poor healing — never stop abruptly (adrenal suppression). They act higher than NSAIDs (block phospholipase A2 → stop prostaglandins AND leukotrienes), giving broader anti-inflammatory cover.

3d · Antibody Quick-Recall

MCQ DRILL

- Crosses placenta = **IgG**; first/largest = **IgM**.
- Secretions/breast milk = **IgA**; allergy = **IgE**.
- Antigen binds the variable (Fab) region.

4 · Hypersensitivity I–IV

3.2 ☆ CLASSIC TRAP

Excessive immune response that damages tissue (needs prior **sensitisation**). Mnemonic "ACID".

TYPE	MEDIATOR	MECHANISM / EG
I Allergic	**IgE** + mast	allergen → degranulation → **histamine**; mins. Hay fever, asthma, **anaphylaxis**
II Cytotoxic	IgG/IgM + comp.	Ab vs **fixed cell-surface Ag** → lysis. ABO, HDN, Graves'
III Complex	IgG complexes	Ag-Ab **deposit in tissue** → inflammation. SLE, GN, RA
IV Delayed	**T cells** (no Ab)	cytokines, **24–72 h**. Contact dermatitis, Mantoux, T1DM, graft rejection

I–III antibody-mediated; IV is T-cell, delayed, NO antibody. II = Ab vs fixed cell; III = circulating complexes.

4b · Anaphylaxis

3.2.2 · SAQ

Severe **systemic Type I**. Mast cells dump **histamine** into the circulation → systemic vasodilation → severe hypotension; airway oedema + bronchoconstriction → respiratory failure.

Mechanism→sign: hypotension = vasodilation; wheeze/SOB = bronchoconstriction + oedema; hives = histamine on skin. **1st-line = adrenaline (NOT antihistamine):** β2 bronchodilates, α1 vasoconstricts/raises BP.

4c · Telling II from III

BOTH IGG

Both use **IgG**, but: **Type II** = antibody binds an antigen fixed on a cell surface → that cell is destroyed (ABO transfusion reaction, haemolytic disease of the newborn, Goodpasture's). **Type III** = antibody binds a soluble antigen → circulating immune complexes deposit in vessels/joints/kidney → complement-driven inflammation (SLE, post-strep glomerulonephritis, serum sickness).

Management across types: avoid the allergen; antihistamines + corticosteroids dampen I–III; adrenaline for anaphylaxis; immunosuppressants for severe autoimmune Type II/III; Type IV (contact dermatitis) → topical steroids. Diagnosis often uses skin-prick (I) or patch testing (IV); raised total/specific IgE supports Type I.

4d · Worked SAQ · Allergy

EXPLAIN IT

Q. Why does a second bee sting cause anaphylaxis but the first did not?

A (cascade): 1st sting sensitises — venom drives **IgE** production that coats **mast cells**. On re-exposure, venom cross-links that IgE → mast-cell **degranulation** → massive **histamine** release → systemic vasodilation (hypotension) + bronchoconstriction + oedema = Type I anaphylaxis. Give **adrenaline** first.

Key word: the *first* exposure causes no symptoms because it only builds the IgE — symptoms need pre-formed IgE on mast cells. The same "sensitisation then re-exposure" logic underlies all four types.

4e · Hypersensitivity Recall

ACID DRILL

- **I** IgE/histamine, immediate; **II** IgG vs fixed cell + complement.
- **III** IgG complexes deposit; **IV** T cells, no Ab, delayed (only IV).

5 · Immunodeficiency & HIV

3.3 ☆

Primary = intrinsic/**genetic** defect (Bruton's = B cell; DiGeorge = T cell; SCID = both). **Secondary (acquired)** = consequence of another factor: corticosteroids/stress, malnutrition, drugs (chemo), infection (HIV, TB), cancer (leukaemia, Hodgkin's).

HIV/AIDS — HIV infects & destroys **helper T (CD4+) cells**; slow decline → broad immune failure (CD4 controls BOTH arms). AIDS = CD4 < 200/mm³ → opportunistic infection (candidiasis, *Pneumocystis*) + cancers. Mx: antiretrovirals + prophylaxis.

Transmission: sexual, blood/needles, mother→child (pregnancy/birth/breastfeeding).

6 · Autoimmunity

3.2.3 ☆

Loss of **self-tolerance** → auto-antibodies / self-reactive T cells attack self-antigens (normally deleted in the **thymus**). Cannot be cured — managed with NSAIDs, **corticosteroids**, anti-TNF, immunosuppressants.

DISEASE	TARGET
Type 1 diabetes	pancreatic β-cells
Graves' / Hashimoto's	thyroid (hyper / hypo)
Multiple sclerosis	CNS **myelin**
SLE	DNA (multi-system)
Rheumatoid arthritis	**synovial joints**

6b · Inflammation Recap

UNDERPINS IT ALL

5 cardinal signs = **redness, heat, swelling, pain, loss of function** (vasodilation + ↑permeability + mediators). Histamine (mast cells) = early; **prostaglandins** = pain/fever (NSAID target). Acute = neutrophils; chronic (>2 wk) = macrophages + lymphocytes + fibrosis.

Exudate types: serous (watery — burns/blisters); fibrinous (sticky, → adhesions); **purulent** (pus → bacterial infection); haemorrhagic (RBCs → worst vessel damage).

6c · Microbiology Scaffold

MOD 2 · INFECTION

Bacteria = prokaryotes (no nucleus/organelles — what antibiotics exploit = *selective toxicity*). Classify by shape (cocci/bacilli), arrangement (clusters=staph, chains=strep), Gram stain, O_2 need.

	GRAM +	GRAM −
Wall	thick peptidoglycan	thin + outer membrane
Stain	**purple**	**pink**
Toxin	**exotoxin** (protein, heat-labile)	**endotoxin** = LPS, heat-stable

Chain of infection: agent → reservoir → exit → transmission → entry → susceptible host (break any link). Viruses = obligate intracellular; not killed by antibacterials.

Antibiotic targets (4): cell-wall synthesis (penicillins → lysis), protein synthesis (aminoglycosides, macrolides), DNA/replication (quinolones), folate synthesis (sulfonamides). Resistance via mutation/gene transfer → stewardship. **Selective toxicity** = hit bacterial structures absent from human cells. Endotoxin (LPS) at high dose → **septic shock**; exotoxins (tetanus, botulism, diphtheria) are among the most potent toxins known. Remember: exotoxin = protein/gram-pos/heat-labile; endotoxin = LPS/gram-neg/heat-stable.

7 · Neoplasia & Cancer

MODULE 4 ☆

Neoplasia = new, uncontrolled, **autonomous** growth. Benign vs malignant:

	BENIGN	MALIGNANT
Growth	slow, expansile	rapid, infiltrative
Capsule	encapsulated	invasive
Differentiation	well	poor (anaplastic)
Metastasis	**No**	Yes

Carcinogenesis = multistep initiation → promotion → progression; needs *multiple* mutations passed to daughter cells.

7b · Oncogenes & Spread

GAIN VS LOSS

- **Proto-oncogene** → mutation = **gain of function** → **oncogene** = accelerator stuck ON.
- **Tumour suppressor** (**p53** "guardian", BRCA1/2) → **loss of function** = brakes failed.

Cell cycle **G1→S→G2→M**; cancer = checkpoint failure (esp. G1/S). **Metastasis routes:** local invasion, **lymphatic**, **haematogenous** (blood), transcoelomic seeding.

Grading vs Staging: grading = how abnormal cells *look*; staging = how far it spread (TNM = Tumour, Node, Metastasis). AU risks: tobacco, UV, alcohol, HPV, BRCA, age.

8 · MSK & Pain

MODULE 5 ☆

Osteoporosis — ↓bone density (resorption > formation; post-menopausal ↓oestrogen) → fragility fractures.

Fracture healing: haematoma → soft callus → hard (bony) callus → remodelling. **Compartment syndrome** = ↑pressure in a closed fascial space → ischaemia (the **6 Ps**) — emergency.

Pain cascade (SAQ): tissue injury → mediators (prostaglandins, bradykinin) **sensitise nociceptors** → signal via Aδ/C fibres → dorsal horn → spinothalamic tract → thalamus → cortex (perception). Nociceptive vs neuropathic vs referred.

8b · Arthritis & BPH

5.2 / 4.4

OA = "wear-and-tear" cartilage loss, mechanical, asymmetrical, large weight-bearing joints. **RA** = autoimmune (Type III, synovium), symmetrical small joints, systemic, morning stiffness, RF/anti-CCP.

BPH = benign *hyperplasia* of the peri-urethral prostate (age/DHT) → obstruction (hesitancy, frequency, nocturia, weak stream). Mx: **α1-blockers** ("-osin", relax smooth muscle) + 5α-reductase inhibitors. Prostate cancer = peripheral zone, **PSA** marker, androgen-dependent.

8c · Cell-Cycle Recap

WHERE CANCER BREAKS

G1 → S (DNA synthesis) → G2 → M (mitosis) → cytokinesis. Checkpoints (esp. **G1/S restriction point**) police DNA integrity; **p53** halts or apoptoses damaged cells. Cancer = oncogene accelerator stuck ON *plus* suppressor brakes OFF → checkpoints bypassed → autonomous proliferation.

Cancer treatment (4.2.3): surgery (remove), radiotherapy (DNA damage, local), **chemotherapy** (cytotoxic, hits rapidly dividing cells → AEs: myelosuppression, hair loss, GI/mucositis, nausea), and targeted/hormonal therapy. Diagnosis: biopsy + histology, imaging, tumour markers (PSA, CA-125). The cytotoxic AEs come from hitting *normal* fast-dividing cells (marrow, gut, hair).

9 · Genetics & Inheritance
MODULE 6 ★

46 chromosomes = 23 pairs (22 autosomes + 1 sex pair); gametes **haploid (23)**. Patterns:

- **Autosomal dominant** — one mutant allele suffices; 50% risk (Huntington's).
- **Autosomal recessive** — needs *two* mutant alleles; carriers (Aa) unaffected (cystic fibrosis).
- **X-linked recessive** — males affected more (one X); females carriers (haemophilia).

Aneuploidy: trisomy (Down = trisomy 21) or monosomy (Turner = 45,X). **Point mutation** = single base change → loss or gain of function (match to tumour-suppressor vs oncogene).

9b · Congenital & Teratogens
6.2

Multifactorial = genes + environment (neural tube defects, diabetes). **Teratogens** disrupt development — **TORCH** infections, **alcohol** (FAS), drugs, radiation, low folate (→ neural tube defect). Critical period = **organogenesis (weeks 3–8)**.

10 · Ageing & Pharmacokinetics
6.3.2 ★

Age changes map onto ADME:

STEP	AGE CHANGE → EFFECT
Absorb	↓gastric motility/acid (minor)
Distribute	↑fat, ↓water, **↓albumin → ↑free drug**
Metabolise	↓liver mass/flow → slower
Excrete	↓renal GFR → accumulation (biggest)

Net: ↑levels, ↑half-life, ↑toxicity + polypharmacy → **"start low, go slow."**

10b · Worked · Punnett
RECESSIVE CROSS

Two carriers of cystic fibrosis (**Aa × Aa**):

	A	**A**
A	AA	Aa
a	Aa	aa

Genotype **1 AA : 2 Aa : 1 aa**; phenotype 3 unaffected : 1 affected. So 25% affected (aa), 50% unaffected carriers (Aa). Carriers are healthy but pass the allele on — the key autosomal-recessive MCQ.

10c · Routes & First-Pass
WHY ROUTE MATTERS

Sublingual, rectal, IV, transdermal, inhaled all bypass first-pass hepatic metabolism (no portal vein) → useful for high first-pass drugs (e.g. GTN sublingual). Oral is convenient but loses bioavailability to first pass + incomplete absorption. **IV** = fastest onset, 100% F, but no recall once given.

10d · Genetics MCQ Traps
QUICK RECALL

- **Down syndrome = trisomy 21** (extra chromosome).
- X-linked recessive (haemophilia) affects **males more**.
- Autosomal recessive needs **two** alleles; carriers unaffected.
- Oncogene = gain of function; tumour suppressor = loss of function.
- Teratogen critical period = organogenesis, weeks 3–8.

11 · Neuro Pathophysiology
MODULE 7 ★

Consciousness = arousal (RAS/brainstem) + awareness (cortex); graded by **GCS** (eye/verbal/motor, 3–15).

Raised ICP — Monro-Kellie: the skull is a fixed volume of brain + blood + CSF; ↑one must ↓another or ICP rises. Compensation (displace CSF/venous blood) is exhausted suddenly → steep ICP rise → ↓perfusion (**CPP = MAP − ICP**). **Cushing's triad** (↑BP/wide pulse pressure, **bradycardia**, irregular breathing) = late herniation sign.

11b · Stroke, TBI, Neurodegeneration
7.2–7.3

- **Stroke:** ischaemic (thrombus/embolus, most) vs haemorrhagic (bleed); thrombolysis only for ischaemic; FAST.
- **TBI bleeds:** extradural (arterial, *lucid interval*), subdural (venous), subarachnoid.
- **Alzheimer's:** amyloid plaques + tau tangles, **↓ACh** → AChE-inhibitor Rx.
- **Parkinson's:** loss of **dopaminergic** neurons (substantia nigra) → tremor, rigidity, bradykinesia; levodopa.
- **MS** = autoimmune CNS **demyelination**; **MND** = motor-neuron loss, sensory spared.

12 · The ANS
7.4.1 ★

Controls **involuntary** muscle/glands; two antagonistic branches via a 2-neuron chain (pre → ganglion → post).

- **SNS** "fight/flight", **thoracolumbar** (T1–L2).
- **PNS** "rest/digest", **craniosacral** (CN III, VII, IX, X; S2–S4).

ALL preganglionic + ALL PNS postganglionic = ACh on nicotinic/muscarinic; MOST SNS postganglionic = noradrenaline on α/β. Exceptions: sweat glands = cholinergic; adrenal medulla = nicotinic, dumps adrenaline.

12b · SNS vs PNS Effects
OPPOSITE ACTIONS

ORGAN	SNS	PNS
Pupils	dilate	constrict
Heart	**↑ rate/force**	↓ rate
Bronchi	dilate	constrict
GI	↓ motility	↑ motility/secretion
Bladder	retain	void
Vessels/BP	vasoconstrict ↑BP	—

12c · Seizures & SCI
7.2

Seizure = abnormal synchronous neuronal discharge; focal (one area) vs generalised (both hemispheres, LOC). **Spinal cord injury**: complete vs incomplete; **spinal/neurogenic shock** (loss of sympathetic tone → hypotension + bradycardia); autonomic dysreflexia above the lesion.

12d · Raised-ICP SAQ
EXPLAIN THE SPIRAL

Cascade: mass/bleed/oedema adds volume → CSF + venous blood displaced (compensated, ICP stays normal) → compensation exhausted → **ICP rises steeply** → **CPP = MAP − ICP** falls → brain ischaemia → more oedema (vicious cycle) → herniation. Late sign = **Cushing's triad** (↑BP, bradycardia, irregular breathing). Manage by lowering ICP and supporting MAP.

13 · Adrenergic Pharmacology
7.4.2 ★ MCQ GOLD

NA acts on G-protein adrenoceptors, cleared by **uptake-1** then **MAO**/COMT.

RECEP.	SITE → EFFECT	AGONIST / BLOCKER
α1	vessels → **vasoconstrict ↑BP**	phenylephrine / **-osin** (prazosin)
α2	presynaptic → ↓NA (feedback)	clonidine
β1	**heart** → ↑rate/force	dobutamine / **-olol**
β2	bronchi → **dilate**	salbutamol (SABA)

"β1 = 1 heart, β2 = 2 lungs." SABA (salbutamol) = reliever; LABA (salmeterol) = preventer. β2-agonist AEs: tremor, tachycardia, **hypokalaemia**. Use cardioselective (β1) blockers in asthmatics.

14 · Cholinergic Pharmacology
7.4.3 ★

ACh → receptor → broken by **acetylcholinesterase (AChE)**. **Muscarinic** (M1 gastric, **M2 heart ↓rate**, M3 smooth muscle/glands); **nicotinic** (ganglia + skeletal NMJ).

- **Muscarinic agonist** (bethanechol, pilocarpine) = *more PNS:* bradycardia, secretions, miosis ("SLUDGE").
- **Antimuscarinic** (**atropine**, ipratropium, oxybutynin) = *less PNS:* "can't see/pee/spit/poo" + tachycardia.
- **AChE inhibitors** (neostigmine; donepezil) ↑ACh → myasthenia gravis & Alzheimer's.
- **Suxamethonium** = depolarising NM blocker (fasciculations, irreversible); **atracurium** = non-depolarising (reversible by neostigmine).

14b · Drug → Receptor Logic
MATCH IT

Examiners give a drug, ask the receptor (or vice versa). The reflex:

DRUG	ACTION	USE
Salbutamol	β2 agonist	acute asthma
Prazosin	α1 block	HTN / BPH
Metoprolol	β1 block	angina, post-MI
Clonidine	α2 agonist	↓BP
Atropine	M block	bradycardia, pre-op
Bethanechol	M agonist	urinary retention

14c · Worked SAQ · Adrenaline
MULTI-RECEPTOR

Adrenaline in anaphylaxis hits several receptors at once: α1 → vasoconstriction → ↑BP (reverses hypotension); β1 → ↑cardiac output; β2 → bronchodilation + ↓mast-cell mediator release. One drug, three life-saving actions — the classic "explain why adrenaline" SAQ.
Contrast: a β-blocker would *worsen* anaphylaxis and bronchospasm — never give one here. Likewise non-selective β-blockers can trigger bronchospasm in asthmatics → use cardioselective β1 agents. β-blockers are also contraindicated in heart block and cardiogenic shock.

14d · Autonomic Recall
MCQ DRILL

- SNS post = **NA** (α/β); PNS post = **ACh** (muscarinic); all pre = ACh/nicotinic.
- Atropine blocks muscarinic ("can't see/pee/spit/poo").
- AChE inhibitors ↑ ACh (myasthenia, Alzheimer's).

15 · Pharmacokinetics · ADME
★ "BODY → DRUG"

Absorption · **D**istribution · **M**etabolism · **E**xcretion.

ABSORPTION & BIOAVAILABILITY

Enteral (oral, SL, rectal) vs parenteral (IV, IM, SC). IV = 100% bioavailability, fastest, no first-pass. **Bioavailability (F)** = fraction reaching circulation unchanged. Absorption depends on lipid solubility, ionisation/pH, GI motility, surface area, blood flow and food.

DISTRIBUTION

Drugs bind **albumin**; only free (unbound) drug is active. ↓albumin / displacement → ↑free drug → interaction. **Vd** high = lipophilic/tissue; low = stays in plasma.

METABOLISM & EXCRETION

Liver (Phase I **CYP450**; Phase II conjugation) → water-soluble. **First-pass**: oral drug via portal vein → liver *before* circulation → ↓oral F. Kidney excretes; **renal impairment → accumulation**.

15b · Kinetic Parameters
DOSING

Half-life (t½) = time for conc. to fall 50%; **~4–5 t½** to clear OR reach **steady state** (rate in = rate out). **Loading dose** = reach level fast; **maintenance dose** = replace what's eliminated. CYP **inducers** ↓ levels, **inhibitors** ↑ levels/toxicity.

15c · Worked · Half-Life
SHOW THE STEPS

A drug with t½ = 8 h, started at 80 mg/L, no more dosing:

TIME	CONC.	# T½
0 h	80	0
8 h	40	1
16 h	20	2
24 h	10	3
40 h	~2.5	5 → cleared

⇒ ~5 half-lives (40 h) to essentially clear; the same ~5 t½ on regular dosing reaches steady state. A **loading dose** skips this wait by filling the volume of distribution up front.

15d · ADRs & Interactions
7.5.4 QUM

Type A ADR = dose-related, predictable (opioid respiratory depression); **Type B** = idiosyncratic/hypersensitivity, unpredictable (penicillin anaphylaxis). **Interactions:** PK (protein-binding displacement, CYP450 induction/inhibition, altered excretion) or PD (additive/synergistic/antagonistic). Elderly + polypharmacy = high risk. **QUM** = right drug/patient/dose/route/time + monitor.

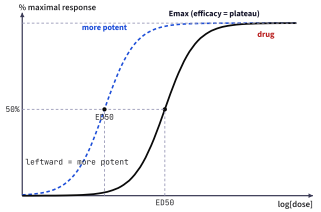
Worked interaction: a CYP450 *inhibitor* added to warfarin (narrow TI) slows warfarin metabolism → ↑plasma warfarin → bleeding. An *inducer* does the opposite (↓effect, clot risk). This is why narrow-TI drugs are monitored when co-prescribed. Protein-binding displacement (e.g. by a second highly-bound drug) similarly raises free active drug. Always check renal and hepatic function before dosing in the elderly. The five rights — right drug, patient, dose, route, time — plus monitoring effect and ADRs are the safety backbone of quality use of medicines.

16 · Pharmacodynamics
★ "DRUG → BODY"

Drugs bind receptors ("lock & key", e.g. GPCRs).

- **Agonist** — binds + **activates** (affinity + efficacy).
- **Partial agonist** — submaximal even when fully bound.
- **Antagonist** — binds, **no effect**, blocks agonist (affinity, no efficacy).

Competitive antagonist = same site, reversible, surmountable (↑agonist overcomes; shifts curve right, max unchanged). **Non-competitive** = irreversible/allosteric, insurmountable (↓max).



Dose-response. ED50 = dose for 50% of max effect (potency); Emax plateau = efficacy. A **left-shifted** curve is more potent.

16b · Potency, Efficacy, TI
DON'T CONFUSE

Potency ≠ efficacy: potency = dose needed (lower ED50/EC50 = left-shift); efficacy = max effect (curve height). A weaker, lower-dose drug can be *more potent* yet *less efficacious* than another — they are independent (e.g. a strong opioid vs paracetamol). **ED50** = effect in 50%; **LD50/TD50** = lethal/toxic in 50%.

THERAPEUTIC INDEX
`TI = LD50 / ED50 (or TD50/ED50)`
`high TI = safer; narrow = monitor`

Narrow-TI drugs: **warfarin, digoxin, lithium, gentamicin. Tolerance** = ↓response on repeat use (receptor downregulation, e.g. opioids). **Tachyphylaxis** = rapid tolerance over short repeated doses.

16c · Antagonist Curve Shifts
READ THE GRAPH

Competitive (surmountable): shifts the dose-response curve right, *same* Emax (more agonist overcomes it). **Non-competitive (insurmountable):** lowers Emax (the plateau drops; extra agonist can't recover it). **Partial agonist** = own ceiling below full Emax and can *block* a full agonist if both present.

Therapeutic window = plasma range between minimum effective and toxic concentrations — dosing keeps the concentration-time curve inside it. A **narrow window** (digoxin, lithium) means small dose changes tip from ineffective to toxic → therapeutic drug monitoring.

On the concentration-time curve: **Cmax** (peak), **Tmax** (time to peak), and **trough** (just before the next dose). Onset = crossing MEC up; duration = time above MEC; the danger zone = above the toxic level. Repeated dosing builds toward steady state, oscillating between peak and trough within the window — keeping the trough above MEC and the peak below the toxic level is the dosing goal. Narrow-window drugs are measured at the trough to confirm safety.

17 · NSAIDs & COX
1.3 / 5.3

Inhibit **cyclo-oxygenase (COX)** → ↓**prostaglandins** → anti-inflammatory, analgesic, antipyretic (+ antiplatelet for aspirin).

COX-1 = housekeeping (gastric mucosa, platelets, renal flow); **COX-2** = inducible (inflammation). Non-selective NSAIDs → GI ulcers/bleed, renal impairment. **Coxibs** (celecoxib) spare gut but ↑**cardiovascular risk**.

Paracetamol = analgesic/antipyretic, NOT anti-inflammatory, gentle on stomach (central action). **Corticosteroids** block **phospholipase A2** (stop prostaglandins + leukotrienes); AEs: hyperglycaemia, osteoporosis, infection, poor healing.

18 · Analgesic Ladder & Opioids
5.3.2

WHO ladder (escalate by severity; non-opioids/adjuvants continue at every step):

1. **Mild:** non-opioids — paracetamol, NSAIDs.
2. **Moderate:** weak opioids — codeine.
3. **Severe:** strong opioids — morphine, oxycodone, fentanyl.

Opioids bind opioid receptors centrally → ↓pain. AEs: respiratory depression (the danger sign) + sedation, constipation, nausea, tolerance, dependence. **Adjuvants**: some antidepressants/anticonvulsants; local anaesthetics block **Na⁺ channels**.

19 · High-Yield MCQ Trap-Bank
LAST LOOK

- Innate = no memory; adaptive = memory (B/antibody, T/cell).
- IgM first+largest; IgG most abundant + placenta; IgE allergy.
- Hypersensitivity **I IgE**, II cytotoxic, III complex, **IV T-cell delayed**. Anaphylaxis → **adrenaline**.
- AIDS = CD4 < 200; HIV kills CD4 helper T.
- Benign = no metastasis; **grading = looks, staging = TNM**.
- Oncogene = gain; suppressor (p53/BRCA) = loss.
- IV = 100% F, no first-pass; only free drug active; ~5 t½ = cleared/steady state.
- **β1 heart, β2 lungs**; atropine = "can't see/pee/spit/poo"; AChE-I ↑ ACh.
- Competitive = surmountable; high TI = safer.
- Opioid danger = respiratory depression; paracetamol ≠ anti-inflammatory.

SIA → *For SAQs, always show the cascade (trigger→mechanism→sign) and name a drug's mechanism of action, not just its name – that's where the marks live.*

20 · CNS / Mental-Health Drugs
7.5.3

- **Antidepressants** — SSRIs ↑ synaptic serotonin (reuptake block); SNRIs add noradrenaline.
- **Anxiolytics** — benzodiazepines enhance **GABA** (sedation, dependence risk).
- **Antipsychotics** — block **dopamine D2** (extrapyramidal AEs).
- **Mood stabiliser** — lithium (narrow TI → monitor levels).
- **Alzheimer's** — AChE inhibitors (donepezil) ↑ ACh; **Parkinson's** — levodopa ↑ dopamine.

SAQ reflex: answer the *verb* — "differentiate" = give the contrast, "explain" = give the cascade; for any drug, state the **mechanism of action** + one key AE. Define a term before applying it (define metastasis, then say why it makes a tumour malignant).

good luck. revise smart.