Study Guide 5

This guide covers chapters 9 and 10. Chapter 9 is integrative physiology: the gut, the endocrine axes, reproduction and the exercising body, all running on signals and negative feedback. Chapter 10 opens the chemistry domain with the four families of biomolecules and the enzymes that handle them. The board tests both chapters by asking you to follow one link and predict what happens when it breaks: a missing hormone, a missing enzyme, a changed amino acid. Work one chapter at a time, study the diagram, cover the steps of each worked case, then finish with the ten board-style items. The cram sheet at the end puts both chapters on one page.

WHAT THIS GUIDE COVERS

- Chapter 9 · the enteric nervous system and motility, salivary, gastric and pancreatic secretion, the parietal cell, the GI hormones, carbohydrate, protein and fat digestion and absorption, the liver, bile and bilirubin, hormone classes and receptors, the pituitary axes and primary versus secondary disease, GH, prolactin, thyroid and cortisol, insulin, glucagon and the fed and fasted states, PTH, vitamin D and bone remodeling, the male and female axes, pregnancy and menopause, and exercise and heat illness.
- Chapter 10 · monosaccharides, isomers and glycosidic bonds, polysaccharides, GAGs and proteoglycans of the disc, fatty acids, membranes, sphingolipidoses, cholesterol, eicosanoids and lipoproteins, amino acids and protein structure, collagen, elastin, hemoglobin and myoglobin, enzyme kinetics, Lineweaver Burk plots and inhibition, regulation, vitamin coenzymes, clinical enzymes, DNA and RNA, replication, transcription, translation, mutations and uric acid.

CHAPTER 9

Gastrointestinal, Endocrine, Reproductive and Exercise Physiology

Read it in full: **Chapter 9 in the review book**. Practice it: **the practice exams** (Exam 5 covers this chapter) and **the flashcards**.

What to know

The **myenteric (Auerbach) plexus** runs motility and the **submucosal (Meissner) plexus** runs secretion. Parasympathetic input speeds the gut; sympathetic input slows it and closes sphincters. Loss of inhibitory nitric oxide neurons gives achalasia (the lower esophageal sphincter will not relax) and Hirschsprung disease (absent ganglion cells in the distal colon). Interstitial cells of Cajal make **slow waves** that set the maximum contraction rate (stomach about 3, duodenum about 12 per minute); contraction needs spikes on top of them. The migrating motor complex, driven by motilin, sweeps the fasting gut about every 90 minutes.

The parietal cell secretes acid through the **H+/K+ ATPase** and makes intrinsic factor. Acetylcholine (M3) and gastrin raise calcium, histamine (H2) raises cAMP, and they potentiate one another, so an H2 blocker dulls all three. The alkaline tide is bicarbonate entering the blood after a meal. Pancreatic ducts secrete bicarbonate to secretin; acinar cells secrete enzymes to CCK. Enterokinase activates trypsinogen, and trypsin activates the rest; premature activation is the core of acute pancreatitis.

GI hormones: **gastrin** (G cells) raises acid; **CCK** (I cells, fat and protein) empties the gallbladder, releases enzymes and slows emptying; **secretin** (S cells, acid) releases bicarbonate; **GIP and GLP-1** are incretins, so oral glucose gives more insulin than IV glucose; **motilin** drives the fasting MMC; **somatostatin** inhibits nearly everything. A gastrinoma (Zollinger Ellison) causes multiple ulcers.

Only monosaccharides are absorbed: glucose and galactose by **SGLT1** with sodium (the basis of oral rehydration), fructose by GLUT5, all out by GLUT2. Lactase deficiency gives osmotic diarrhea and gas. Fats are emulsified by bile, split by lipase with colipase, carried in micelles, re-esterified and sent out as **chylomicrons** into the lacteals. Fat malabsorption causes steatorrhea and deficiency of A, D, E and K. Iron and calcium are absorbed in the duodenum; **B12 with intrinsic factor and bile salts in the terminal ileum**. Cholera toxin locks Gs on and opens CFTR.

The liver gets about 25% of cardiac output, three quarters by the portal vein. Bile salts are made from cholesterol (7α-hydroxylase), and about 95% are reabsorbed in the terminal ileum (enterohepatic circulation). Bilirubin from heme travels unconjugated on albumin; the liver

conjugates it with glucuronic acid. Hemolysis and Gilbert syndrome raise unconjugated bilirubin; obstruction raises conjugated bilirubin with dark urine, pale stools and itching. B12 deficiency (pernicious anemia, ileal disease, metformin, vegan diet) can present with back pain plus numb feet and an unsteady gait.

Peptide hormones are stored, travel free, act on membrane receptors through second messengers and last minutes. Steroids are made from cholesterol on demand, travel bound, act on nuclear receptors and last hours. Thyroid hormone acts like a steroid. Gs and cAMP: ACTH, TSH, LH, FSH, glucagon, PTH, V2. Gq: GnRH, TRH, oxytocin, V1, angiotensin II, alpha 1. Tyrosine kinase: insulin, IGF-1. JAK-STAT: GH, prolactin, EPO. Free hormone is the active fraction; pregnancy raises TBG and total T4 but not free T4.

In **primary** disease the target gland fails and the pituitary hormone moves the opposite way: primary hypothyroidism has low free T4 and **high TSH**. In **secondary** disease both are low. TSH is the best single thyroid screen. Graves disease has high T4 and suppressed TSH. Addison disease has low cortisol, high ACTH, hyperpigmentation and aldosterone loss (high potassium, low sodium); secondary adrenal insufficiency spares aldosterone and skin color. Exogenous steroids are the commonest cause of Cushing syndrome. **Prolactin** is held down by dopamine, so stalk damage or D2 blockers raise it; a prolactinoma gives amenorrhea, galactorrhea and bitemporal hemianopia.

GH is released in pulses during deep sleep and acts through **IGF-1**; it opposes insulin. Excess after the growth plates close is acromegaly (screen with IGF-1). Thyroid hormone raises metabolic rate and beta 1 receptors; hypothyroidism brings fatigue, cold intolerance, delayed reflex relaxation, myalgia and carpal tunnel syndrome. Cortisol raises glucose, breaks down protein, suppresses inflammation and inhibits bone formation, so long-term oral steroids are a major cause of osteoporotic compression fractures: take a medication history before a thrust technique.

Glucose enters the beta cell by GLUT2, is phosphorylated by glucokinase, raises ATP, **closes ATP-sensitive K+ channels**, depolarizes the cell, opens calcium channels and releases insulin (sulfonylureas close the same channel). C-peptide marks the body's own insulin. Insulin moves GLUT4 into muscle and fat membranes, stores fuel and drives potassium into cells. Glucagon,

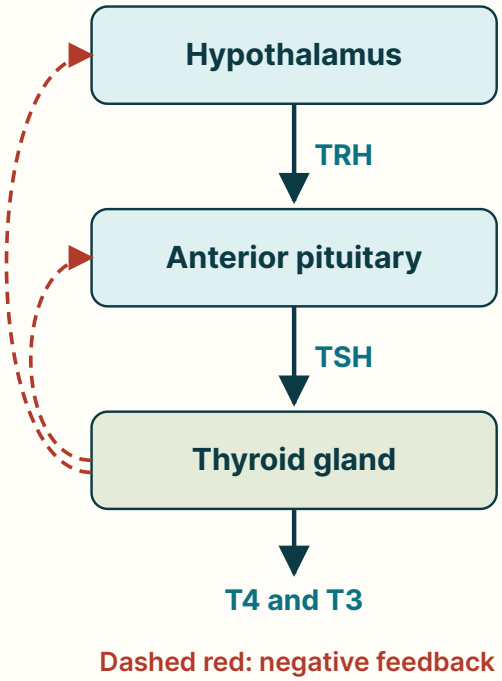
epinephrine, cortisol and GH defend glucose. Type 1 diabetes leads to DKA; type 2 to the hyperosmolar state. Diabetes: fasting glucose 126 mg/dL or more, HbA1c 6.5% or more. Exercise moves GLUT4 without insulin.

PTH raises calcium and lowers phosphate (bone resorption through osteoblast RANKL, distal calcium reabsorption, phosphaturia, 1α-hydroxylase on). **Calcitriol** raises both by absorbing them from the gut. Calcitonin plays a minor role. 25-hydroxyvitamin D is the best status test. The **RANKL to OPG ratio** sets resorption: PTH, glucocorticoids and cytokines raise it, estrogen lowers it. Labs: osteoporosis has normal calcium, phosphate and PTH; osteomalacia has low calcium or phosphate and high ALP; primary hyperparathyroidism has high calcium, low phosphate and high PTH (stones, bones, groans, psychiatric overtones).

Pulsatile GnRH drives LH and FSH. In men, LH drives Leydig cell testosterone, FSH drives Sertoli cells and inhibin B trims FSH; DHT shapes the external genitalia and prostate; estrogen closes the growth plates. Anabolic steroids shrink the testes. In women, LH makes theca cells produce androgens and FSH makes granulosa cells aromatize them to estradiol. Sustained high estradiol flips feedback to positive and triggers the **LH surge** and ovulation; the luteal phase is fixed at about 14 days. hCG rescues the corpus luteum. Menopause (12 months without menses, average 51) raises FSH and accelerates bone loss. The female athlete triad is low energy availability, amenorrhea and low bone density.

In exercise, cardiac output rises from about 5 to 20 to 25 L/min, systolic pressure rises, diastolic pressure stays about the same and TPR falls. **VO2 max is limited mainly by maximal cardiac output**; endurance training raises stroke volume and lowers resting heart rate, but maximal heart rate (about 220 minus age) does not change. The lactate threshold predicts endurance better than VO2 max. One MET is 3.5 mL O2/kg/min. **Exertional heat stroke** is a core temperature above 40 °C with CNS dysfunction: cool first by cold water immersion, then transport.

One axis, two kinds of failure: reading thyroid labs



Pattern	Free T4	TSH	Level
Primary hypothyroid	↓	↑	Gland
Secondary hypothyroid	↓	↓	Pituitary
Graves disease	↑	↓	Gland
TSH-secreting tumor	↑	↑	Pituitary

Opposite directions: the gland is the problem.
Same direction: the pituitary is the problem.

The same rule reads every axis: compare the pituitary hormone with the end hormone (TSH with T4, ACTH with cortisol, FSH with estradiol).

Feedback locates the lesion. If the pituitary hormone and the end hormone move in opposite directions the gland has failed; if they move together the pituitary is at fault.

LOCK THESE IN

- Myenteric plexus: motility. Submucosal plexus: secretion. Slow waves from interstitial cells of Cajal.
- Gastrin acid, secretin bicarbonate, CCK enzymes and bile, GIP and GLP-1 incretins, motilin MMC, somatostatin inhibits.
- SGLT1 for glucose and galactose; micelles to chylomicrons; B12 and bile salts in the terminal ileum.
- Primary failure: end hormone low, pituitary hormone high. Secondary: both low.
- Prolactin is held down by dopamine; prolactinoma gives amenorrhea, galactorrhea, bitemporal hemianopia.
- Beta cell: glucose, ATP, K-ATP channel closes, calcium in, insulin out.
- PTH raises calcium and lowers phosphate; calcitriol raises both.
- LH surge from sustained estradiol; luteal phase about 14 days; VO2 max limited by cardiac output.

Endocrine lab patterns

Condition	End hormone / pituitary hormone	Clue
Primary hypothyroidism (Hashimoto)	Free T4 low / TSH high	Most common pattern
Secondary hypothyroidism	Free T4 low / TSH low or normal	Pituitary disease
Graves disease	T4 high / TSH suppressed	Thyroid stimulating antibody
Addison disease	Cortisol low / ACTH high	Hyperpigmentation, high K+, low Na+
Secondary adrenal insufficiency	Cortisol low / ACTH low	Aldosterone spared
Primary hyperparathyroidism	Calcium high / PTH high	Phosphate low
Menopause or primary ovarian failure	Estradiol low / FSH high	FSH is the best marker
Prolactinoma	Prolactin high / LH, FSH low	Amenorrhea, galactorrhea
Acromegaly	IGF-1 high / GH not suppressed by glucose	Carpal tunnel, arthropathy

GI hormones

Hormone (cell)	Stimulus	Main action
Gastrin (G, antrum)	Peptides, distension, vagus	Raises acid; trophic to mucosa
CCK (I, duodenum)	Fat, amino acids	Gallbladder contraction, enzymes, slower emptying
Secretin (S, duodenum)	Acid below pH 4.5	Pancreatic and biliary bicarbonate
GIP (K) and GLP-1 (L)	Glucose, fat	Incretins: more insulin
Motilin (M)	Fasting	Starts the MMC
Somatostatin (D)	Luminal acid	Inhibits nearly everything

Worked cases

WORKED CASE 1 · READING THYROID LABS

Hannah, 44, has fatigue, weight gain, cold intolerance, aching muscles and night numbness in both hands. Free T4 is low and TSH is high.

STEP 1 · DECIDE WHICH WAY EACH MOVED

The end hormone (T4) is low and the pituitary hormone (TSH) is high: they moved in opposite directions.

STEP 2 · APPLY FEEDBACK

Low T4 removes negative feedback, so a healthy pituitary pours out TSH. The gland itself has failed.

STEP 3 · NAME IT

Primary hypothyroidism, most often Hashimoto thyroiditis.

STEP 4 · LINK THE HANDS

Hypothyroidism is a cause of carpal tunnel syndrome, so treat the wrist findings as part of a systemic picture and coordinate care.

CONTRAST

Low T4 with a low or normal TSH would point to the pituitary (secondary disease).

WORKED CASE 2 · AMENORRHEA AND A FIELD DEFECT

A 29-year-old has had no periods for eight months, notes milk from both breasts, and bumps into door frames on both sides.

STEP 1 · NAME THE FIELD DEFECT

Bumping into things on both sides suggests loss of both temporal fields: bitemporal hemianopia from chiasm compression.

STEP 2 · CONNECT THE HORMONES

Milk production and absent periods point to high prolactin, which inhibits GnRH.

STEP 3 · NAME THE LESION

A prolactin-secreting pituitary macroadenoma (prolactinoma), the most common functioning pituitary adenoma.

STEP 4 · RECALL TREATMENT LOGIC

Dopamine normally holds prolactin down, so dopamine agonists (cabergoline, bromocriptine) are first line. Refer.

WORKED CASE 3 · WHY ORAL GLUCOSE BEATS IV GLUCOSE

The same glucose load given by mouth produces a larger insulin rise than when it is given intravenously.

STEP 1 · NAME THE EFFECT

The incretin effect.

STEP 2 · FIND THE HORMONES

Glucose in the gut releases GIP from K cells and GLP-1 from L cells.

STEP 3 · TRACE THE ACTION

Both act on beta cells to amplify glucose-stimulated insulin release.

STEP 4 · APPLY IT

GLP-1 also slows gastric emptying and promotes satiety, the basis of GLP-1 agonist drugs.

TRAPS PEOPLE FALL INTO

- **Slow waves.** They are not action potentials and do not cause contraction by themselves.
- **Secondary adrenal insufficiency.** Aldosterone is largely spared because renin and angiotensin, not ACTH, control the glomerulosa.
- **Total versus free T4.** Pregnancy and oral estrogen raise TBG and total T4; free T4 and thyroid status stay normal.
- **PTH and phosphate.** PTH raises calcium but lowers plasma phosphate by causing phosphaturia.
- **Fixed phase.** The luteal phase is fixed at about 14 days; the follicular phase varies.

- **Heat stroke versus exhaustion.** Heat stroke is above 40 °C with CNS dysfunction; heat exhaustion has normal mental status.

Chapter 9 self-test · ten board-style items

1. Acidic chyme entering the duodenum releases which hormone?

A. Gastrin
B. Gastric inhibitory peptide
C. Secretin
D. Motilin

C. Secretin S cells respond to acid by releasing secretin, which drives pancreatic and biliary bicarbonate secretion.

2. Why does an H2 blocker reduce acid stimulated by gastrin and acetylcholine too?

A. Gastrin acts on H2 receptors directly
B. Acetylcholine is released from ECL cells
C. H2 blockers inhibit the proton pump
D. The three stimulants potentiate one another

D. The three stimulants potentiate one another ACh, gastrin and histamine amplify each other at the parietal cell, and gastrin acts partly by releasing histamine from ECL cells.

3. After an ileal resection, a patient develops macrocytic anemia and diarrhea. Why?

A. Lost B12 and bile salt absorption
B. Lost pancreatic enzyme secretion
C. Lost iron and calcium absorption
D. Lost lactase and sucrase activity

A. Lost B12 and bile salt absorption The terminal ileum absorbs B12 with intrinsic factor and reclaims bile salts; losing both gives megaloblastic anemia and fat malabsorption.

4. Low free T4 with a high TSH indicates which disorder?

A. Secondary hypothyroidism
B. Primary hypothyroidism
C. Euthyroid sick syndrome
D. Graves disease

B. Primary hypothyroidism The gland has failed and the pituitary responds to absent feedback with high TSH.

5. Which pattern fits primary adrenal insufficiency?

A. High cortisol, low ACTH, low potassium
B. Low cortisol, low ACTH, normal potassium
C. High cortisol, high ACTH, normal potassium
D. Low cortisol, high ACTH, high potassium

D. Low cortisol, high ACTH, high potassium Addison disease removes cortisol and aldosterone; ACTH rises (with hyperpigmentation) and potassium climbs.

6. Which step directly triggers insulin release from the beta cell?

A. Closure of ATP-sensitive K+ channels
B. Activation of glucagon receptors
C. Opening of GLUT4 transporters
D. Opening of K-ATP channels by ATP

A. Closure of ATP-sensitive K+ channels Rising ATP closes K-ATP channels, the cell depolarizes, voltage-gated calcium channels open and insulin is released.

7. Which lab pattern fits primary hyperparathyroidism?

A. High calcium, high phosphate, low PTH
B. Low calcium, high phosphate, high PTH
C. High calcium, low phosphate, high PTH
D. Normal calcium, normal phosphate, normal PTH

C. High calcium, low phosphate, high PTH PTH increases resorption and calcium reabsorption and causes phosphaturia. The second option fits renal secondary hyperparathyroidism.

8. What triggers the midcycle LH surge?

A. Inhibin B climbing
B. Estradiol high for days
C. Progesterone falling away
D. A sudden drop in FSH

B. Estradiol high for days Estradiol held above a threshold for about two days switches feedback from negative to positive.

9. In a healthy young adult, which link in the oxygen chain sets the ceiling on VO2 max?

A. Ventilation per minute
B. Diffusion in the lung
C. Delivery by the heart
D. Mitochondrial density

C. Delivery by the heart Maximal cardiac output limits VO2 max; ventilation and diffusion are rarely the limit in healthy people.

10. A runner collapses in the heat, confused, with a rectal temperature of 41 °C. What comes first?

A. Transport first, then cooling
B. Cold water immersion, then transport
C. Oral fluids and rest in the shade
D. Massage and elevate the legs

B. Cold water immersion, then transport Exertional heat stroke is an emergency; whole-body cold water immersion is the fastest cooling and comes before transport.

CHAPTER 10

Biomolecules: Carbohydrates, Lipids, Proteins, Enzymes and Nucleic Acids

Read it in full: **Chapter 10 in the review book**. Practice it: **the practice exams** (Exam 5 covers this chapter) and **the flashcards**.

What to know

Monosaccharides are aldoses or ketoses and are named by carbon count. Natural sugars are D; natural amino acids are L. **Epimers** differ at one chiral carbon (glucose and galactose at C4, glucose and mannose at C2). **Anomers** differ only at the anomeric carbon made by ring closure (C1 in glucose); β-D-glucose is the more stable. A free anomeric carbon makes a reducing sugar, and the same chemistry drives glycation (HbA1c, stiffened collagen in diabetes).

Disaccharides: maltose (glucose α-1,4), lactose (galactose β-1,4 glucose), and **sucrose** (glucose α-1,β-2 fructose), which is **nonreducing** because both anomeric carbons are bonded. Starch (amylose and amylopectin) and glycogen use α-1,4 chains with α-1,6 branches; glycogen branches more often, giving many ends for fast release. Cellulose is β-1,4 and indigestible fiber.

Glycosaminoglycans are long, unbranched, strongly negative chains that attract cations and water. Hyaluronic acid is the only GAG that is not sulfated and not on a core protein; chondroitin

sulfate is the most abundant. **Aggrecan** carries chondroitin and keratan sulfate and binds hyaluronic acid; trapped in a collagen net, it swells and gives cartilage and the **nucleus pulposus** their compression resistance. With degeneration, proteoglycan falls, the disc dehydrates (black disc on T2 MRI) and load shifts to the annulus and facets. Mucopolysaccharidoses: Hurler (corneal clouding), Hunter (X-linked), Morquio (odontoid hypoplasia).

Fatty acids are mostly even numbered; cis double bonds kink the chain and raise fluidity; trans fats raise LDL and lower HDL. **Linoleic (ω-6) and α-linolenic (ω-3) acids are essential.** Triglycerides store about 9 kcal/g. Phosphatidylcholine (lecithin) dominates the outer membrane leaflet and lung surfactant; phosphatidylserine flips outward in apoptosis; PIP2 gives IP3 and DAG; cardiolipin is the syphilis test antigen. Sphingomyelin is in myelin. Sphingolipidoses: Tay-Sachs (hexosaminidase A), Niemann-Pick (sphingomyelinase), **Gaucher** (glucocerebrosidase; bone pain, femoral head necrosis), Fabry (X-linked), Krabbe, metachromatic leukodystrophy.

Cholesterol is made from acetyl CoA with **HMG-CoA reductase** as the rate-limiting step (statins). It is the parent of bile acids, steroid hormones and vitamin D, and it buffers membrane fluidity. **Phospholipase A2** (blocked by corticosteroids) releases arachidonic acid. **COX** (blocked by aspirin and NSAIDs) makes prostaglandins, prostacyclin (endothelium: dilates, inhibits platelets) and thromboxane A2 (platelets: constricts, aggregates). Aspirin acetylates COX irreversibly, and anucleate platelets cannot replace it for 7 to 10 days. Lipoxygenase makes leukotrienes (LTB4 chemotaxis; LTC4, D4, E4 bronchoconstriction).

Lipoproteins: **chylomicrons** (intestine, dietary fat, apoB-48), VLDL (liver fat, apoB-100), IDL, **LDL** (cholesterol to tissues, apoB-100, atherogenic) and **HDL** (reverse cholesterol transport, apoA-I activates LCAT). ApoC-II activates lipoprotein lipase; apoE clears remnants. Familial hypercholesterolemia (LDL receptor defect) brings tendon xanthomas, often on the Achilles tendon, and early coronary disease.

Amino acids are L and zwitterions at body pH; **histidine** (pKa near 6) buffers best. Essential: PVT TIM HaLL. Leucine and lysine are purely ketogenic. The **peptide bond** is rigid and planar (partial double bond). Primary structure is sequence; secondary structure (α-helix, β-sheet) rests on **backbone** hydrogen bonds; tertiary structure rests on side chains, the hydrophobic effect and

disulfide bonds; quaternary is subunit assembly. Denaturation unfolds a protein without breaking peptide bonds. Proline breaks helices.

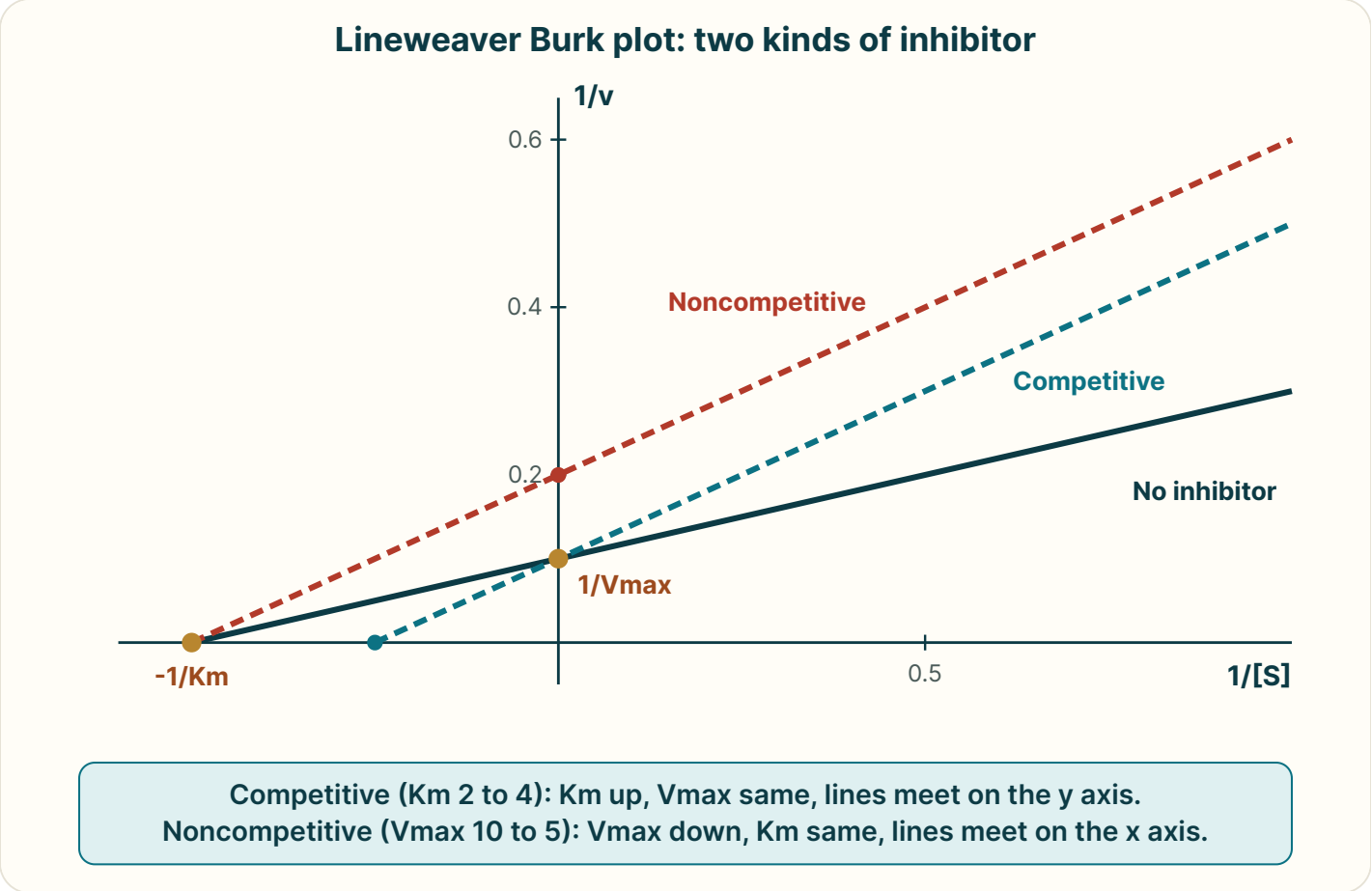
Collagen is Gly-X-Y, three chains in a triple helix; glycine fits the crowded center. Prolyl and lysyl hydroxylation need **vitamin C** (scurvy) and iron; lysyl oxidase cross-links need **copper** (Menkes). Type I is bone, tendon, ligament, skin, annulus and late scar (osteogenesis imperfecta); type II is cartilage and nucleus pulposus; type III is vessels and early granulation tissue (vascular Ehlers-Danlos); type IV is basement membrane. Repair starts with type III and remodels to type I over months. **Elastin** (ligamentum flavum, arteries, lung) is cross-linked by desmosine on a fibrillin scaffold (Marfan).

Myoglobin has one heme and a hyperbolic curve (P50 about 1 to 3 mm Hg). Hemoglobin (α2β2) binds cooperatively (T to R state), giving a sigmoidal curve with P50 about 27. CO2, H+ (Bohr), heat and 2,3-BPG shift it right; HbF, CO, alkalosis and cold shift it left. Methemoglobin has Fe3+. Sickle cell disease is glutamate to valine at β6.

Enzymes lower activation energy; they never change ΔG or the equilibrium. In Michaelis Menten kinetics, **Km** is the substrate concentration giving half of Vmax (low Km means high affinity) and **Vmax** reflects enzyme amount. Hexokinase has a low Km and is product inhibited; glucokinase (liver, beta cell) has a high Km. On a **Lineweaver Burk** plot the y-intercept is 1/Vmax and the x-intercept is -1/Km. **Competitive**: Km up, Vmax same, lines meet on the y axis (statins, methotrexate). **Noncompetitive**: Vmax down, Km same, lines meet on the x axis. Uncompetitive: both down, parallel. Irreversible: aspirin, organophosphates, penicillin.

Rate-limiting enzymes are often allosteric and feedback inhibited: PFK-1 (glycolysis), HMG-CoA reductase, carnitine acyltransferase I (inhibited by malonyl CoA), acetyl CoA carboxylase. Phosphorylation by PKA turns glycogen phosphorylase on and glycogen synthase off. Zymogens are activated by cleavage. Coenzymes: B1 TPP (pyruvate and α-ketoglutarate dehydrogenase), B2 FAD, B3 NAD+, B5 CoA, **B6 PLP (transamination)**, B7 biotin (carboxylation), B9 folate (one-carbon), B12 (methionine synthase, methylmalonyl CoA mutase), C (hydroxylation), K (γ-carboxylation). Clinical enzymes: CK-MM muscle, ALT liver, AST liver plus heart and muscle, **ALP bone or liver (GGT says liver)**, lipase pancreas. Very high ALP with normal calcium suggests Paget disease.

Purines (A, G) have two rings; pyrimidines (C, T, U) one. DNA is an antiparallel right-handed helix; A-T has two hydrogen bonds and G-C three. Replication is semiconservative and always 5′ to 3′: helicase unwinds, topoisomerase relieves coiling (gyrase is the fluoroquinolone target), primase lays RNA primers, the leading strand runs continuously and the lagging strand in **Okazaki fragments** joined by ligase. RNA polymerase II makes mRNA, which is capped, polyadenylated and spliced. Ribosomes are 80S in humans and 70S in bacteria. Mutations: silent, missense (sickle cell), nonsense, frameshift (Duchenne), trinucleotide repeats (Huntington CAG). **Xanthine oxidase** makes uric acid (allopurinol); urate crystals are needle shaped and negatively birefringent; podagra is acute gout of the first MTP joint.



Read the intercepts. The y-intercept is 1/Vmax and the x-intercept is -1/Km, so where the lines meet tells you the type of inhibitor.

LOCK THESE IN

- Glucose and galactose are C4 epimers; α and β glucose are anomers; sucrose is nonreducing.
- Hyaluronic acid: not sulfated, no core protein. Aggrecan plus collagen net = disc swelling pressure.
- Linoleic and α-linolenic acids are essential; HMG-CoA reductase is rate limiting for cholesterol.
- Corticosteroids block phospholipase A2; aspirin blocks COX irreversibly; TXA2 aggregates, PGI2 opposes.
- Chylomicrons apoB-48; VLDL and LDL apoB-100; HDL apoA-I.
- Collagen Gly-X-Y needs vitamin C and copper; type I bone and ligament, type II cartilage and nucleus.
- Competitive: Km up, Vmax same. Noncompetitive: Vmax down, Km same. Enzymes never change equilibrium.
- Purines two rings; G-C three hydrogen bonds; Okazaki fragments on the lagging strand; xanthine oxidase makes urate.

Enzyme inhibition

Type	Km and Vmax	Lineweaver Burk and examples
Competitive	Km up; Vmax unchanged	Lines meet on the y axis; statins, methotrexate
Noncompetitive	Km unchanged; Vmax down	Lines meet on the x axis; allosteric inhibitors
Uncompetitive	Both down	Parallel lines; lithium on inositol monophosphatase
Irreversible	Acts like loss of enzyme	Aspirin on COX, organophosphates, penicillin

Molecules tied to musculoskeletal tissue

Molecule	Where	Clinical link
Aggrecan and chondroitin sulfate	Cartilage, nucleus pulposus	Loss dehydrates the disc
Hyaluronic acid	Synovial fluid, aggrecan backbone	Viscosity of joint fluid
Collagen type I	Bone, tendon, ligament, annulus	Osteogenesis imperfecta; slow remodeling
Collagen type II	Hyaline cartilage, nucleus pulposus	Chondrodysplasias
Collagen type III	Vessels, early scar	Vascular Ehlers-Danlos
Elastin on fibrillin	Ligamentum flavum, aorta	Marfan syndrome
Glucocerebroside	Macrophages (Gaucher)	Bone pain, femoral head necrosis
Alkaline phosphatase	Osteoblasts, bile ducts	Paget disease, blastic metastases
Uric acid	Joints	Gout, punched-out erosions

Worked cases

WORKED CASE 1 · READING MICHAELIS MENTEN NUMBERS

An enzyme has Vmax = 100 µmol/min and Km = 5 mM.

STEP 1 · AT [S] = KM

v = 100 × 5 / (5 + 5) = 50 µmol/min, half of Vmax, as the definition of Km says.

STEP 2 · AT [S] = 15 MM

v = 100 × 15 / (5 + 15) = 75 µmol/min.

STEP 3 · AT [S] = 45 MM

v = 100 × 45 / (5 + 45) = 90 µmol/min: approaching Vmax, near zero order.

STEP 4 · ADD A COMPETITIVE INHIBITOR THAT DOUBLES KM TO 10 MM

At 10 mM substrate, v = 100 × 10 / 20 = 50. Enough substrate still reaches Vmax of 100, so Vmax is unchanged.

LINEWEAVER BURK CHECK

Without inhibitor the x-intercept is -1/5 = -0.2; with it, -1/10 = -0.1. The y-intercept stays at 1/100 = 0.01, so the lines meet on the y axis.

WORKED CASE 2 · BONE PAIN AND A HIGH ALP

Arthur, 72, has deep aching in the right tibia and pelvis and a hat that no longer fits. ALP is markedly raised; calcium, phosphate and GGT are normal.

STEP 1 · FIND THE SOURCE OF ALP

ALP comes mainly from bone (osteoblasts) or liver (bile ducts). A normal GGT says the source is not the liver.

STEP 2 · READ THE PATTERN

Very high bone ALP with normal calcium and phosphate fits intense osteoblast activity.

STEP 3 · NAME THE LIKELY DISEASE

Paget disease of bone; films show coarse trabeculae and cortical thickening.

KEEP THE RED FLAG IN MIND

A very high ALP with lytic or sclerotic lesions and a cancer history suggests metastasis instead; that changes management.

WORKED CASE 3 · A HOT BIG TOE OVERNIGHT

Dorian, 52, wakes with a red, swollen, exquisitely painful first MTP joint after a heavy meal with beer. He takes a thiazide diuretic.

STEP 1 · NAME THE PICTURE

Podagra: acute gout of the first metatarsophalangeal joint.

STEP 2 · FIND THE CHEMISTRY

Uric acid is the end product of purine breakdown by xanthine oxidase; above about 6.8 mg/dL, urate exceeds its solubility.

STEP 3 · LIST HIS RISK FACTORS

Underexcretion from the thiazide and alcohol; purine-rich food.

STEP 4 · RECALL THE CRYSTALS

Needle-shaped, negatively birefringent monosodium urate.

STEP 5 · ACT

Do not manipulate the inflamed joint; refer for medical management of the flare and of urate.

TRAPS PEOPLE FALL INTO

- **Epimer versus anomer.** An anomer differs only at the anomeric carbon made by ring closure; an epimer can differ at any one chiral carbon.
- **Hydrogen bonds in secondary structure.** They are between backbone atoms, not side chains. Disulfides are tertiary.
- **Enzymes and equilibrium.** Enzymes change the rate only, never ΔG or the equilibrium constant.
- **Low Km.** A low Km means high affinity, not low activity.
- **Aspirin and platelets.** The effect lasts the platelet lifespan, 7 to 10 days, because platelets cannot make new COX.
- **Gout versus pseudogout.** Gout crystals are needles, negatively birefringent; pseudogout crystals are rhomboid, weakly positive.

Chapter 10 self-test · ten board-style items

1. In which common disaccharide are both anomeric carbons locked in the bond?

A. Maltose
B. Lactose
C. Isomaltose
D. Sucrose

D. Sucrose With glucose C1 and fructose C2 both bonded, sucrose cannot open and is nonreducing.

2. Which glycosaminoglycan is neither sulfated nor attached to a core protein?

A. Hyaluronic acid
B. Heparan sulfate
C. Chondroitin sulfate
D. Keratan sulfate

A. Hyaluronic acid Hyaluronic acid forms the backbone strand to which aggrecan attaches through link protein.

3. Corticosteroids block the production of both prostaglandins and leukotrienes because they inhibit

A. thromboxane synthase
B. cyclooxygenase-1
C. phospholipase A2
D. 5-lipoxygenase

C. phospholipase A2 Phospholipase A2 releases arachidonic acid, the shared starting material for both branches.

4. Which apolipoprotein is made only in the intestine and marks chylomicrons?

A. ApoA-I
B. ApoB-48
C. ApoC-II
D. ApoB-100

B. ApoB-48 ApoB-48 is made only by enterocytes. VLDL and LDL carry apoB-100; apoA-I marks HDL; apoC-II activates lipoprotein lipase.

5. Bleeding gums, perifollicular hemorrhages and poor wound healing reflect failure of which step?

A. Hydroxylation of proline and lysine
B. Copper-dependent cross-linking
C. Glycosylation in the Golgi
D. Cleavage of procollagen peptides

A. Hydroxylation of proline and lysine Prolyl and lysyl hydroxylases need vitamin C. This is scurvy.

6. The α-helix is stabilized mainly by

A. ionic bonds between side chains
B. hydrophobic packing of side chains
C. hydrogen bonds between backbone groups
D. disulfide bonds between cysteines

C. hydrogen bonds between backbone groups Secondary structure rests on backbone C=O to N-H hydrogen bonds. Disulfides and side-chain interactions are tertiary.

7. An inhibitor raises Km and leaves Vmax unchanged. What type is it?

A. Uncompetitive
B. Competitive
C. Irreversible
D. Noncompetitive

B. Competitive It competes for the active site, so enough substrate restores full speed but half speed needs more substrate.

8. Which vitamin-derived coenzyme is required by ALT and AST?

A. Thiamine pyrophosphate (B1)
B. Tetrahydrofolate (B9)
C. Biotin (B7)
D. Pyridoxal phosphate (B6)

D. Pyridoxal phosphate (B6) Transamination uses pyridoxal phosphate. TPP serves oxidative decarboxylation; biotin serves carboxylation.

9. Why is the lagging strand made in pieces?

A. Primase works only on one strand
B. Polymerases add only to a 3′ end
C. Helicase opens only one strand
D. Ligase cannot work continuously

B. Polymerases add only to a 3′ end Synthesis must run 5′ to 3′, so on the antiparallel lagging template it runs away from the fork in Okazaki fragments.

10. Allopurinol lowers urate by inhibiting which enzyme?

A. HGPRT
B. Adenosine deaminase
C. Xanthine oxidase
D. Uricase

C. Xanthine oxidase Xanthine oxidase converts hypoxanthine to xanthine and xanthine to uric acid. Humans lack uricase.

Cram sheet

Both chapters on one page. Cover the right columns and rebuild each row from memory. If a row will not come back, go back to that chapter.

GI, endocrine, reproduction and exercise

Topic	Rule	Board hook
Enteric plexuses	Myenteric motility; submucosal secretion	Achalasia, Hirschsprung
Acid	H+/K+ ATPase; ACh, gastrin, histamine	Alkaline tide
GI hormones	Gastrin, CCK, secretin, GIP, GLP-1, motilin, somatostatin	Incretin effect
Absorption	SGLT1, GLUT5, GLUT2; micelles, chylomicrons	B12 and bile salts in terminal ileum
Bilirubin	Unconjugated in hemolysis; conjugated in obstruction	Dark urine, pale stool
Hormone classes	Peptide membrane; steroid nuclear	JAK-STAT: GH, prolactin
Axes	Primary: pituitary hormone high; secondary: both low	TSH best thyroid screen
Insulin	K-ATP closes, calcium in	C-peptide marks own insulin
Calcium	PTH up Ca, down PO4; calcitriol up both	RANKL to OPG ratio
Reproduction	LH surge from estradiol; luteal 14 days	FSH high in menopause
Exercise	VO2 max limited by cardiac output	Heat stroke above 40 °C with CNS signs

Biomolecules

Topic	Rule	Board hook
Sugars	Epimers one carbon; anomers at C1	Sucrose nonreducing
Polysaccharides	α-1,4 with α-1,6 branches	Cellulose β-1,4 fiber
GAGs	Negative, hold water; aggrecan on HA	Black disc on T2
Lipids	Essential: linoleic, α-linolenic	Gaucher bone and AVN
Eicosanoids	PLA2, COX, lipoxygenase	Aspirin 7 to 10 days on platelets
Lipoproteins	B-48 chylomicron; B-100 LDL; A-I HDL	Achilles xanthomas in FH
Protein structure	Backbone H bonds secondary; disulfides tertiary	Denaturation keeps sequence
Collagen	Gly-X-Y; vitamin C; copper	I bone, II cartilage, III vessel, IV basement
Kinetics	Km half Vmax; LB intercepts	Competitive Km up; noncompetitive Vmax down
Coenzymes	B1 TPP, B6 PLP, B7 biotin, B12	ALP plus GGT says liver
Nucleic acids	Purines two rings; GC three bonds	Okazaki fragments; urate from xanthine oxidase

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