Human Anatomy, Physiology and Pathophysiology II (Theory)

Course code: BP203T

A Textbook for the B. Pharm Second Semester (BP203T)

As per the new Pharmacy Council of India (PCI) Syllabus 2026 (NEP 2020)

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PREFACE

This book was written for one reader: the second-semester pharmacy student meeting the human body as a working machine for the first time, and needing to understand it well enough to pass the BP203T examination and to make sense of the pharmacology that follows. Everything in it is shaped to that purpose. The anatomy is taught only to the depth the physiology needs, the physiology only to the depth the diseases need, and each system closes by pointing at where a future drug will act, so that no fact feels abstract to a student of pharmacy.

The subject is large, and the temptation in a book like this is to pile up facts. The plan here is the opposite. A small number of ideas, named at the start and returned to throughout, carry the whole book: that structure serves function, that the body defends a steady internal state by feedback, that chemical signalling runs the body, and that disease is the failure of a normal process. A student who holds these four ideas will find that the diseases explain themselves, because each is simply a healthy mechanism gone wrong. Throughout, the writing assumes the reader is intelligent and busy, and tries to be clear, exact and honest rather than exhaustive.

The book follows the BP203T syllabus unit by unit: the nervous system, the gastrointestinal system, the respiratory and urinary systems, the endocrine system, and the reproductive system with cancer. Every topic the syllabus lists is covered, with original figures drawn for clarity in black and white, comparison tables for revision, worked examples where the subject is quantitative, and a full set of self-assessment questions in the pattern of the university examination at the end of each chapter. The figures are kept deliberately simple and labelled, so that a student can reproduce them in an answer.

No book is the work of one hand alone, and this one rests on the standard reference texts of the subject, listed at the end of each chapter and gathered at the back. Students are encouraged to read this book first to build the framework, and then to turn to those larger texts for greater detail where their interest or their examination requires it.

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COURSE OBJECTIVES

The objectives of this course are to:

1. Understand the anatomy and physiology of major body systems.

2. Learn mechanisms of neurological, gastrointestinal, respiratory, renal, endocrine, and reproductive functions.

3. Identify common pathophysiological conditions affecting each organ system.

4. Correlate structural and functional abnormalities with disease symptoms.

5. Equip students with foundational knowledge for interpreting disease processes and planning rational pharmacotherapy.

COURSE OUTCOMES

Upon successful completion of this course, the students will be able to:

1. Describe the structural organization of the nervous, gastrointestinal, respiratory, urinary, endocrine and reproductive systems.

2. Explain the physiological mechanisms that regulate the functions of nervous, endocrine and reproductive systems.

3. Illustrate the etiology and development of common diseases affecting different organ systems including cancer.

4. Analyze the pathophysiological alterations associated with disorders of the nervous, gastrointestinal, respiratory, renal and endocrine systems.

5. Interpret clinical manifestations and case findings related to organ system dysfunctions.

Syllabus

Unit	Topics	No. of lectures
I	Nervous System a) Organization of nervous system, neuron, neuroglia, classification and properties of nerve fibre, electrophysiology, action potential, nerve impulse, receptors, synapse and neurotransmitters. Central nervous system: Meninges, ventricles of brain and cerebrospinal fluid. Structure and functions of brain (cerebrum, brain stem and cerebellum), spinal cord (gross structure, functions of afferent and efferent nerve tracts, reflex activity). b) Pathophysiology of epilepsy, Parkinson's disease, stroke, migraine, depression, schizophrenia, Alzheimer's disease and meningitis.	14 hours
II	Gastrointestinal System a) Anatomy of GI tract with special reference to anatomy and functions of stomach (acid production in the stomach and its regulation through parasympathetic nervous system; role of pepsin in protein digestion). Anatomy and functions of small intestine and large intestine. Anatomy and functions of salivary glands, pancreas and liver. Movements of GIT, digestion and absorption of nutrients. b) Pathophysiology of inflammatory bowel diseases, peptic ulcer, jaundice, hepatitis, typhoid and alcoholic and non alcoholic fatty liver disease.	12 hours
III	a) Respiratory System Anatomy of respiratory system with special reference to anatomy of lungs. Mechanism of respiration and regulation of respiration. Lung volumes and capacities, transport of respiratory gases, artificial respiration and resuscitation	12 hours

	methods. b) Pathophysiology of asthma, chronic obstructive pulmonary diseases and tuberculosis. c) Urinary System Anatomy of urinary tract with special reference to anatomy of kidney and nephrons. Functions of kidney and urinary tract. Physiology of urine formation, micturition reflex and role of kidneys in acid-base balance. Role of Renin Angitensin Aldosterone System in kidney. d) Pathophysiology of acute and chronic renal failure and urinary tract infections.	
IV	Endocrine System a) Classification of hormones and mechanism of hormone action. Structure and functions of pituitary gland, thyroid gland, parathyroid gland, adrenal gland, pancreas, pineal gland and thymus. b) Pathophysiology of diabetes, hypothyroidism, hyperthyroidism, goitre and polycystic ovary syndrome.	10 hours
V	Reproductive System and Cancer a) Anatomy of male and female reproductive system. Functions of male and female reproductive system, sex hormones, physiology of menstruation, fertilization, spermatogenesis, oogenesis, pregnancy and parturition. b) Pathophysiology of sexually transmitted diseases: AIDS, syphilis and gonorrhea. c) Etiology and pathogenesis of cancer.	12 hours

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Chapter 1: Organization of the Nervous System, the Neuron and the Nerve Impulse

Learning outcomes

After working through this chapter the student will be able to:

1. Describe the structural and functional organization of the nervous system into its central, peripheral, somatic and autonomic divisions.
2. Draw and label a typical neuron and explain how its parts match its job of carrying signals.
3. Name the types of neuroglia and state one function of each.
4. Classify nerve fibres by diameter and conduction speed, and explain the properties of a nerve fibre that an exam asks for.
5. Explain how the resting membrane potential is set up and how an action potential is generated, conducted and made faster by myelin.
6. Describe how a chemical synapse transmits a signal, and classify receptors and the major neurotransmitters.

1.1 Why the body needs a fast signalling system

Pick up a hot cup, feel the burn, and your hand is already moving before you have finished the thought. Something carried that message from skin to spinal cord and back to muscle in a fraction of a second. The body has two systems for sending signals. One is the endocrine system, which floats hormones through the blood and works in minutes to hours. The other is the nervous system, which fires electrical signals down wires and works in milliseconds. When speed matters, the nervous system does the job.

This chapter builds the wire and the signal. First the layout of the whole system, so you know the map. Then the neuron, the single cell that does the carrying. Then the electrical event itself, the action potential, which is the one piece of this chapter that every later chapter leans on. Get the action potential clear here and the heart in Chapter 9, the airway in Chapter 6, and every drug that works on a nerve will make sense later. Rush it, and those topics turn into memorising.

A pharmacy student has a sharper reason to learn this well. Most of the drugs in a pharmacology syllabus act somewhere on this pathway: on a channel, on a receptor, on the enzyme that destroys a transmitter, or on the pump that recycles it. Local anaesthetics block the sodium channel you will meet in section 1.6. Antidepressants block the reuptake of

transmitters you will meet in section 1.8. So the nervous system is not background anatomy. It is the map of where drugs work.

1.2 Organization of the nervous system

The nervous system is split two ways, by location and by control. Both splits matter and both are examined, so keep them separate in your head.

By location, there is the central nervous system and the peripheral nervous system. The **central nervous system (CNS)** is the brain and the spinal cord. It is the processor: it receives information, decides what to do, and issues commands. The **peripheral nervous system (PNS)** is everything else, the nerves that run out to the rest of the body. The PNS is the cabling that connects the processor to the sensors and the muscles.

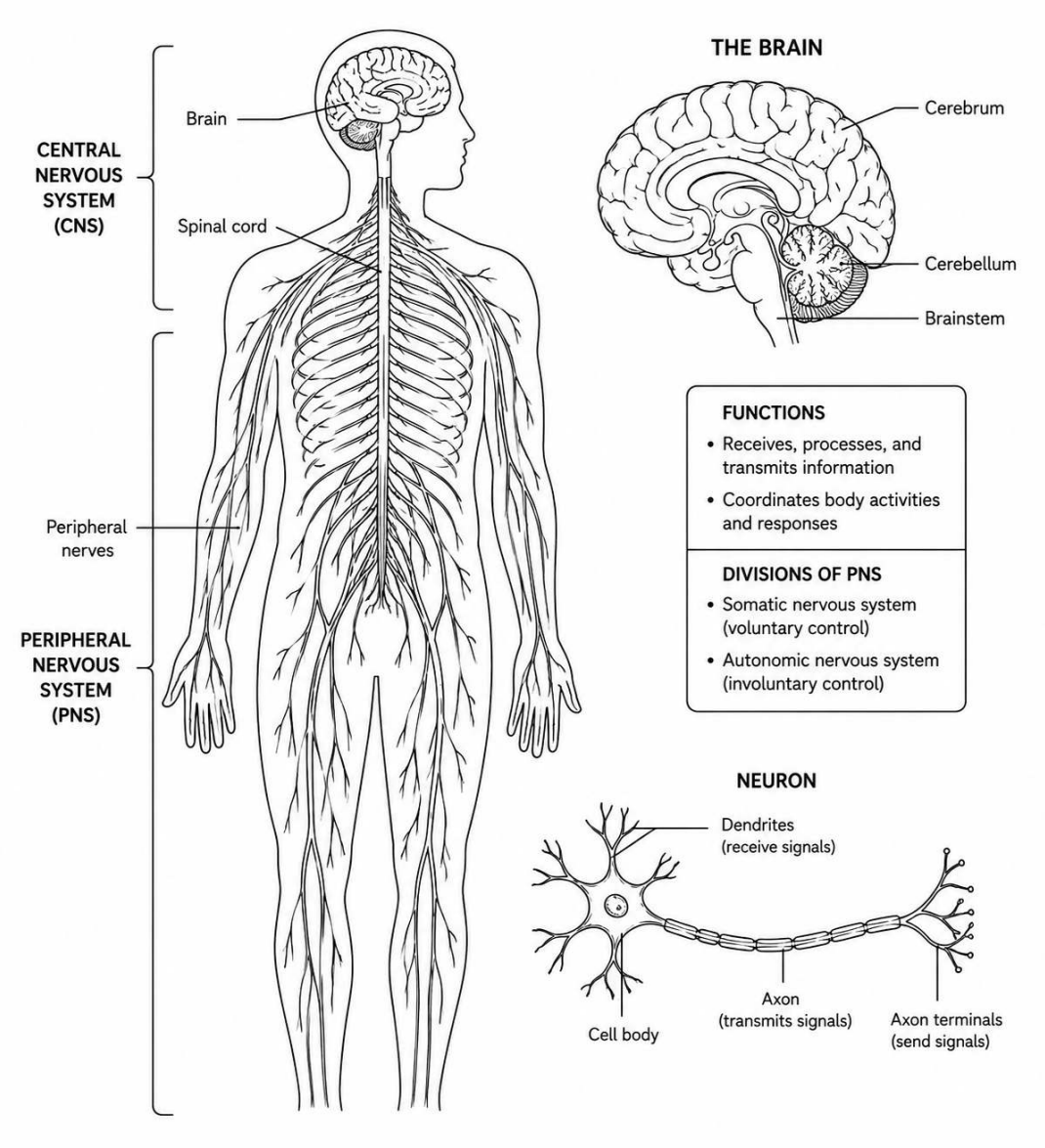


Figure 1.1 Nervous system

The PNS carries traffic in two directions. **Afferent (sensory) neurons** carry signals inward, from sense organs and the body toward the CNS. **Efferent (motor) neurons** carry signals outward, from the CNS to the muscles and glands that act. A simple way to hold the words: afferent arrives at the centre, efferent exits. Mix these up and the reflex arc in Chapter 2 will not make sense.

By control, the efferent side splits again into the somatic and the autonomic nervous systems. The **somatic nervous system** carries voluntary commands to skeletal muscle. You decide to lift your arm, and the somatic system delivers the order. The **autonomic nervous system (ANS)** runs the things you do not consciously control: heart rate, gut movement, sweating, the diameter of blood vessels and airways, the secretion of many glands. It works in the background to keep the internal state steady, which is the homeostasis throughline of this book.

The autonomic system has two branches that usually pull in opposite directions, and this opposition is one of the most useful ideas in the whole of pharmacology. The **sympathetic nervous system** is the "fight or flight" branch. It gets the body ready for effort: it speeds the heart, widens the airways, dilates the pupils, and shifts blood to muscle. The **parasympathetic nervous system** is the "rest and digest" branch. It slows the heart, narrows the airways, and turns on digestion, including the gastric acid you will meet in Chapter 4. Most organs receive both, and the balance between them sets the organ's state at any moment.

This dual control is worth fixing now because it returns again and again. When you read in Chapter 4 that the vagus nerve drives gastric acid, you are reading parasympathetic action. When you read in Chapter 6 that the airway tightens in asthma, the parasympathetic side is part of the story. When you read in Chapter 8 that the adrenal medulla pours out adrenaline, that is the sympathetic side given a hormonal voice. One map, used many times. Figure 1.2 lays the whole organization out as a tree.

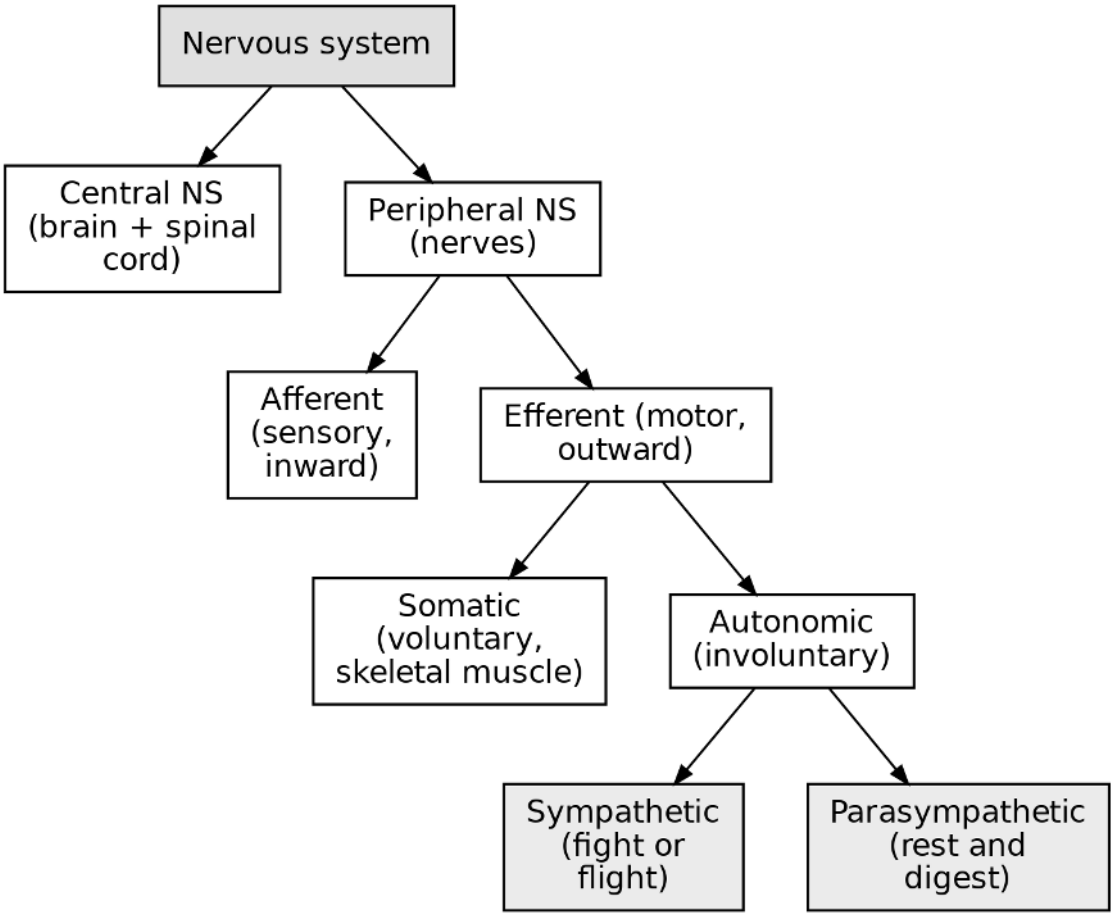


Figure 1.2 *Organization of the nervous system.*

> **Quick-recall box 1.1: Organization at a glance** CNS = brain + spinal cord (the processor). PNS = nerves (the cabling). Afferent arrives, efferent exits. Efferent splits into somatic (voluntary, to skeletal muscle) and autonomic (involuntary). Autonomic splits into sympathetic (fight or flight) and parasympathetic (rest and digest).

1.3 The neuron: structure built for the job

The working cell of the nervous system is the **neuron**. There are around eighty-six billion of them in the human brain, and although they vary in shape, they share a plan that suits their one job: receive a signal at one end, carry it along, and pass it on at the other end. Look at the structure in Figure 1.3 with that job in mind and every part explains itself.

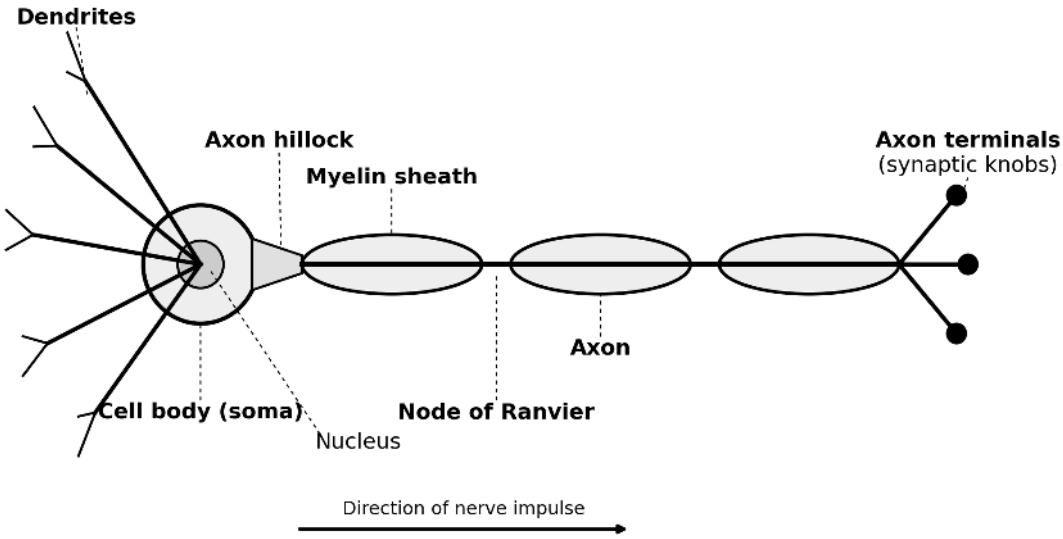


Figure 1.3 *Structure of a typical neuron.*

The **cell body**, also called the soma or perikaryon, holds the nucleus and most of the machinery that keeps the cell alive: ribosomes, mitochondria, and the protein factories that supply the rest of the cell. The cell body is the metabolic headquarters, not mainly the signalling part.

The **dendrites** are the short, branching processes that spread out from the cell body like the bare twigs of a tree. They are the receiving end. A single neuron can carry thousands of dendritic contacts, and the more surface a dendrite tree offers, the more incoming signals the neuron can sample. Signals picked up by dendrites travel toward the cell body.

The **axon** is the single long process that carries the outgoing signal away from the cell body. It begins at a cone-shaped region called the axon hillock, which is the trigger zone where the action potential is born. An axon can be very long: the one running from the spinal cord to the foot is around a metre in an adult. At its far end the axon branches into fine terminals, and each terminal ends in a swelling, the **synaptic knob**, which is where the signal is handed to the next cell.

Many axons are wrapped in **myelin**, a fatty insulating sheath laid down in segments. The gaps between segments are the **nodes of Ranvier**. Myelin is the single feature that makes nerve conduction fast, and section 1.6 explains exactly how. For now, hold the picture: a cell body that runs the cell, dendrites that listen, an axon that speaks, and a sheath that speeds the speaking.

Classifying neurons

Neurons are grouped two ways. By function they are sensory (afferent, carrying information in), motor (efferent, carrying commands out), or interneurons, which sit between the two inside the CNS and do the connecting and processing. Interneurons are the most numerous by far, because most of the nervous system's work is internal wiring rather than input or output. By structure they are classed by how many processes leave the cell body: multipolar neurons have one axon and many dendrites and are the common type in the CNS; bipolar neurons have one axon and one dendrite and are found in special sense organs such as the retina; unipolar (strictly, pseudounipolar) neurons have a single process that splits, and they are the typical sensory neuron of the PNS.

1.4 Neuroglia: the supporting cells

Neurons get the attention, but they are outnumbered by the **neuroglia**, also called glial cells, the support cells of nervous tissue. Glia do not fire action potentials. They feed, insulate, defend and tidy up around neurons, and without them neurons would not survive or signal properly. There are six types worth knowing, four in the CNS and two in the PNS, and the cleanest way to learn them is by what each one does.

In the CNS, **astrocytes** are star-shaped cells that anchor neurons to their blood supply and form a large part of the blood–brain barrier, the selective wall that controls what passes from blood into brain tissue. That barrier matters enormously to a pharmacist, because a drug that cannot cross it cannot act on the brain. **Oligodendrocytes** make the myelin sheath in the CNS; one oligodendrocyte wraps several axons. **Microglia** are the immune cells of the CNS, small wandering scavengers that engulf debris and pathogens. **Ependymal cells** line the cavities of the brain and spinal cord and help make and move the cerebrospinal fluid you will meet in Chapter 2.

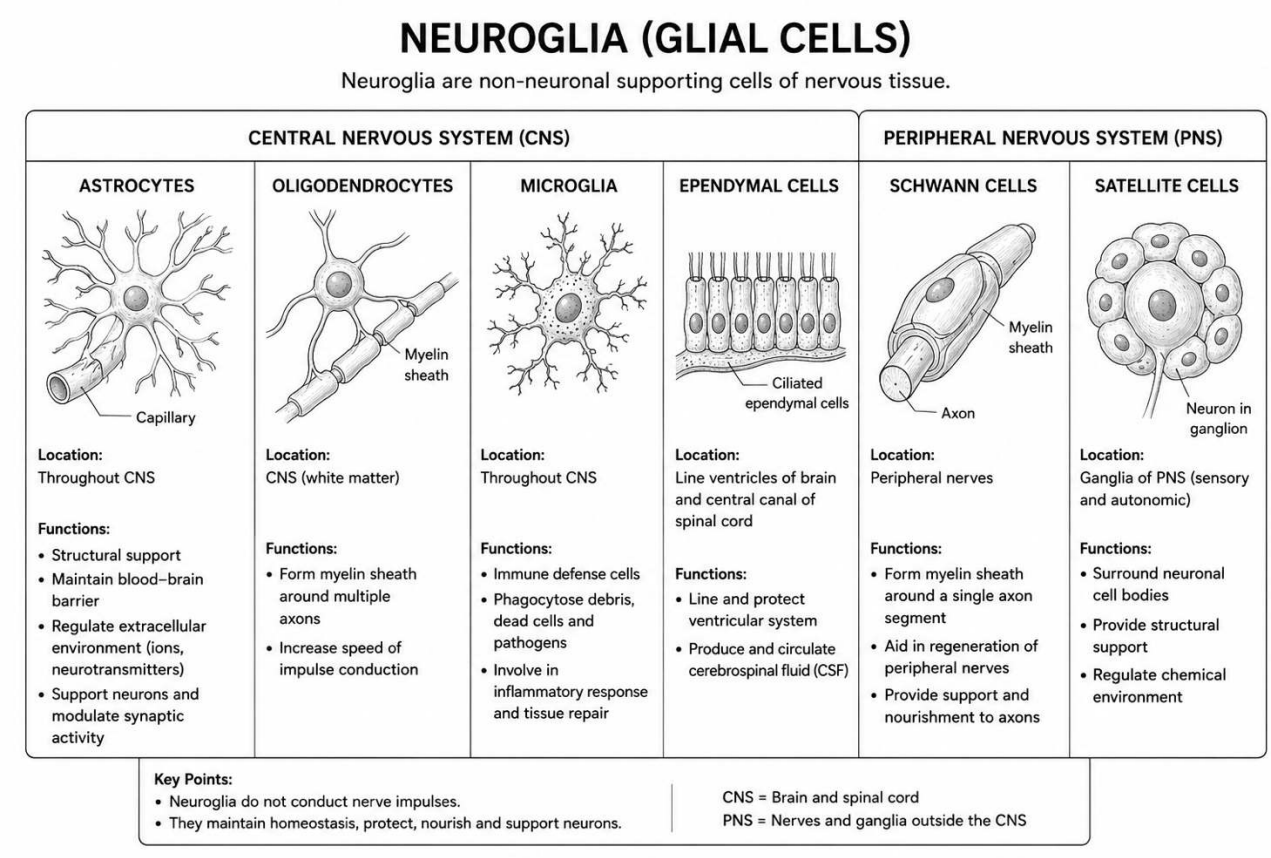


Figure 1.4 Types of neuroglia

In the PNS, **Schwann cells** make the myelin sheath, but unlike oligodendrocytes each Schwann cell wraps just one segment of one axon. **Satellite cells** surround and support the cell bodies of neurons in peripheral ganglia. Table 1.1 sets the six types side by side so you can revise them quickly.

Table 1.1: The six types of neuroglia

Glial cell	Location	Main function
Astrocyte	CNS	Anchors neurons to blood vessels; forms the blood–brain barrier
Oligodendrocyte	CNS	Makes the myelin sheath (one cell wraps several axons)
Microglia	CNS	Immune scavenger; engulfs debris and pathogens
Ependymal cell	CNS	Lines brain cavities; helps make and circulate CSF
Schwann cell	PNS	Makes the myelin sheath (one cell wraps one segment)
Satellite cell	PNS	Supports the cell bodies of neurons in ganglia

A small clinical hook makes the glia stick. In multiple sclerosis the body's own immune system attacks CNS myelin, so oligodendrocytes lose their sheaths and conduction slows or

fails. The symptoms of that disease are, at root, the loss of the speed that section 1.6 is about. The brain tumours called gliomas arise from glia, not neurons, which is why the support cells are not a footnote.

1.5 Nerve fibres: classification and properties

A **nerve fibre** is an axon together with its sheaths. Out in the body, many fibres run together inside a connective-tissue wrapping, and that bundle is a **nerve**. Fibres differ in two linked ways that decide how fast they carry a signal: their diameter and whether they are myelinated. Thicker fibres conduct faster, and myelinated fibres conduct faster than unmyelinated ones of the same size.

Physiologists sort fibres into classes by these properties. The common scheme labels them A, B and C. **Type A fibres** are the thickest and most heavily myelinated, so they are the fastest; they carry skeletal motor commands and fine touch and are subdivided (alpha, beta, gamma, delta) by decreasing size and speed. **Type B fibres** are thinner, lightly myelinated, of moderate speed, and carry autonomic signals to the ganglia. **Type C fibres** are the thinnest and have no myelin at all, so they are the slowest; they carry dull, aching pain and many autonomic outputs. The pattern to remember is one line: thicker plus myelinated equals faster. Everything else in the classification hangs off that.

This is also a neat place to see why two kinds of pain feel different. Sharp, immediate pain travels on faster, thinly myelinated fibres; the dull, lingering ache that follows travels on slow type C fibres. The lag you feel between the two is the speed difference made conscious.

Properties of a nerve fibre

Examiners ask for the “properties of a nerve fibre” as a set, so learn them as a list, each as a full point.

- **Excitability:** the fibre can respond to a stimulus by generating an action potential. A stimulus must reach a minimum strength, the **threshold**, to do this.
- **Conductivity:** once generated, the action potential travels along the whole length of the fibre without dying away.
- **All-or-none response:** a stimulus at or above threshold produces a full-sized action potential; a stimulus below threshold produces none. There is no half-sized signal. The fibre either fires fully or not at all, like a camera flash rather than a dimmer.
- **Refractory period:** for a brief time after firing, the fibre cannot fire again (absolute refractory period) or can fire only to a strong stimulus (relative refractory period). This

sets an upper limit on how often a fibre can signal and forces the impulse to travel one way.

- **Summation:** several below-threshold stimuli arriving close together in time or space can add up to cross threshold, even though each alone would fail.

The all-or-none rule raises an obvious question. If every action potential is the same size, how does the body signal a strong stimulus differently from a weak one? It does it two ways: by **frequency**, firing more action potentials per second for a stronger stimulus, and by **recruitment**, bringing more fibres into play. Strength is coded in how many and how often, never in how big. This is the kind of point an exam rewards, so do not let the all-or-none rule pass without noticing the puzzle it sets.

1.6 Electrophysiology: the resting membrane potential and the action potential

This is the core of the chapter. Everything before it was the wiring; this is the signal that runs through the wire. Take it slowly, because the same mechanism reappears in the heart, the gut and the secreting cell, and learning it once here saves learning it four times later.

The resting membrane potential

A neuron that is not signalling is not switched off. It sits charged, like a loaded spring, ready to fire. Across its membrane there is a voltage of about **−70 mV**, with the inside negative relative to the outside. This is the **resting membrane potential (RMP)**, and three things together create it.

First, the ions are unevenly spread. Sodium (Na^+) is concentrated outside the cell; potassium (K^+) is concentrated inside. These gradients are the stored energy the signal will spend. Second, the resting membrane is far more leaky to potassium than to sodium, because more potassium channels sit open at rest. So potassium drifts out down its gradient, carrying positive charge with it and leaving the inside negative. Third, the **sodium–potassium pump** works constantly in the background, pushing three Na^+ out for every two K^+ it brings in, spending ATP to keep the gradients from running down. The pump does not create the voltage moment to moment; it maintains the gradients that make the voltage possible. (You met this pump in the first-semester HAP course; here it is the engine behind every signal in this book.)

So the resting state is the potassium leak setting the voltage, on top of gradients the pump keeps charged. Hold that picture, because the action potential is simply what happens when the membrane briefly stops favouring potassium and lets sodium have its way.

The action potential, step by step

An **action potential (AP)** is a rapid, brief, all-or-none reversal of the membrane voltage that travels along the axon. It is the nerve impulse the syllabus names. It runs through four stages, and the gatekeepers throughout are the **voltage-gated sodium and potassium channels**, channels that open and close in response to the membrane voltage itself. Follow the voltage trace in Figure 1.5 as you read.

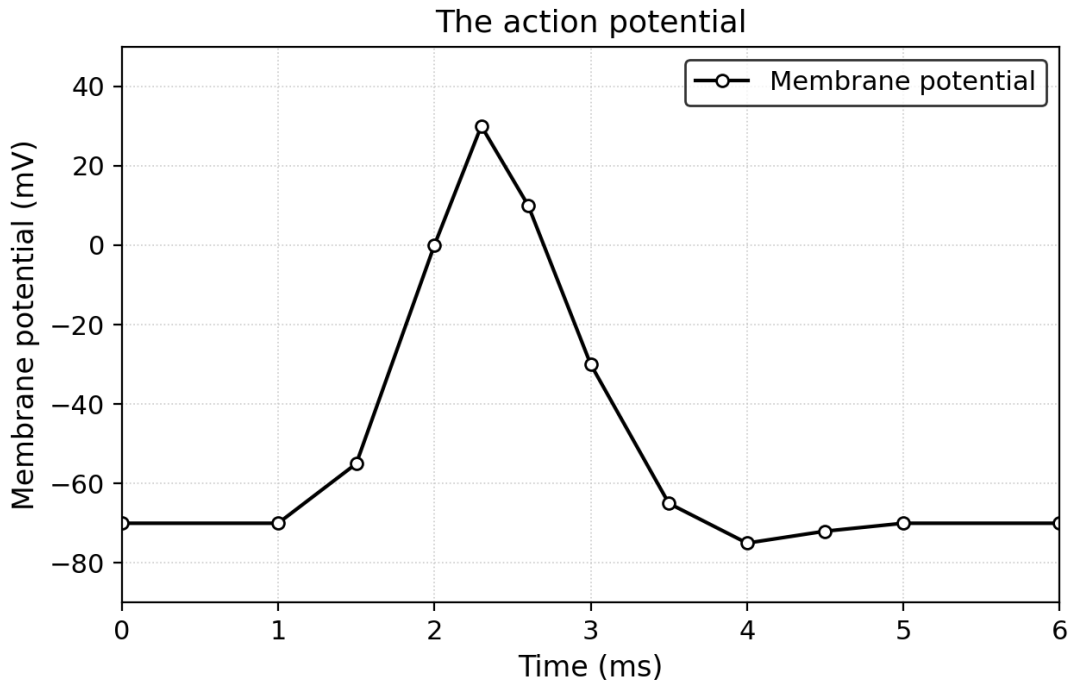


Figure 1.5 *The action potential: membrane potential against time.*

1. **Resting state.** The membrane sits at −70 mV. The voltage-gated sodium and potassium channels are shut. The cell waits.
2. **Depolarization.** A stimulus pushes the voltage up toward threshold, about −55 mV. At threshold the voltage-gated sodium channels snap open. Sodium floods in down its steep gradient, and because sodium is positive the inside rushes from negative toward positive, overshooting to about +30 mV. This inrush is fast and self-reinforcing: the more the membrane depolarizes, the more sodium channels open. That positive feedback is what makes the AP all-or-none. Once threshold is crossed, the spike completes itself.
3. **Repolarization.** The sodium channels close quickly (they inactivate), and now the slower voltage-gated potassium channels are fully open. Potassium pours out, carrying positive charge with it, and the inside falls back toward negative. The voltage drops from +30 mV back down toward rest.

4. **Hyperpolarization and recovery.** The potassium channels are slow to close, so a little too much potassium leaves and the voltage dips briefly below −70 mV before the sodium–potassium pump and the leak channels restore the exact resting value. During the early part of this recovery the membrane is in its absolute refractory period and cannot fire again, which is what forces the impulse to keep moving forward rather than backward.

A clean way to remember the ion movements: **sodium in to fire, potassium out to reset.** That single line is the heart of the action potential, and it is the line to write first in any exam answer on this topic.

It is worth naming the common misconception here, because students lose marks on it every year. The action potential does not undo the concentration gradients. Only a tiny number of ions cross during a single spike, far too few to flatten the gradients. The gradients stay almost unchanged, and the pump quietly tops them up afterward. So a neuron can fire hundreds of times a second without "running out" of gradient. Read the AP as a brief change in which channels are open, not as a draining of the battery.

How the impulse travels, and why myelin makes it fast

An action potential at one point depolarizes the patch of membrane just ahead of it, pushing that patch to threshold so it fires in turn, and so on along the axon. The signal regenerates itself at every step, which is why it does not fade. In an unmyelinated fibre this happens continuously, patch by patch, and it is slow.

Myelin changes the game. Where the axon is wrapped in myelin, the membrane is insulated and ions cannot cross, so the action potential cannot regenerate there. It can only regenerate at the bare **nodes of Ranvier** between the myelin segments. So the impulse appears to jump from node to node, a mode called **saltatory conduction** (from the Latin *saltare*, to leap). Because it skips the insulated stretches and fires only at the nodes, it travels far faster and uses less energy, since fewer patches of membrane have to be restored by the pump. This is the payoff of myelin promised in section 1.3, and it is why the demyelinating diseases slow conduction to a crawl.

> **Quick-recall box 1.2: The action potential in one breath** Rest −70 mV (K^+ leak sets it, pump maintains gradients). Threshold −55 mV opens voltage-gated Na^+ channels: Na^+ in, depolarize to +30 mV. Na^+ channels close, K^+ channels open: K^+ out, repolarize. Brief hyperpolarization, then pump restores rest. Sodium in to fire, potassium out to reset. Myelin gives saltatory conduction, node to node, fast.

A pharmacology hook closes the section. Local anaesthetics such as lignocaine block the voltage-gated sodium channel. Block that channel and step 2 cannot happen, so no action potential forms, so no pain signal reaches the brain from that patch of tissue. The whole of local anaesthesia is the deliberate failure of the step you just learned.

1.7 The synapse: passing the signal on

A signal that reaches the end of an axon has to cross to the next cell, and the two cells do not touch. The junction between them is the **synapse**, and the tiny gap is the **synaptic cleft**. Most synapses in the human nervous system are chemical: the electrical signal is converted into a chemical messenger, sent across the gap, and converted back into an electrical signal on the other side. The cell sending the signal is the **presynaptic** neuron; the cell receiving it is the **postsynaptic** neuron.

Transmission across a chemical synapse runs as a short sequence, shown in Figure 1.6:

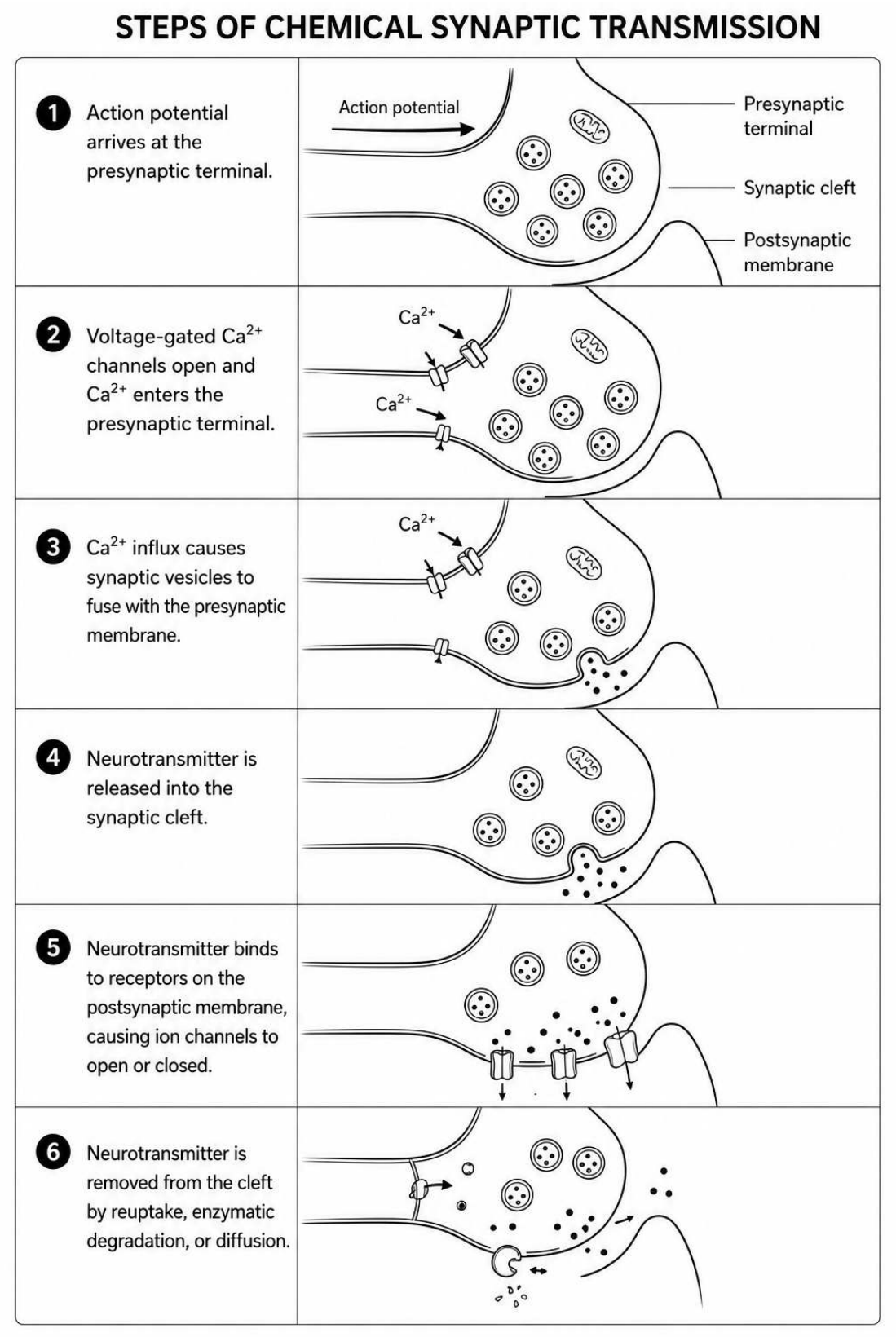


Figure 1.6 *Steps of chemical synaptic transmission.*

1. The action potential arrives at the presynaptic synaptic knob.
2. Its depolarization opens **voltage-gated calcium channels**, and calcium (Ca^{2+}) enters the knob. Calcium is the trigger that links the electrical event to chemical release.
3. The calcium causes synaptic vesicles, small membrane sacs filled with **neurotransmitter**, to fuse with the presynaptic membrane and empty their contents into the synaptic cleft.
4. The neurotransmitter diffuses across the cleft and binds to **receptors** on the postsynaptic membrane.
5. Binding opens or closes ion channels in the postsynaptic cell, changing its membrane voltage. If the change pushes the postsynaptic cell toward threshold it is an **excitatory postsynaptic potential (EPSP)**; if it pushes the cell away from threshold, making it harder to fire, it is an **inhibitory postsynaptic potential (IPSP)**.
6. The signal is then switched off. The transmitter is cleared from the cleft, either broken down by an enzyme, taken back up into the presynaptic neuron (reuptake), or carried away by diffusion. Clearance matters as much as release: a signal that is never switched off is as useless as one never sent.

Two features of this chain are worth dwelling on because they explain a great deal of pharmacology. The synapse is a **one-way valve**: only the presynaptic side has vesicles and only the postsynaptic side has receptors, so a signal can cross in just one direction. And the synapse is where the postsynaptic neuron **adds up** its inputs. A single EPSP is usually too small to fire the cell. The neuron sums many EPSPs and IPSPs arriving across its dendrites and cell body, and only if the total reaches threshold at the axon hillock does it fire. This summation, met as a fibre property in section 1.5, is where the nervous system does its real computing.

The clearance step is the richest drug target in the whole chapter. Block the enzyme that breaks down a transmitter and the transmitter lingers and acts longer. Block reuptake and the same thing happens. Many antidepressants work exactly this way, by blocking the reuptake of serotonin or noradrenaline so that more transmitter stays in the cleft. You will meet that mechanism again as a cause of disease relief in Chapter 3 and as a drug class in pharmacology.

1.8 Receptors and neurotransmitters

Receptors

A **receptor** is a protein, here on the postsynaptic membrane, that recognises a particular neurotransmitter and responds when the transmitter binds. The same transmitter can have

different effects in different places because the receptor, not the transmitter, decides the response. Acetylcholine speeds nothing by itself; what it does depends on which receptor it meets. This is why receptors, not transmitters, are usually the precise drug target.

Receptors fall into two broad families by how fast and how they act. **Ionotropic receptors** are themselves ion channels: the transmitter binds and the channel opens directly, changing the voltage in a millisecond. They are fast and short-lived, suited to moment-to-moment signalling. **Metabotropic receptors** do not open a channel directly. They are coupled to internal signalling molecules (G-proteins and second messengers) that set off a slower chain inside the cell. They are slower to start but their effects last longer and can be amplified. You will meet this same two-family split again in Chapter 8, where hormones act through the very same kinds of receptor. One idea, two systems.

Neurotransmitters

A **neurotransmitter** is the chemical messenger released at a synapse. There are many, but a handful carry most of the traffic and turn up repeatedly in disease and in pharmacology, so learn this short list well. Table 1.2 sets out the major ones with where they act and why they matter.

- **Acetylcholine** is the transmitter at the neuromuscular junction (where nerve meets skeletal muscle), at all autonomic ganglia, and at the parasympathetic endings. It is cleared by the enzyme acetylcholinesterase, an enzyme that is itself a major drug target.
- **Noradrenaline (norepinephrine)** is the main transmitter of the sympathetic endings and is widespread in the brain, where it affects mood and alertness.
- **Dopamine** controls movement and reward in the brain. Its loss in one brain region causes Parkinson’s disease, and its excess activity is linked to schizophrenia, both met in Chapter 3.
- **Serotonin (5-HT)** affects mood, sleep and appetite; low serotonin signalling is tied to depression, and raising it is how a large class of antidepressants works.
- **GABA (gamma-aminobutyric acid)** is the main inhibitory transmitter of the brain. It quietens neurons, and drugs that boost it, such as the benzodiazepines, calm anxiety and stop seizures.
- **Glutamate** is the main excitatory transmitter of the brain. Too much of it is toxic to neurons and contributes to the damage in stroke.

Table 1.2: Major neurotransmitters at a glance

Neurotransmitter	Main site / role	Linked disease	Drug relevance
Acetylcholine	Neuromuscular junction, autonomic ganglia, parasympathetic endings	Myasthenia gravis	Anticholinesterases, muscle relaxants
Noradrenaline	Sympathetic endings; brain (mood, alertness)	Depression (part)	Reuptake inhibitors
Dopamine	Brain: movement and reward	Parkinson's (low), schizophrenia (high)	L-dopa, antipsychotics
Serotonin (5-HT)	Brain: mood, sleep, appetite	Depression	SSRIs
GABA	Brain: main inhibitory transmitter	Epilepsy, anxiety	Benzodiazepines
Glutamate	Brain: main excitatory transmitter	Stroke damage (excess)	Neuroprotective targets

Notice the pattern across that list: nearly every transmitter is paired with a disease of too little or too much, and with a drug that nudges it back. That pairing is the bridge from this chapter to the whole of neuro-pharmacology, and it is why the short list above is worth memorising cold. The transmitters are the vocabulary; Chapter 3 is the first place you will read the sentences.

The neuromuscular junction: a synapse worth knowing by name

One synapse deserves a closer look because it is the cleanest example of everything in section 1.7 and because it is a heavily examined drug target. The neuromuscular junction is the synapse where a motor neuron meets a skeletal muscle fibre. The transmitter is acetylcholine. When the action potential reaches the motor nerve ending, calcium enters, acetylcholine is released into the cleft, and it binds nicotinic receptors on the muscle membrane. Those receptors are ionotropic, so they open at once, sodium enters the muscle fibre, the muscle membrane depolarizes, and the muscle contracts. The acetylcholine is then broken down in the cleft by acetylcholinesterase, which resets the junction for the next signal.

This one junction explains several drug and poison actions a pharmacist will meet. Curare-like drugs block the nicotinic receptor, so acetylcholine cannot act and the muscle is paralysed; that is how muscle relaxants work in surgery. Drugs that block

acetylcholinesterase let acetylcholine pile up and act longer, which strengthens a weak junction in the disease myasthenia gravis. The same enzyme is the target of organophosphate pesticides, where too much blockade floods the junction and causes dangerous overactivity. The point is general: a synapse has at least four drug targets (release, receptor, enzyme, reuptake), and the neuromuscular junction shows three of them in one place.

1.9 Chapter summary

The nervous system is the body's fast signalling network, split by location into the central system (brain and spinal cord) and the peripheral system (the nerves), and split by control into the somatic system for voluntary muscle and the autonomic system for the involuntary background, the latter balanced between its sympathetic and parasympathetic branches. The working cell is the neuron, with a cell body that runs it, dendrites that receive, an axon that sends, and a myelin sheath that speeds the sending. Around the neurons, six types of neuroglia feed, insulate, defend and tidy, and two of them build the myelin that makes conduction fast. Nerve fibres are classed by size and myelination into types A, B and C, with the rule that thicker and myelinated means faster, and they show the properties of excitability, conductivity, the all-or-none response, a refractory period and summation.

The signal itself is electrical. A resting neuron holds about −70 mV across its membrane, set by a potassium leak and kept charged by the sodium–potassium pump. A stimulus that reaches threshold opens voltage-gated sodium channels and sodium floods in, reversing the voltage to about +30 mV; sodium channels then close, potassium channels open, potassium leaves, and the membrane resets. Sodium in to fire, potassium out to reset. The impulse regenerates itself along the axon and, where myelin insulates the fibre, leaps from node to node by saltatory conduction. At the journey's end the signal crosses a synapse by chemical means: calcium entry triggers neurotransmitter release, the transmitter binds a receptor on the next cell, and the signal is then cleared by enzyme, reuptake or diffusion. Receptors come in fast ionotropic and slower metabotropic families, and a small set of transmitters, acetylcholine, noradrenaline, dopamine, serotonin, GABA and glutamate, carries most of the traffic and sits behind most neurological disease and most of the drugs that treat it. That last fact is the door into Chapter 3.

1.10 Self-assessment

A. Multiple-choice questions

1. The central nervous system consists of:
   (a) brain and peripheral nerves (b) brain and spinal cord (c) spinal cord and ganglia
   (b) brain and autonomic nerves. Answer: (b).

2. Afferent neurons carry signals:
   (a) away from the CNS (b) to skeletal muscle only (c) toward the CNS (d) within muscle. Answer: (c).
3. The resting membrane potential of a typical neuron is about:
   (a) 0 mV (b) +30 mV (c) −55 mV (d) −70 mV. Answer: (d).
4. During the depolarization phase of the action potential, the ion that moves into the cell is: (a) potassium (b) calcium (c) sodium (d) chloride. Answer: (c).
5. Saltatory conduction occurs in: (a) unmyelinated fibres (b) myelinated fibres
   (c) dendrites (d) the cell body. Answer: (b).
6. The myelin sheath in the central nervous system is made by:
   (a) Schwann cells (b) astrocytes (c) oligodendrocytes (d) microglia. Answer: (c).
7. The main inhibitory neurotransmitter in the brain is:
   (a) glutamate (b) GABA (c) dopamine (d) acetylcholine. Answer: (b).
8. Calcium entry at the synaptic knob directly triggers:
   (a) reuptake of transmitter (b) release of neurotransmitter (c) repolarization
   (b) closure of sodium channels. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Define resting membrane potential and state the two factors that establish it. The resting membrane potential is the steady voltage of about −70 mV across the membrane of an unstimulated neuron, with the inside negative to the outside. It is established mainly by the resting membrane being more permeable to potassium than to sodium, so potassium leaks out and leaves the inside negative, and it is maintained by the sodium–potassium pump, which keeps the ion gradients charged by pumping three Na^+ out for every two K^+ in. *(High-yield.)*

2. Explain the all-or-none response of a nerve fibre. How then is stimulus strength coded? A stimulus at or above threshold produces a full-sized action potential, while a stimulus below threshold produces none at all; the action potential cannot be partial. Because every action potential is the same size, stimulus strength is coded not by size but by frequency (more action potentials per second for a stronger stimulus) and by recruitment (more fibres firing).

3. Differentiate between the somatic and autonomic nervous systems. The somatic nervous system carries voluntary motor commands to skeletal muscle and is under conscious control. The autonomic nervous system controls involuntary functions such as heart rate, gut movement and gland secretion, works without conscious control, and is divided into the sympathetic (fight or flight) and parasympathetic (rest and digest) branches.

4. Why does conduction fail or slow in a demyelinating disease such as multiple sclerosis? Myelin insulates the axon and forces the action potential to regenerate only at the nodes of Ranvier, giving fast saltatory conduction. When myelin is lost the insulation fails, the impulse can no longer leap from node to node, and conduction slows or stops, producing the weakness and sensory loss of the disease.

5. List the six types of neuroglia and give one function of each. Astrocytes anchor neurons to blood vessels and help form the blood–brain barrier; oligodendrocytes make CNS myelin; microglia are the immune scavengers of the CNS; ependymal cells line the brain cavities and help make cerebrospinal fluid; Schwann cells make PNS myelin; satellite cells support the cell bodies of peripheral ganglia.

6. What is a synaptic cleft, and why does a chemical synapse transmit in only one direction? The synaptic cleft is the narrow gap between the presynaptic and postsynaptic neurons at a chemical synapse. Transmission is one-way because only the presynaptic terminal stores and releases neurotransmitter while only the postsynaptic membrane carries the receptors, so the signal can cross in just one direction.

C. Long-answer questions (10 marks)

1. Describe the generation and conduction of an action potential along a nerve fibre. Add a note on the role of myelin. A complete answer defines the action potential as a rapid all-or-none reversal of membrane voltage; describes the resting state at −70 mV set by the potassium leak and the sodium–potassium pump; explains threshold at about −55 mV opening voltage-gated sodium channels with sodium influx and depolarization to +30 mV; explains closure of sodium channels and opening of potassium channels with potassium efflux and repolarization, then brief hyperpolarization and recovery; states that the impulse regenerates along the axon; and explains saltatory conduction at the nodes of Ranvier in myelinated fibres as the basis of fast, efficient conduction. A labelled voltage-versus-time graph (Figure 1.3) should be drawn. *(High-yield.)*

2. With a suitable diagram, explain the structure of a neuron and the transmission of a signal across a chemical synapse. A full answer labels the neuron (cell body, dendrites, axon, axon hillock, myelin sheath, nodes of Ranvier, synaptic knob) and matches each part to its function; then describes synaptic transmission as the arrival of the action potential, calcium entry, vesicle fusion and neurotransmitter release, diffusion across the cleft, binding to postsynaptic receptors producing an EPSP or IPSP, and clearance of the transmitter by enzyme, reuptake or diffusion. Mentioning a drug that acts on clearance (a reuptake-blocking antidepressant) earns the applied mark.

3. Classify nerve fibres and explain the properties of a nerve fibre. A full answer classifies fibres into types A, B and C by diameter and myelination, with type A thickest and fastest and type C thinnest, unmyelinated and slowest, noting the rule that thicker and myelinated equals faster; then explains the properties of excitability, conductivity, the all-or-none response, the refractory period (absolute and relative) and summation, each as a full point.

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Chapter 2: The Central Nervous System: Brain and Spinal Cord

Learning outcomes

After working through this chapter the student will be able to:

1. Name the three meninges in order and state how they protect the central nervous system.
2. Describe the ventricles of the brain and explain how cerebrospinal fluid is formed, circulates and is reabsorbed.
3. State the functions of cerebrospinal fluid and explain why a blockage is dangerous.
4. Identify the main parts of the brain (cerebrum, brain stem and cerebellum) and give the chief function of each.
5. Describe the gross structure of the spinal cord and the role of its ascending and descending tracts.
6. Explain a reflex arc and the value of reflex activity.

2.1 Protecting a soft organ

The brain has the consistency of soft jelly and weighs about 1.4 kg, yet it sits inside a hard skull that would bruise it with every step if nothing came between them. The body solves this with two layers of defence. It wraps the brain and spinal cord in three protective membranes, and it floats them in a cushion of fluid. Chapter 1 built the cells and the signal. This chapter builds the organ those cells make, and it starts with how that organ is kept safe, because the protection explains a great deal of the clinical picture later. When a membrane gets infected you have meningitis, the disease that closes Chapter 3. When the fluid cannot drain you have raised pressure inside the skull. So the covering is not packaging to skim over. It is where several diseases begin.

The central nervous system is the brain and the spinal cord, the processor introduced in Chapter 1. Everything in this chapter is that processor: first its coverings and fluid, then the brain itself, then the cord that links the brain to the body.

2.2 The meninges

The **meninges** are the three connective-tissue membranes that wrap the brain and spinal cord. From the outside in they are the dura mater, the arachnoid mater and the pia mater, and the easiest way to keep them in order is to picture them as a tough outer case, a loose webbed middle, and a thin inner skin glued to the surface.

- The **dura mater** is the outermost layer, thick, tough and fibrous (its name means “hard mother”). It lines the inside of the skull and forms a strong protective bag.
- The **arachnoid mater** is the middle layer, a delicate membrane with a web-like space beneath it (the name comes from its spider-web look). That space, the **subarachnoid space**, is filled with cerebrospinal fluid and is where the cushioning fluid sits.
- The **pia mater** is the innermost layer, a thin membrane that follows every fold and groove of the brain surface closely, carrying the small blood vessels that supply the tissue (its name means “tender mother”).

Between and around these layers are spaces that matter in disease and in practice. A collection of blood above the dura is an extradural haemorrhage; below it, a subdural haemorrhage. Bleeding into the subarachnoid space is a subarachnoid haemorrhage, and you will meet it as a type of stroke in Chapter 3. The subarachnoid space is also where a lumbar puncture draws fluid from, low in the back where the cord has ended but the fluid still runs, so a needle can sample cerebrospinal fluid without touching the cord.

2.3 The ventricles and cerebrospinal fluid

Deep inside the brain is a connected set of four fluid-filled cavities called the **ventricles**. There are two lateral ventricles, one in each cerebral hemisphere, a third ventricle in the midline, and a fourth ventricle between the brain stem and the cerebellum. They are linked by narrow channels so that fluid made in one can flow to the next. The fluid they make and hold is **cerebrospinal fluid (CSF)**, the clear watery fluid that bathes and protects the whole central nervous system.

How CSF is formed and where it goes

CSF is made by the **choroid plexuses**, networks of capillaries that hang inside the ventricles, mainly in the lateral ventricles. They filter and secrete fluid from the blood at a steady rate, so the total volume is replaced several times a day. The circulation follows a fixed path, shown in Figure 2.1:

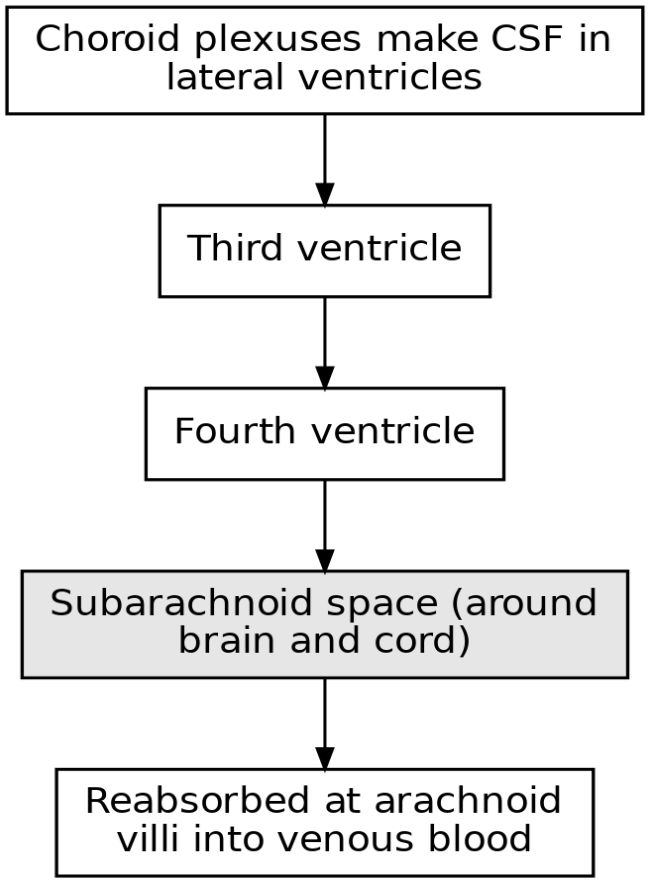


Figure 2.1 *Formation and circulation of cerebrospinal fluid.*

1. CSF forms in the lateral ventricles.
2. It flows into the third ventricle, then down a narrow channel into the fourth ventricle.
3. From the fourth ventricle it escapes through small openings into the subarachnoid space around the brain and cord, the same space held by the arachnoid mater.
4. It is reabsorbed back into the venous blood through the arachnoid villi, small projections that act as one-way valves into the large veins of the skull.

This is a balance, and the balance is the point. CSF is made and reabsorbed at matching rates, so the volume and the pressure stay steady. Block the flow anywhere along the path, say at the narrow channel between the third and fourth ventricles, and fluid keeps forming behind the block with nowhere to go. The pressure rises and the ventricles swell, a condition called hydrocephalus. In an infant whose skull bones have not yet fused the head enlarges; in an adult whose skull is fixed the rising pressure squeezes the brain. The lesson to carry forward is simple. A fluid that is made continuously must be drained continuously, and most CSF disease is a drainage problem.

What CSF does

CSF earns its place by doing several jobs at once, and they are worth learning as a list because examiners ask for them directly.

- **Protection by flotation.** The brain floats in CSF, which reduces its effective weight to a fraction of its real weight, so it is not crushed under its own mass.
- **Cushioning.** The fluid absorbs shocks and softens the blows the skull would otherwise pass straight to the tissue.
- **Constant environment.** CSF keeps the chemical surroundings of neurons steady, supporting the homeostasis that nervous tissue needs to signal.
- **Exchange.** It carries nutrients to the tissue and removes waste, acting as a circulating medium where there is no blood directly bathing the cells.

A diagnostic use closes the section. Because CSF surrounds the whole central nervous system, a sample drawn by lumbar puncture mirrors what is happening inside. Cloudy CSF full of white cells points to bacterial meningitis; blood in the CSF can signal a subarachnoid haemorrhage. The fluid is both a cushion and a window.

2.4 The brain

The brain is the large part of the central nervous system held within the skull. It is described in three main parts: the cerebrum, the brain stem and the cerebellum. Figure 2.2 sets out these divisions, and the sections below take each in turn. Hold one idea as you read: the brain is organised so that the newest, most complex functions sit on top in the cerebrum, while the oldest, most automatic functions sit lower in the brain stem, close to the spinal cord.

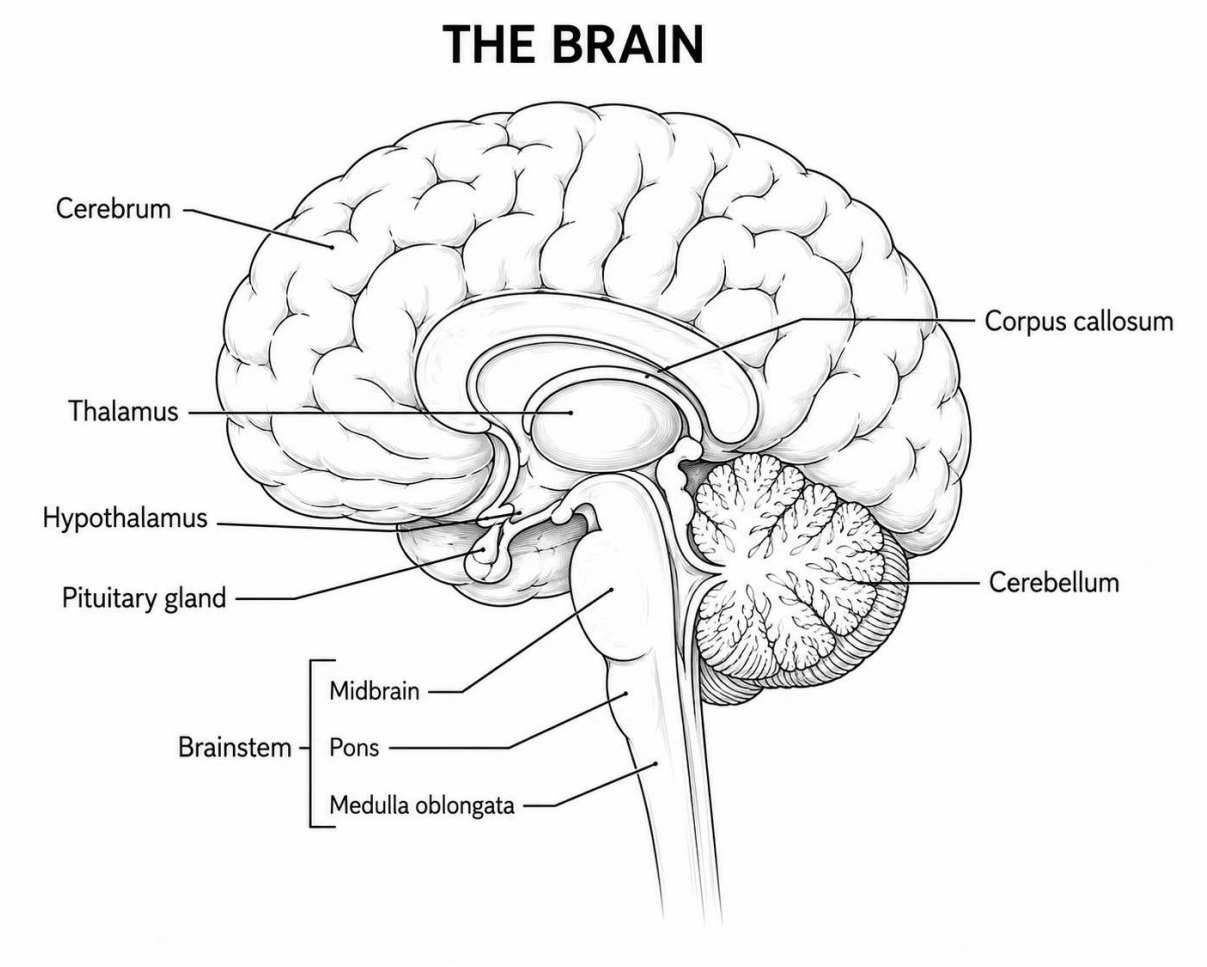


Figure 2.2 *The brain.*

The cerebrum

The **cerebrum** is the largest part of the brain, the folded mass that fills most of the skull. It is split into two halves, the right and left cerebral hemispheres, joined deep in the middle by a thick band of nerve fibres called the corpus callosum, which lets the two sides communicate. Its surface is thrown into folds, which increases the area of the outer layer.

That outer layer is the **cerebral cortex**, a sheet of grey matter (nerve cell bodies) a few millimetres thick. The cortex is where conscious thought, perception, voluntary movement and language happen. Beneath it lies white matter, the myelinated axons that connect cortical areas to each other and to the rest of the nervous system. The grey-on- the-outside, white-underneath pattern is worth noticing now, because the spinal cord later reverses it, and the reversal is a favourite exam point.

Each hemisphere is divided into four lobes, named after the skull bones over them, and each lobe has a broad specialisation:

- The **frontal lobe** at the front handles voluntary movement, planning, decision-making and personality, and contains the motor area that issues movement commands.
- The **parietal lobe** behind it handles sensation: touch, temperature, pain and the sense of where the body is.
- The **temporal lobe** at the side handles hearing and is central to memory.
- The **occipital lobe** at the back handles vision.

A point students often blur is worth fixing. Each hemisphere controls and receives from the **opposite** side of the body, because the major tracts cross over on their way down. So damage to the right cerebrum, as in many strokes, shows up as weakness on the left side of the body. That crossing is why a left-sided weakness sends the doctor looking at the right side of the brain.

Deep within the cerebrum sit three structures the syllabus expects you to place. The **thalamus** is a relay station that sorts incoming sensory signals and passes them up to the cortex. The **hypothalamus**, just below it, is small but controls a great deal: body temperature, hunger and thirst, sleep, and, through its link to the pituitary gland, much of the endocrine system you will meet in Chapter 8. The hypothalamus is the bridge between the nervous and endocrine systems, the two signalling networks named at the start of Chapter 1.

The third group is the **basal ganglia**, masses of grey matter buried deep in the cerebrum that help control and smooth voluntary movement. They work alongside the motor cortex, setting muscle tone and suppressing unwanted movements so that an intended action comes out clean. Their role matters far beyond this chapter, because the basal ganglia depend on the neurotransmitter dopamine, met in Chapter 1. When the dopamine supply to them fails, movement becomes slow, stiff and tremulous, which is Parkinson's disease in Chapter 3. So learn the basal ganglia now as the movement-tuning centre, and the cause of Parkinson's will already be half explained when you reach it.

A small but useful point connects this section to drug treatment. The brain is shielded by the blood–brain barrier built largely by astrocytes, met in Chapter 1, so many drugs cannot reach brain tissue at all. A drug meant to act in the brain must be designed to cross that barrier, which is why the dopamine lost in Parkinson's cannot simply be given as dopamine and is given as a precursor that can cross instead. The anatomy of protection becomes a rule of pharmacology.

The brain stem

The **brain stem** connects the cerebrum to the spinal cord and runs the automatic functions that keep you alive. It has three parts stacked from top to bottom: the **midbrain**, the **pons** and

the **medulla oblongata**. The midbrain relays signals for sight and sound and helps control movement. The pons (the name means “bridge”) links the two halves of the cerebellum and carries signals between the higher brain and the cord, and it helps regulate breathing.

The **medulla oblongata** is the lowest part, where the brain stem meets the spinal cord, and it is the most vital piece of the whole brain for staying alive. It holds the control centres for heart rate, the force and rhythm of breathing, and the diameter of blood vessels, along with reflexes such as swallowing, coughing, sneezing and vomiting. This is why an injury to the brain stem is so dangerous: the cerebrum can be damaged and a person can survive, but damage to the medulla stops the heartbeat and breathing it controls. The medulla is also where many of the great tracts cross from one side to the other, the crossing that explains the opposite-side rule above.

The cerebellum

The **cerebellum** sits behind the brain stem, beneath the back of the cerebrum, and looks like a smaller folded brain of its own. Its job is to coordinate movement and balance. It does not start movements; the cerebrum does that. The cerebellum makes them smooth, accurate and well-timed, comparing the movement the cerebrum intended with the movement the body is actually making and correcting the difference moment by moment. When the cerebellum is damaged, movements become clumsy and jerky, balance fails, and fine coordination is lost, even though strength is normal. A simple way to hold it: the cerebrum decides to move, the cerebellum makes the move graceful.

> **Quick-recall box 2.1: The brain in one line each** Cerebrum: thought, sensation, voluntary movement (cortex = grey matter, outside). Thalamus: sensory relay. Hypothalamus: temperature, hunger, thirst, links to endocrine. Brain stem (midbrain, pons, medulla): automatic life support; medulla runs heart and breathing. Cerebellum: coordination and balance.

2.5 The spinal cord

The **spinal cord** is the long column of nervous tissue that runs from the base of the brain stem down through the protective canal of the backbone. It is the main cable between the brain and the body below the neck, and it is also a processing centre in its own right for reflexes. It ends around the first or second lumbar vertebra, which is why a lumbar puncture lower than that can sample CSF without harming the cord.

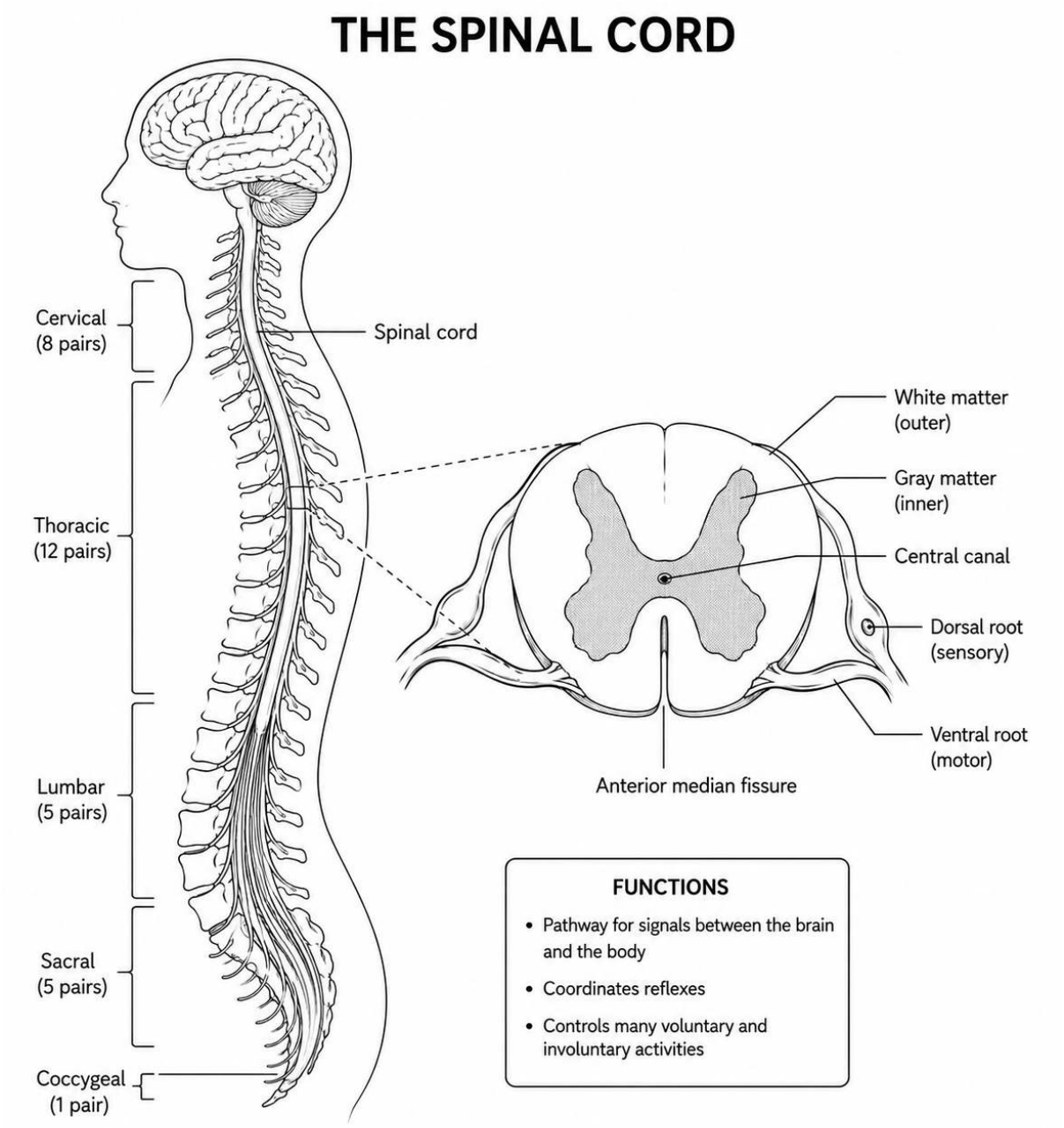


Figure 2.3 The spinal cord

Gross structure

Cut the spinal cord across and you see a pattern that is the mirror image of the cerebrum. In the centre is **grey matter**, shaped like a butterfly or the letter H, made of nerve cell bodies. Around it is **white matter**, made of myelinated axon tracts running up and down. So in the cord the grey matter is inside and the white matter is outside, the reverse of the cerebrum, and this reversal is exactly the kind of contrast an exam likes to test.

Thirty-one pairs of **spinal nerves** branch off the cord along its length and run out to the body. Each spinal nerve joins the cord by two roots. The **dorsal (posterior) root** carries sensory (afferent) fibres into the cord; its swelling, the dorsal root ganglion, holds the cell bodies of those sensory neurons. The **ventral (anterior) root** carries motor (efferent) fibres out of the cord. Sensory in at the back, motor out at the front: this clean separation, met as afferent and efferent in Chapter 1, is the wiring that makes the reflex arc below work.

Ascending and descending tracts

The white matter of the cord is organised into **tracts**, bundles of axons that all carry the same kind of traffic in the same direction. There are two families.

Ascending tracts carry sensory information upward, from the body to the brain. They are the afferent pathways: signals for touch, pain, temperature and body position travel up these tracts to reach the sensory cortex, where they become conscious sensation.

Descending tracts carry motor commands downward, from the brain to the muscles. They are the efferent pathways: a command formed in the motor cortex of the frontal lobe travels down these tracts to the spinal nerves and out to the muscle. The best known is the corticospinal tract, which carries the commands for voluntary movement and crosses to the opposite side in the medulla, the crossing that explains why one side of the brain moves the other side of the body. Table 2.1 sets the two families side by side.

Table 2.1: Ascending and descending tracts of the spinal cord

Feature	Ascending tracts	Descending tracts
Direction	Body to brain (upward)	Brain to body (downward)
Type of signal	Sensory (afferent)	Motor (efferent)
Carries	Touch, pain, temperature, body position	Voluntary movement commands
Example	Spinothalamic tract	Corticospinal tract (crosses in the medulla)
Enters/leaves cord by	Dorsal (posterior) root	Ventral (anterior) root

A point worth stressing, because it ties the chapter together: the cord is a two-way street. Sensation flows up, commands flow down, and the grey matter in the middle is where local connections are made, including the reflexes that need no brain at all.

2.6 Reflex activity

A **reflex** is a rapid, automatic, involuntary response to a stimulus. Pull your hand off a hot surface, blink when something nears your eye, or jerk your leg when the knee tendon is tapped: each is a reflex, fast because it does not wait for the brain to think. The pathway that makes a reflex happen is the **reflex arc**, and it is the simplest complete circuit in the whole nervous system. Its five parts run in order, shown in Figure 2.3:

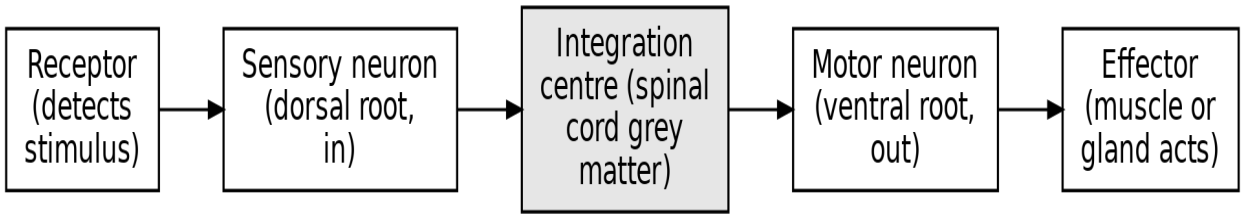


Figure 2.3 *The reflex arc.*

1. **Receptor:** the sense ending that detects the stimulus, for example a pain receptor in the skin.
2. **Sensory (afferent) neuron:** carries the signal from the receptor into the spinal cord through the dorsal root.
3. **Integration centre:** in the cord's grey matter, where the signal is passed on, directly or through an interneuron, to a motor neuron. In the simplest reflexes this is a single synapse.
4. **Motor (efferent) neuron:** carries the command out of the cord through the ventral root to the effector.
5. **Effector:** the muscle or gland that acts, for example the muscle that pulls the hand away.

The value of the reflex arc is speed and protection. Because the loop is completed in the spinal cord and does not have to travel up to the brain and back, the response happens in a fraction of the time. Your hand leaves the hot surface before you consciously feel the pain; the conscious feeling arrives a moment later, once the signal has also reached the cortex by the ascending tracts. The reflex protects the body first and informs the mind second. This is also why reflexes are tested clinically: a knee-jerk that is absent or exaggerated points to a problem somewhere along that arc, from the nerve to the cord, and gives the examiner a quick read on the nervous system without any equipment.

2.7 Chapter summary

The central nervous system is the brain and spinal cord, and it is protected two ways: by the three meninges (the tough dura, the webbed arachnoid and the thin pia) and by cerebrospinal

fluid, which floats and cushions the tissue. CSF is made by the choroid plexuses in the four ventricles, flows from the lateral ventricles through the third and fourth ventricles into the subarachnoid space, and is reabsorbed into venous blood at the arachnoid villi. Made and drained at matching rates, its volume stays steady; block the flow and pressure rises, which is hydrocephalus.

The brain has three main parts. The cerebrum, largest and most complex, carries conscious thought, sensation and voluntary movement in its outer grey cortex, with each hemisphere serving the opposite side of the body, and it houses the thalamus (sensory relay) and the hypothalamus (temperature, hunger, thirst and the link to the endocrine system). The brain stem (midbrain, pons and medulla) runs the automatic functions, and its medulla controls heart rate and breathing, which is why brain-stem injury is so often fatal. The cerebellum coordinates movement and balance, making movements smooth rather than starting them. The spinal cord links brain to body and reverses the cerebral pattern, with grey matter inside and white matter outside; its ascending tracts carry sensation up and its descending tracts carry motor commands down, with sensory fibres entering at the back and motor fibres leaving at the front. Finally, the reflex arc, receptor, sensory neuron, integration centre, motor neuron and effector, lets the cord produce fast protective responses without waiting for the brain. With the processor and its wiring now in place, Chapter 3 turns to what happens when this system fails.

2.8 Self-assessment

A. Multiple-choice questions

1. The outermost and toughest of the meninges is the:
   (a) pia mater (b) arachnoid mater (c) dura mater (d) choroid plexus. Answer: (c).
2. Cerebrospinal fluid is mainly produced by the:
   (a) arachnoid villi (b) choroid plexuses (c) corpus callosum (d) medulla. Answer: (b).
3. The part of the brain that controls heart rate and breathing is the:
   (a) cerebellum (b) thalamus (c) medulla oblongata (d) frontal lobe. Answer: (c).
4. In the spinal cord, the grey matter is located:
   (a) on the outside (b) in the centre (c) only in the dorsal root (d) absent. Answer: (b).
5. The dorsal root of a spinal nerve carries:
   (a) motor fibres out (b) sensory fibres in (c) both equally (d) cerebrospinal fluid. Answer: (b).
6. Coordination of movement and balance is the chief role of the:

(a) cerebrum (b) cerebellum (c) pons (d) hypothalamus. Answer: (b).

7. The structure that links the nervous system to the endocrine system is the:

(a) thalamus (b) hypothalamus (c) corpus callosum (d) arachnoid villi. Answer: (b).

8. A blockage of cerebrospinal fluid flow leads to:

(a) meningitis (b) hydrocephalus (c) stroke (d) epilepsy. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Name the three meninges from outside to inside and give one feature of each. From outside to inside they are the dura mater, the arachnoid mater and the pia mater. The dura mater is the tough fibrous outer bag lining the skull; the arachnoid mater is the delicate middle layer with the cerebrospinal-fluid-filled subarachnoid space beneath it; the pia mater is the thin inner layer that follows the brain surface closely and carries its blood vessels.

2. Trace the circulation of cerebrospinal fluid from formation to reabsorption. CSF is formed by the choroid plexuses in the lateral ventricles, flows into the third ventricle and then the fourth ventricle, escapes through openings into the subarachnoid space around the brain and spinal cord, and is reabsorbed into the venous blood through the arachnoid villi. Formation and reabsorption are balanced, so volume and pressure stay steady. *(High-yield.)*

3. List four functions of cerebrospinal fluid. It floats the brain so it is not crushed under its own weight; it cushions the brain and cord against shocks; it keeps the chemical environment of neurons constant; and it carries nutrients to the tissue and removes waste.

4. Why does damage to the right side of the cerebrum cause weakness on the left side of the body? Because the major motor tracts, chiefly the corticospinal tract, cross from one side to the other in the medulla. So commands from the right cerebrum travel to and control the muscles of the left side of the body, and damage on the right shows up as weakness on the left.

5. State the function of the cerebellum and describe what happens when it is damaged. The cerebellum coordinates movement and balance, making movements smooth, accurate and well-timed, though it does not initiate them. When it is damaged, movements become clumsy and jerky and balance is lost, even though muscle strength itself is normal.

6. Differentiate between the grey and white matter of the spinal cord. Grey matter is made of nerve cell bodies and lies in the centre of the cord in an H or butterfly shape; white matter is made of myelinated axon tracts and lies around the outside. This is the reverse of the cerebrum, where grey matter is on the outside and white matter within.

C. Long-answer questions (10 marks)

1. Describe the structure and functions of the brain under its three main divisions. A full answer covers the cerebrum (two hemisphere, the outer grey cortex for thought, sensation and voluntary movement, the four lobes and their functions, the opposite-side rule, and the thalamus and hypothalamus deep within); the brain stem (midbrain, pons and medulla, with the medulla controlling heart rate and breathing); and the cerebellum (coordination and balance). A labelled diagram of the brain (Figure 2.1) should be included. *(High-yield.)*

2. With a labelled diagram, explain the reflex arc and the importance of reflex activity. A full answer defines a reflex as a rapid, automatic, involuntary response, then describes the five parts of the reflex arc in order, receptor, sensory neuron, integration centre in the spinal cord, motor neuron and effector, and explains that the loop completes in the cord without reaching the brain, giving a fast protective response, with the conscious sensation arriving later by the ascending tracts. The clinical use of testing reflexes should be mentioned.

3. Describe the gross structure of the spinal cord and the role of its ascending and descending tracts. A full answer describes the cord running from the brain stem to about the first lumbar vertebra, the central grey matter and surrounding white matter (the reverse of the cerebrum), the 31 pairs of spinal nerves with sensory fibres entering by the dorsal root and motor fibres leaving by the ventral root, and the white-matter tracts: ascending tracts carrying sensory information up to the brain and descending tracts carrying motor commands down to the muscles, with the corticospinal tract crossing in the medulla.

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Chapter 3: Pathophysiology of the Nervous System

Learning outcomes

After working through this chapter the student will be able to:

1. Define epilepsy and explain its basis as an imbalance between excitation and inhibition.
2. Explain the pathophysiology of Parkinson's disease in terms of dopamine loss and link it to the basal ganglia.
3. Distinguish ischaemic from haemorrhagic stroke and outline how each damages the brain.
4. Describe the pathophysiology and features of migraine, depression and schizophrenia in terms of neurotransmitters.
5. Explain the changes in Alzheimer's disease and relate them to its symptoms.
6. Describe the causes, features and danger of meningitis.

3.1 When the wiring fails

The last two chapters built a working nervous system: a cell that fires, a signal that crosses synapses on the back of a few key transmitters, and an organ that runs thought, movement and the automatic business of staying alive. This chapter is about what happens when those parts fail. The striking thing is that they fail in characteristic ways. Push the balance of excitation and inhibition too far toward excitation and you get the electrical storm of a seizure. Lose one transmitter from one small region and you get the stiffness of Parkinson's. Cut the blood supply for a few minutes and a patch of brain dies. Each disease in this chapter is best read not as a list of symptoms to memorise but as a specific break in the machinery you already understand.

That framing is also the most useful one for a pharmacist, because most of the drugs that treat these conditions act on exactly the broken part: boosting an inhibitory transmitter, replacing a missing one, or blocking an excess. So as each disease is described, the point of attack for treatment is named. The pattern from Chapter 1, a transmitter paired with a disease of too much or too little and a drug that nudges it back, runs straight through this chapter. Table 3.1 collects the main diseases for revision; the sections build them one at a time.

Table 3.1: Nervous system diseases at a glance

Disease	Core problem	Key features	Main drug approach
Epilepsy	Excitation over inhibition; abnormal synchronised firing	Recurrent seizures (generalised or focal)	Enhance GABA or block Na^+ channels
Parkinson's	Loss of dopamine neurons (substantia nigra)	Bradykinesia, rigidity, resting tremor, postural instability	Levodopa (dopamine precursor)
Stroke	Blood supply to brain interrupted	Sudden weakness/speech loss, opposite side	Clot removal (ischaemic) or control bleed
Migraine	Trigeminovascular activation; serotonin	Throbbing one-sided headache, nausea, aura	Triptans (acute), preventers
Depression	Low serotonin/noradrenaline (monoamine)	Persistent low mood, loss of interest	Reuptake inhibitors + therapy
Schizophrenia	Excess dopamine activity	Hallucinations, delusions (positive); withdrawal (negative)	Dopamine receptor blockers
Alzheimer's	Amyloid plaques, tau tangles, loss of acetylcholine	Progressive memory loss, dementia	Acetylcholinesterase inhibitors
Meningitis	Infection of the meninges	Fever, headache, neck stiffness, photophobia	Urgent antibiotics (bacterial)

A note on how to read this table. The middle two columns are what an exam asks you to reproduce, and the pattern across the rows is the lesson of the chapter: a named broken part, a set of signs that follow from it, and a drug aimed at the break. Learn the rows as stories, not as isolated facts, and they hold together.

3.2 Epilepsy

Epilepsy is a chronic disorder marked by recurrent, unprovoked **seizures**, where a seizure is a sudden burst of abnormal, excessive and synchronised electrical activity in a group of brain neurons. The key words are excessive and synchronised: in a seizure, large numbers of neurons that should fire independently instead fire together in a runaway discharge, and the body part those neurons control is driven uncontrollably.

The root of that discharge is an imbalance between the two opposing forces met in Chapter 1. Excitation in the brain is carried mainly by glutamate; inhibition is carried mainly by GABA. Normally the two are balanced, and inhibition keeps neuronal firing in check. In epilepsy the balance tips toward excitation, either because excitatory activity is too high or because GABA-driven inhibition is too weak, and a group of neurons begins to fire together without restraint. Once started, the abnormal activity can stay local or spread.

Seizures are classified by how much of the brain is involved, shown in Figure 3.1. **Generalised seizures** involve both hemispheres from the start and usually impair consciousness; the best known is the tonic-clonic seizure, with stiffening (tonic) then rhythmic jerking (clonic) of the whole body, while an absence seizure is a brief blank spell more common in children. **Focal (partial) seizures** begin in one part of one hemisphere, and the signs depend on what that part controls, for example jerking of one limb; a focal seizure can sometimes spread to become generalised.

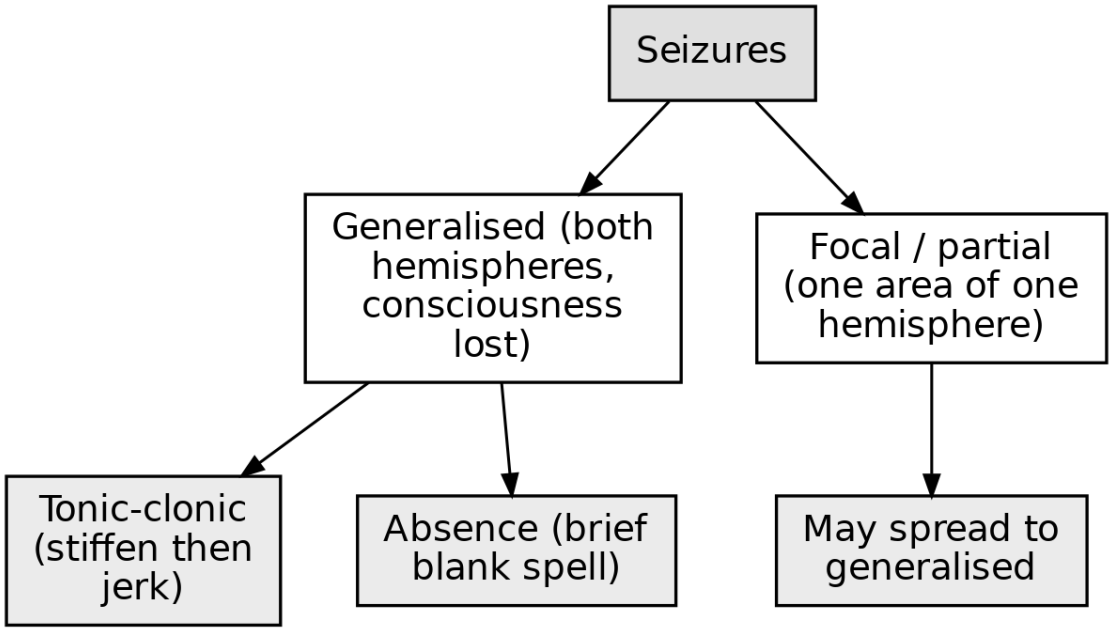


Figure 3.1 *Classification of seizures.*

A seizure in epilepsy may be set off by a trigger even when the underlying tendency is always present. Common triggers include lack of sleep, flashing lights, fever in young children, missed medication, alcohol and stress, and knowing them is part of managing the condition. The cause of the underlying epilepsy is sometimes clear, such as a scar from a past head injury, a stroke, a tumour or an infection, and sometimes no cause is found at all. The diagnosis rests on the description of the attacks together with an electroencephalogram (EEG), the recording of the brain's electrical activity, which can capture the abnormal discharge.

One emergency deserves naming. **Status epilepticus** is a seizure that lasts too long or a run of seizures without recovery between them, and it is a medical emergency because the continuous abnormal firing can damage neurons and threaten breathing. It must be stopped quickly with drugs, usually ones that boost GABA.

The treatment logic falls straight out of the mechanism. Antiepileptic drugs work by restoring the balance toward inhibition: some enhance the action of GABA, and others block the voltage-gated sodium channels met in Chapter 1 so that runaway firing cannot sustain itself. Either way, the aim is to quieten the over-excited circuit. Treatment is usually long-term and aims to keep a person free of seizures with the smallest effective dose, which makes patient counselling on taking the medicine regularly a real part of care.

3.3 Parkinson's disease

Parkinson's disease is a slow, progressive degenerative disorder of movement caused by the loss of dopamine-producing neurons in a small region of the brain. That region is the substantia nigra, part of the basal ganglia introduced in Chapter 2, and its neurons supply dopamine to the movement-tuning circuits there. As these neurons die, the dopamine supply falls, and the basal ganglia can no longer smooth and balance movement. Microscopically, the surviving neurons often contain abnormal protein clumps called Lewy bodies.

Because the basal ganglia normally suppress unwanted movement and help start wanted movement, losing their dopamine produces a recognisable set of signs. The classic four are **bradykinesia** (slowness of movement), **rigidity** (stiff, resistant muscles), a **resting tremor** (a shaking of the hands at rest, often described as pill-rolling), and **postural instability** (poor balance). Symptoms usually appear only after a large fraction of the dopamine neurons are already lost, which is why the disease is well advanced by the time it is diagnosed.

Parkinson's disease is mainly a disease of later life, becoming common above the age of sixty, and it carries more than the movement signs. Non-motor features such as loss of smell, constipation, disturbed sleep, depression and, in late disease, dementia are now recognised as

part of the condition, and they often trouble patients as much as the tremor. A simple way to understand the movement signs is that the basal ganglia normally hold a balance between starting and stopping movement; losing dopamine tips that balance toward stopping, so movement becomes slow and hard to begin.

The treatment is the clearest example of replacing a missing transmitter, and it shows why Chapter 2's blood–brain barrier mattered. Dopamine itself cannot be given as a drug because it does not cross the blood–brain barrier. Instead its precursor, levodopa, is given; it does cross, and the brain converts it to dopamine, topping up the failing supply. Levodopa is usually combined with another drug that stops it being broken down before it reaches the brain, which lets a smaller dose work with fewer side effects. The relief is real but the underlying loss of neurons continues, so over years the disease advances and the medicines control it less smoothly. It is managed, not cured.

3.4 Stroke

A **stroke** is the sudden loss of brain function caused by an interruption of the blood supply to part of the brain. Brain tissue has almost no stored fuel and depends on a constant flow of oxygen and glucose, so when the flow stops the affected neurons begin to die within minutes. The phrase that captures the urgency is that time is brain. There are two main types, shown in Figure 3.2, and telling them apart matters because their treatment is opposite.

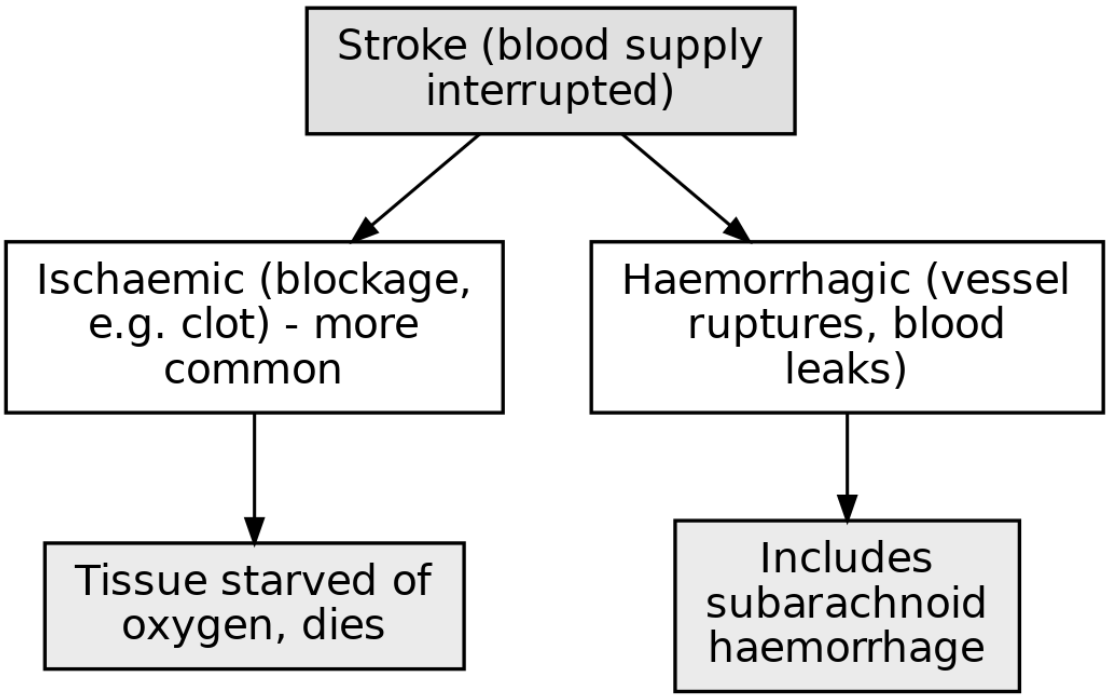


Figure 3.2 *The two main types of stroke.*

An **ischaemic stroke** is caused by a blockage of a blood vessel supplying the brain, most often by a clot, and it is the more common type. The tissue downstream of the block is starved of oxygen and dies. A **haemorrhagic stroke** is caused by the rupture of a blood vessel, so blood leaks into or around the brain; the bleeding both deprives tissue downstream and damages tissue by pressure and irritation. A subarachnoid haemorrhage, the bleed into the space met in Chapter 2, is one form.

Whatever the cause, the dying tissue triggers a wave of damage at the cellular level. Starved neurons lose their ion gradients, depolarise, and release a flood of glutamate, the excitatory transmitter from Chapter 1. In excess, glutamate over-stimulates neighbouring neurons and drives them to death too, a process called excitotoxicity that widens the injury beyond the original patch. The signs of a stroke depend on which part of the brain is affected: a stroke in the motor area of one hemisphere causes weakness on the opposite side of the body, following the crossing rule from Chapter 2, and strokes in language areas impair speech. A short, common warning is the **transient ischaemic attack (TIA)**, sometimes called a mini-stroke, in which the blood supply is blocked only briefly and the symptoms recover fully within a day; it is a warning that a full stroke may follow and must be taken seriously.

The signs of a stroke come on suddenly, and a simple public test, FAST, captures the common ones: Face drooping, Arm weakness, Speech difficulty, and Time to call for help. Speed matters because an ischaemic stroke can sometimes be treated by dissolving the clot, but only within a few hours and only once a bleed has been ruled out, which is why telling the two types apart on a brain scan is the first step in hospital. High blood pressure is the single largest risk factor, and others include smoking, diabetes, high cholesterol, an irregular heartbeat and age. Controlling blood pressure, the subject of the cardiovascular work elsewhere in the course, is therefore also stroke prevention. After a stroke, surviving patients often need long rehabilitation to recover speech and movement, which is part of why stroke is a leading cause of long-term disability.

3.5 Migraine

Migraine is a common disorder of recurrent headache, typically throbbing, often on one side of the head, moderate to severe, and made worse by activity. It is usually accompanied by nausea and by a dislike of light and sound (photophobia and phonophobia), and in some people each attack is preceded by an **aura**, a warning phase of visual or sensory disturbance such as flashing lights or zigzag lines.

Migraine is more than an ordinary headache because its mechanism lies in the brain and its blood vessels, not in muscle tension. The current understanding centres on the **trigeminovascular system**, the network of nerves around the blood vessels of the head.

During an attack these nerves are activated and release chemicals that widen and inflame the vessels, and the pain pathways become over-sensitive. Serotonin, the transmitter from Chapter 1, is closely involved in setting off and controlling this process, which is why several anti-migraine drugs act on serotonin receptors to narrow the dilated vessels and calm the pain pathway. The aura is thought to come from a slow wave of altered electrical activity spreading across the cortex. A classic attack moves through phases that are worth knowing: a prodrome of mood or appetite changes hours before, the optional aura, the headache itself lasting from hours to a few days, and a postdrome of tiredness afterwards. Attacks are often set off by triggers such as certain foods, stress, lack of sleep, hormonal changes around menstruation, or bright light, and migraine is more common in women.

Treatment has two halves a pharmacist should separate. Drugs taken to stop an attack once it starts, such as the serotonin-acting triptans and ordinary painkillers, are different from drugs taken every day to prevent attacks in people who get them often. Migraine is not dangerous in the way a stroke is, but it is disabling and very common, and a pharmacist meets it often because much of its treatment is by medicine.

3.6 Depression

Depression is a mood disorder marked by persistent low mood, loss of interest or pleasure in things once enjoyed, and a cluster of other features such as disturbed sleep and appetite, fatigue, poor concentration, feelings of worthlessness, and in severe cases thoughts of self-harm. To count as the illness rather than ordinary sadness, the low mood lasts for weeks and interferes with daily life.

The leading biological account is the **monoamine hypothesis**, which links depression to a shortage of the monoamine transmitters in the brain, chiefly serotonin and noradrenaline, both met in Chapter 1, with dopamine also involved. According to this view, too little transmitter activity at the synapses that regulate mood produces the symptoms, and raising that activity relieves them. This is exactly what the common antidepressants do: by blocking the reuptake of serotonin (and in some drugs noradrenaline), they leave more transmitter in the synaptic cleft, the reuptake mechanism described in Chapter 1. The hypothesis does not explain everything, since the drugs raise transmitter levels within hours but lift mood only after weeks, so the full picture is more complex, but the monoamine account remains the backbone of how depression is understood and treated. Depression ranges from mild to severe, and it is shaped by life events, long-term stress and a family tendency as well as by brain chemistry, so good treatment usually combines medicine with talking therapy and support. Depression is a serious illness, and because it raises the risk of self-harm it is treated as a condition needing proper professional care. This is a sensitive topic, and anyone troubled

by these feelings should be encouraged to seek help from a doctor or a trusted person rather than face them alone.

3.7 Schizophrenia

Schizophrenia is a severe, chronic psychiatric disorder in which a person loses some contact with reality. Its features are grouped into two kinds. **Positive symptoms** are additions to normal experience: hallucinations (most often hearing voices), delusions (fixed false beliefs), and disordered thought and speech. **Negative symptoms** are losses: blunted emotion, withdrawal, lack of motivation, and poverty of speech. The positive symptoms are often the more obvious; the negative symptoms are often the more disabling in the long run.

The main biological account is the **dopamine hypothesis**, which links the positive symptoms to overactivity of dopamine, the transmitter from Chapter 1, in certain pathways of the brain. Where Parkinson's is a disease of too little dopamine in the movement circuits, schizophrenia is understood, in part, as a disease of too much dopamine activity in the pathways that handle perception and thought, a useful contrast to hold in mind. The evidence is that drugs which block dopamine receptors reduce the positive symptoms, while drugs that raise dopamine can trigger psychotic symptoms. This is why the antipsychotic drugs are dopamine receptor blockers, and it is also why they can produce Parkinson-like stiffness as a side effect, since they lower dopamine action in the movement circuits as well. The neat mirror between the two diseases, one too little and one too much of the same transmitter, is worth carrying into pharmacology.

Schizophrenia usually begins in late adolescence or early adulthood and follows a long course, often with relapses. Newer drugs, the so-called atypical antipsychotics, act on serotonin receptors as well as dopamine and tend to treat the negative symptoms a little better while causing less of the Parkinson-like stiffness, though they bring their own side effects such as weight gain. Because the illness is long-term, steady treatment and family support change the outlook a great deal, and a pharmacist has a real part in helping patients keep to their medicines.

3.8 Alzheimer's disease

Alzheimer's disease is the most common cause of dementia, a progressive degeneration of the brain that slowly destroys memory and thinking. It usually begins with difficulty remembering recent events and advances over years to confusion, loss of language, changes in personality and, eventually, an inability to carry out daily life.

Two abnormal protein changes define the disease in the brain tissue. The first is the build-up of **amyloid plaques**, clumps of a protein fragment called beta-amyloid that collect outside the neurons. The second is the formation of **neurofibrillary tangles**, twisted threads of a protein called tau that form inside the neurons. Together these damage and kill brain cells, and the brain gradually shrinks, especially in the regions that handle memory. A further change matters for treatment: there is a marked loss of neurons that use **acetylcholine**, the transmitter from Chapter 1, and this cholinergic loss is closely tied to the memory failure. That is the basis of the main drug treatment, which uses acetylcholinesterase inhibitors to block the enzyme that breaks down acetylcholine, so the remaining transmitter lasts longer and works harder. The treatment slows symptoms for a time rather than stopping the disease, because it cannot replace the neurons already lost.

Age is the biggest risk factor, and the disease becomes much more common in the very old; a family history and certain genes add to the risk. The course runs over several years through worsening stages, from mild forgetfulness to a complete dependence on others for daily care, and the later stages place a heavy burden on families and carers. There is no cure, so much of the care is supportive: keeping the person safe, treating other illnesses, and helping the family. Telling Alzheimer's apart from the ordinary forgetfulness of age, and from other causes of confusion such as depression or an underactive thyroid, is an important part of diagnosis, because some of those other causes can be reversed.

3.9 Meningitis

Meningitis is inflammation of the meninges, the protective membranes around the brain and spinal cord described in Chapter 2. It is most often caused by infection, and the cause matters enormously, because **bacterial meningitis** is a medical emergency that can kill or disable within hours, while **viral meningitis** is usually milder and self-limiting.

The classic features come directly from the inflamed, irritated meninges and the rising pressure inside the skull: fever, severe headache, a stiff neck (because bending the inflamed membranes hurts), dislike of light, drowsiness and, in severe cases, a falling level of consciousness. In meningococcal infection a characteristic skin rash may appear. Because the meninges are bathed in cerebrospinal fluid, the diagnosis is confirmed by a lumbar puncture, the procedure met in Chapter 2: in bacterial meningitis the CSF is cloudy, full of white cells, and altered in its glucose and protein, while in viral meningitis the changes are milder. Bacterial meningitis is treated urgently with antibiotics, and the speed of treatment decides the outcome, which is why recognising the signs early is part of every health professional's training. This is also the disease that best closes the nervous-system unit, because it is a failure of the very protection that Chapter 2 began with.

Two bedside tests support the diagnosis and are worth knowing by name. Kernig's sign is pain and resistance when the examiner straightens the knee while the hip is bent, and Brudzinski's sign is an involuntary lifting of the legs when the neck is bent forward; both appear because stretching the inflamed meninges hurts. The common bacterial causes vary with age but include the meningococcus, the pneumococcus and, in young children before vaccination, Haemophilus influenzae type b. Several of these are now prevented by vaccines on the childhood schedule, so meningitis is one of the few diseases in this chapter that can be stopped before it starts. The serious complications of the bacterial form, including deafness, seizures and brain damage, are the reason the early signs must never be dismissed as ordinary flu.

> **Quick-recall box 3.1: The transmitter behind each disease** Epilepsy: excitation (glutamate) over inhibition (GABA). Parkinson's: too little dopamine in the basal ganglia. Stroke: blood supply cut, glutamate excitotoxicity. Migraine: trigeminovascular activation, serotonin involved. Depression: too little serotonin and noradrenaline. Schizophrenia: too much dopamine activity. Alzheimer's: amyloid plaques, tau tangles, loss of acetylcholine. Meningitis: infection of the meninges.

3.10 Chapter summary

The diseases of the nervous system are best understood as specific failures of the machinery built in Chapters 1 and 2. Epilepsy is an electrical disorder in which the balance between glutamate-driven excitation and GABA-driven inhibition tips toward excitation, so groups of neurons fire together in seizures, classified as generalised or focal; treatment restores inhibition. Parkinson's disease is the loss of dopamine-producing neurons in the substantia nigra of the basal ganglia, giving bradykinesia, rigidity, resting tremor and postural instability, and treated by giving levodopa, which crosses the blood–brain barrier that dopamine cannot. Stroke is the sudden loss of blood supply to the brain, either ischaemic (a blockage, the common type) or haemorrhagic (a bleed), with glutamate excitotoxicity widening the damage and the deficits depending on the region struck.

Migraine is a recurrent throbbing headache arising from activation of the trigeminovascular system, with serotonin closely involved and sometimes an aura. Depression, a disorder of persistent low mood, is explained by the monoamine hypothesis as a shortage of serotonin and noradrenaline and is treated by drugs that raise their levels at the synapse. Schizophrenia, a disorder of lost contact with reality with positive and negative symptoms, is linked by the dopamine hypothesis to excess dopamine activity, the mirror image of Parkinson's, and is treated with dopamine blockers. Alzheimer's disease, the commonest dementia, is marked by

amyloid plaques, neurofibrillary tangles and a loss of acetylcholine neurons, and is eased for a time by acetylcholinesterase inhibitors. Meningitis is inflammation of the meninges, usually by infection, with the bacterial form a true emergency diagnosed by lumbar puncture. Across the whole chapter the lesson holds: name the broken part of the system, and both the symptoms and the treatment follow. Unit II now turns from signalling to the system that feeds the body, the gastrointestinal tract.

3.11 Self-assessment

A. Multiple-choice questions

1. A seizure is best described as:
   (a) loss of blood supply to the brain (b) abnormal excessive synchronised neuronal firing
   (b) inflammation of the meninges (d) loss of dopamine neurons. Answer: (b).
2. Parkinson's disease results from the loss of neurons that produce:
   (a) GABA (b) acetylcholine (c) dopamine (d) serotonin. Answer: (c).
3. The more common type of stroke is:
   (a) haemorrhagic (b) ischaemic (c) subarachnoid (d) subdural. Answer: (b).
4. The monoamine hypothesis links depression to a shortage of:
   (a) dopamine and GABA (b) serotonin and noradrenaline (c) glutamate (d) acetylcholine. Answer: (b).
5. The dopamine hypothesis explains the positive symptoms of:
   (a) Parkinson's disease (b) epilepsy (c) schizophrenia (d) Alzheimer's disease. Answer: (c).
6. The protein that forms plaques outside neurons in Alzheimer's disease is:
   (a) tau (b) beta-amyloid (c) dopamine (d) myelin. Answer: (b).
7. A stiff neck, fever and dislike of light suggest:
   (a) migraine (b) stroke (c) meningitis (d) epilepsy. Answer: (c).
8. Levodopa is given instead of dopamine in Parkinson's disease because:
   (a) it is cheaper (b) dopamine cannot cross the blood–brain barrier (c) it has no side effects (d) it cures the disease. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Define epilepsy and explain its basis in terms of excitation and inhibition. Epilepsy is a chronic disorder of recurrent, unprovoked seizures, a seizure being a sudden burst of abnormal, excessive and synchronised electrical activity in a group of neurons. It arises when

the normal balance between excitation (glutamate) and inhibition (GABA) tips toward excitation, either from too much excitatory activity or too little inhibition, so neurons fire together uncontrollably. *(High-yield.)*

2. Describe the pathophysiology and the four classic signs of Parkinson's disease. Parkinson's disease is caused by the progressive loss of dopamine-producing neurons in the substantia nigra of the basal ganglia, reducing the dopamine that smooths movement. The four classic signs are bradykinesia (slow movement), rigidity (stiff muscles), resting tremor and postural instability (poor balance).

3. Differentiate between ischaemic and haemorrhagic stroke. An ischaemic stroke is caused by a blockage of a brain blood vessel, usually a clot, starving the tissue downstream of oxygen; it is the more common type. A haemorrhagic stroke is caused by the rupture of a blood vessel, so blood leaks into or around the brain, damaging tissue by loss of supply and by pressure.

4. What is the monoamine hypothesis of depression, and how do antidepressants act on it? The monoamine hypothesis proposes that depression results from a shortage of monoamine transmitters in the brain, chiefly serotonin and noradrenaline. Antidepressants act by blocking the reuptake of these transmitters, leaving more in the synaptic cleft and raising their activity, which relieves the symptoms over a few weeks.

5. Why is bacterial meningitis treated as an emergency, and how is it diagnosed? Bacterial meningitis can kill or cause permanent disability within hours, so it must be treated urgently with antibiotics; the speed of treatment decides the outcome. It is diagnosed by lumbar puncture, which in bacterial meningitis shows cloudy cerebrospinal fluid full of white cells with altered glucose and protein.

6. Contrast the role of dopamine in Parkinson's disease and schizophrenia. In Parkinson's disease there is too little dopamine in the movement circuits of the basal ganglia, causing slow, stiff, tremulous movement. In schizophrenia there is thought to be too much dopamine activity in the pathways handling perception and thought, causing the positive symptoms. The two are mirror images, which is why a drug for one can worsen the other.

C. Long-answer questions (10 marks)

1. Discuss the pathophysiology, clinical features and basis of treatment of Parkinson's disease. A full answer defines Parkinson's as a progressive degenerative movement disorder; explains the loss of dopaminergic neurons in the substantia nigra of the basal ganglia and the resulting dopamine deficiency, with Lewy bodies as a microscopic marker; lists the four classic signs (bradykinesia, rigidity, resting tremor, postural instability); and explains

treatment with levodopa, the dopamine precursor that crosses the blood–brain barrier, noting that the disease is managed not cured. *(High-yield.)*

2. Write notes on epilepsy and stroke. For epilepsy: definition as recurrent unprovoked seizures, the excitation–inhibition imbalance, the classification into generalised (tonic- clonic, absence) and focal seizures, and the principle of treatment by restoring inhibition. For stroke: definition as sudden loss of brain function from interrupted blood supply, the ischaemic and haemorrhagic types, glutamate excitotoxicity widening the damage, region- dependent deficits with the opposite-side rule, and high blood pressure as the main risk factor.

3. Describe the causes, clinical features and significance of meningitis. A full answer defines meningitis as inflammation of the meninges; gives the infective causes and the crucial difference between the emergency of bacterial meningitis and the milder viral form; lists the features (fever, severe headache, neck stiffness, photophobia, drowsiness, possible rash); explains diagnosis by lumbar puncture and the CSF changes; and stresses urgent antibiotic treatment for the bacterial form.

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Chapter 4: The Gastrointestinal System: Anatomy and Physiology

Learning outcomes

After working through this chapter the student will be able to:

1. Describe the general plan of the gastrointestinal tract and the layers of its wall.
2. Explain the anatomy and functions of the stomach, including how gastric acid is produced and regulated and how pepsin digests protein.
3. Describe the anatomy and functions of the small and large intestine.
4. State the functions of the salivary glands, pancreas and liver in digestion.
5. Describe the movements of the gastrointestinal tract.
6. Explain how carbohydrates, proteins and fats are digested and absorbed.

4.1 A disassembly line

The food on a plate is built from molecules far too large to enter the blood. A protein in a piece of meat is a chain of hundreds of amino acids; the starch in rice is a chain of thousands of sugar units. None of these can cross the wall of the gut as they are. So the gastrointestinal system has one central task: take large food molecules apart into pieces small enough to absorb, then pass those pieces into the blood and send the waste out. It is a disassembly line, with each station doing one part of the job.

This chapter follows food along that line, from the mouth to the anus, and at each station it asks two questions: what is the structure here, and what does it do. The two are always linked, which is the structure-serves-function throughline of the book. The stomach is built to churn and to make acid; the small intestine is built to absorb, with a surface area the size of a tennis court folded into a few metres; the large intestine is built to reclaim water. Three accessory organs, the salivary glands, the pancreas and the liver, pour their secretions in to help. By the end you should be able to trace a mouthful of food the whole way and name what happens to it at each step. For a pharmacy student there is a further payoff: this same tract is the route most drugs take into the body, so its acid, its enzymes and its absorbing surface decide how a tablet behaves.

4.2 The general plan of the gut

The **gastrointestinal tract (GIT)**, also called the alimentary canal, is a long muscular tube running from the mouth to the anus, about nine metres in length in life. Along its course it

forms the mouth, pharynx, oesophagus, stomach, small intestine and large intestine, ending at the anus. Connected to it but lying outside the tube are the accessory organs: the salivary glands, the pancreas, the liver and its gallbladder, all of which deliver secretions into the tube through ducts.

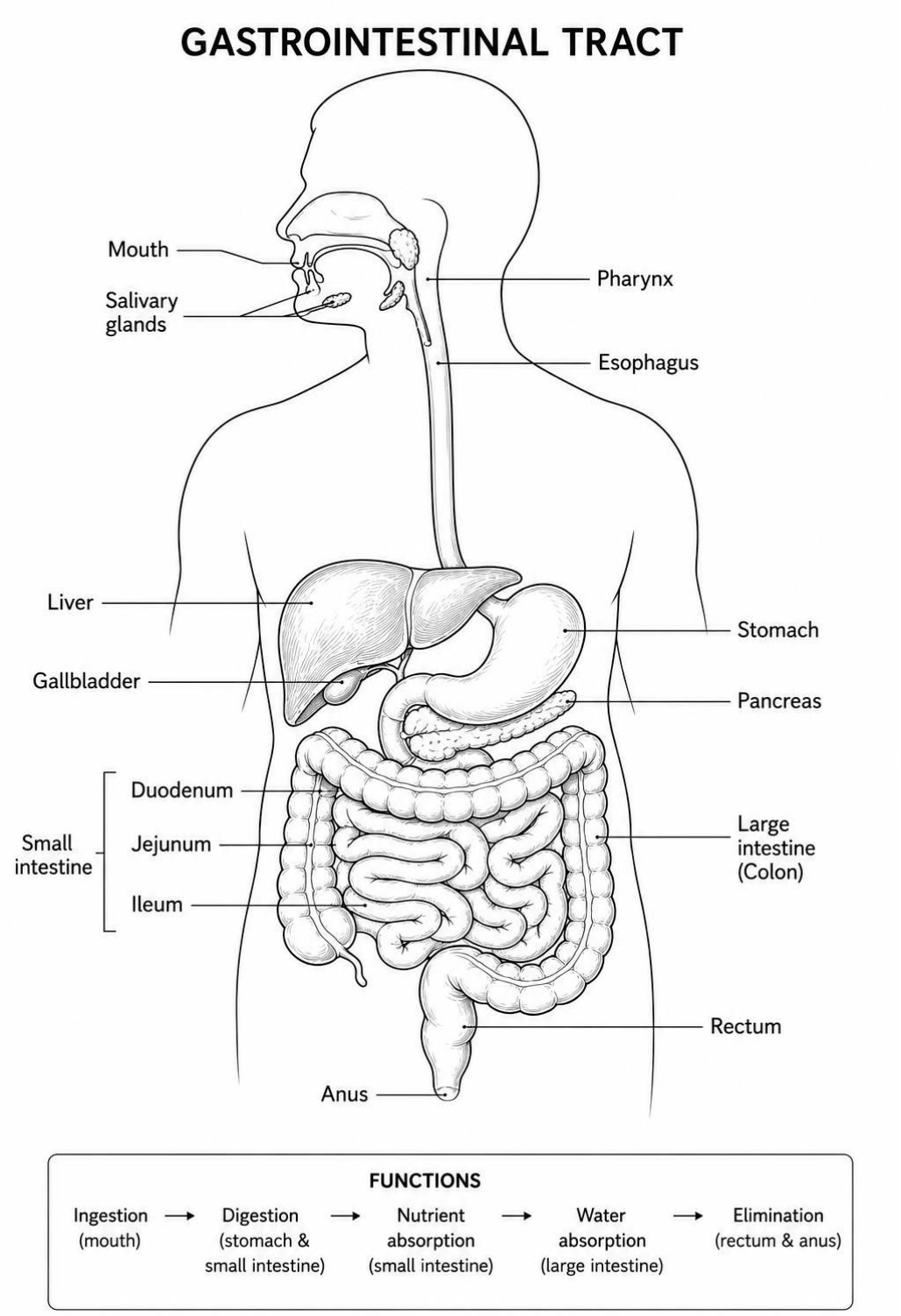


Figure 4.1 The Gastrointestinal Tract

The wall of the tube has the same four layers along almost its whole length, and knowing them once saves describing them again at every organ. From the inside out they are:

- The **mucosa**, the innermost lining that faces the food. It secretes mucus, enzymes and hormones and, in the absorbing regions, takes up the digested nutrients.
- The **submucosa**, a layer of connective tissue beneath the mucosa carrying blood vessels, lymph vessels and nerves.
- The **muscularis (muscle layer)**, usually two sheets of smooth muscle, an inner circular and an outer longitudinal layer, whose contractions mix and move the contents.
- The **serosa**, the outer protective covering.

Running within the wall is the gut's own nervous network, the **enteric nervous system**, sometimes called the gut brain because it can control digestion on its own. It works hand in hand with the autonomic nervous system from Chapter 1, and the parasympathetic supply, carried largely by the vagus nerve, generally stimulates digestion while the sympathetic supply slows it. Keep that vagus link in mind, because it is central to how the stomach is controlled.

4.3 The mouth and oesophagus: the start of the line

Digestion begins in the **mouth**. The teeth break food into smaller pieces (mechanical digestion) while the tongue mixes it and the salivary glands pour in saliva. **Saliva** does several jobs at once: it moistens the food so it can be swallowed, it dissolves some of it so it can be tasted, and it begins the chemical digestion of starch through an enzyme called salivary amylase. There are three pairs of salivary glands, the parotid, submandibular and sublingual glands, and together they produce more than a litre of saliva a day. The chewed, moistened ball of food, now called a bolus, is swallowed into the pharynx and passes into the oesophagus.

Swallowing, properly called **deglutition**, is more controlled than it looks and happens in three stages. The first is voluntary: the tongue pushes the bolus to the back of the mouth. The second is the pharyngeal stage, a reflex that takes over once the bolus reaches the pharynx; in it the soft palate rises to seal off the nose and a small flap, the epiglottis, folds down to cover the windpipe, so food is steered into the oesophagus and not the airway. The third is the oesophageal stage, in which peristalsis carries the bolus down to the stomach. The reflex protection of the airway is why talking or laughing while swallowing can make a person choke: the airway has been left open at the wrong moment.

The **oesophagus** is a muscular tube that carries the bolus from the pharynx to the stomach. It does not digest; it transports. It moves the bolus by **peristalsis**, a wave of muscle contraction

behind the food and relaxation in front of it that squeezes the bolus along, the same mechanism that moves contents through the whole tract. So strong is the wave that a person can swallow even upside down. At the lower end a ring of muscle, the lower oesophageal (cardiac) sphincter, opens to let food into the stomach and then closes to stop the stomach's acid contents flowing back up. When that sphincter is weak, acid does flow back, which is the heartburn of reflux disease met in Chapter 5.

4.4 The stomach

The **stomach** is a J-shaped muscular bag in the upper left of the abdomen, the widest part of the gut, where food is stored, churned and partly digested. The syllabus gives the stomach special attention, and for good reason: it is where the body makes a strong acid on purpose, and the control of that acid is a model of how the nervous system, hormones and local signals work together.

Structure

The stomach has four regions: the cardia where the oesophagus enters, the dome-shaped fundus above, the large central body, and the funnel-shaped pylorus that leads to the small intestine and ends in the pyloric sphincter, a ring of muscle guarding the exit. The muscle layer of the stomach is unusually thick and has a third, oblique layer in addition to the usual two, which gives it the power to churn food vigorously. The lining is folded into ridges called rugae that flatten as the stomach fills, letting it expand to hold a meal.

The mucosa is dotted with millions of **gastric glands** that open into pits in the surface, and these glands hold the cells that do the stomach's chemical work. Three are worth knowing:

- **Parietal (oxyntic) cells** secrete hydrochloric acid and intrinsic factor (a substance needed to absorb vitamin B12 later in the small intestine).
- **Chief cells** secrete pepsinogen, the inactive form of the protein-digesting enzyme.
- **Mucous cells** secrete mucus and bicarbonate that coat and protect the stomach lining from its own acid.

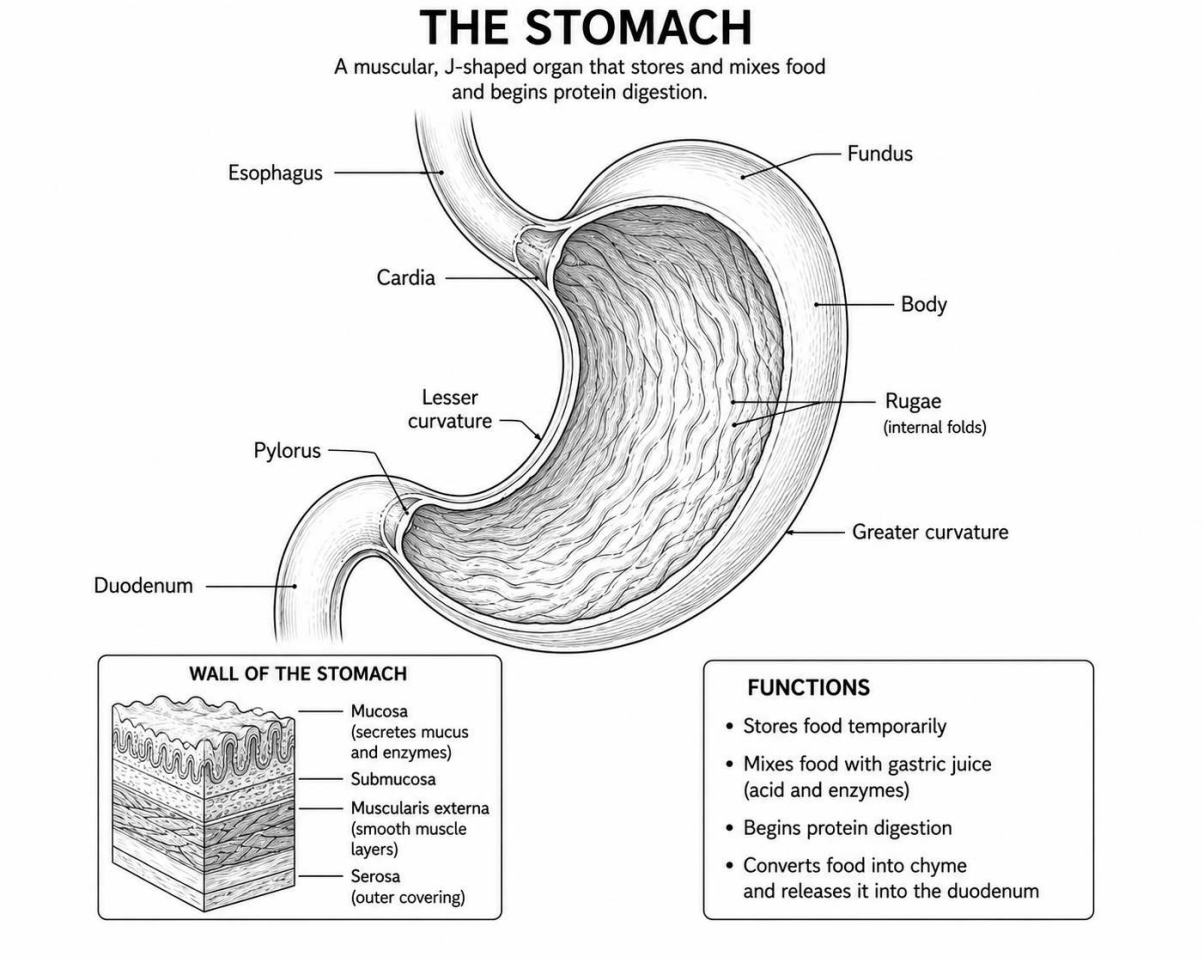


Figure 4.2 The stomach

Functions of the stomach

The stomach does four things. It stores a meal so the body need not eat continuously. It churns the food, mixing it with gastric juice into a creamy, acidic paste called **chyme**. It begins protein digestion through pepsin. And it releases the chyme slowly into the small intestine in controlled amounts through the pyloric sphincter, so the intestine is not overwhelmed.

Gastric acid: how it is produced

The parietal cells make **gastric acid**, a solution of hydrochloric acid (HCl) strong enough to bring the stomach contents to about pH 1.5 to 3.5, more acidic than vinegar. This serves real purposes: it kills most bacteria swallowed with food, it unfolds proteins so enzymes can reach them, and it provides the acid conditions that the enzyme pepsin needs to work.

The acid is made inside the parietal cell and pumped into the stomach by a transport protein in the cell membrane called the **proton pump (the H^+/K^+ ATPase)**, which pushes hydrogen ions (H^+) out into the stomach in exchange for potassium ions, spending ATP to do it. This

pump is the final common step of all acid secretion, and it is a major drug target: the proton-pump inhibitor drugs, among the most used medicines in the world, switch off this pump to treat ulcers and reflux. The acid-making machinery met here is exactly what those drugs act on.

Gastric acid: how it is regulated through the parasympathetic nervous system

Making a strong acid is dangerous, so the body controls its production tightly, switching it on when food is coming and off when digestion is done. The control comes from three directions that work together, and the syllabus highlights the parasympathetic part.

The **parasympathetic** control runs through the **vagus nerve**, the major parasympathetic nerve from Chapter 1. The sight, smell, taste and even the thought of food makes the brain send signals down the vagus to the stomach before any food arrives, the so-called cephalic (head) phase. The vagus stimulates the parietal cells to secrete acid, both directly and by triggering the release of substances that drive acid production. This is why a hungry person's stomach is already acidic at the smell of cooking. Because the vagus drives acid, cutting it (an operation called vagotomy, once common for ulcers) reduces acid secretion, which is direct evidence of its role.

Two other controls act alongside the vagus. The **hormone gastrin**, released from the stomach wall when food (especially protein) arrives and stretches the stomach, travels in the blood back to the parietal cells and strongly stimulates acid. And the local messenger **histamine**, released near the parietal cells, also stimulates them; this is why antihistamine drugs of a particular type reduce stomach acid. So the parietal cell receives three "make acid" signals, from the vagus (nerve), gastrin (hormone) and histamine (local), and only when they combine is acid produced in full. Figure 4.3 sets out this control as a flowchart. Once the meal has passed into the intestine and the stomach empties, these signals fall away and acid production switches off.

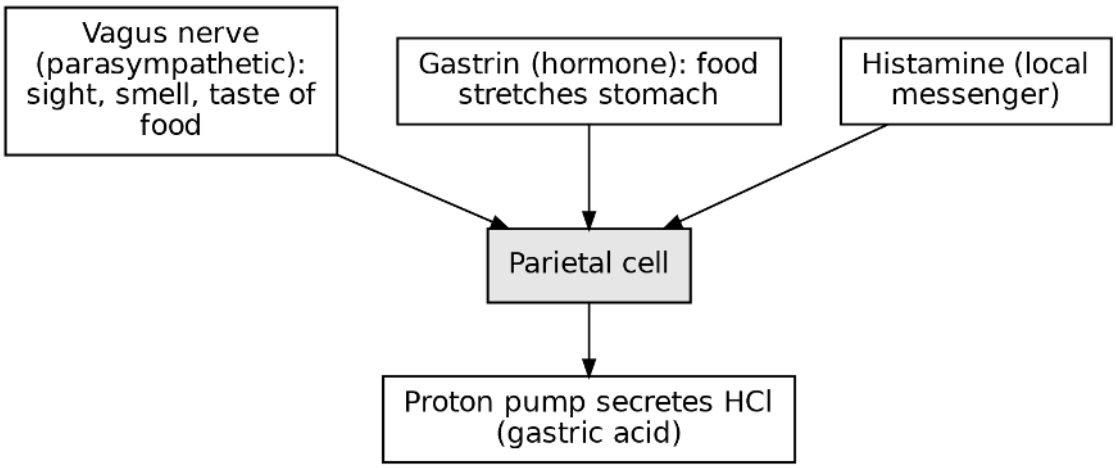


Figure 4.3 *Control of gastric acid secretion.*

The three phases of gastric secretion

The control above plays out over a meal in three overlapping phases, named for where the trigger comes from. Learning them as a sequence makes the whole regulation easier to reproduce in an exam.

The **cephalic phase** happens before food even reaches the stomach. The sight, smell, taste or thought of food, sensed by the brain, drives the vagus nerve to start acid and pepsinogen secretion, so the stomach is primed and ready. This phase is purely nervous and accounts for a notable share of the acid produced for a meal.

The **gastric phase** begins when food actually enters the stomach. The arrival of food stretches the stomach wall and, especially with protein present, triggers the release of gastrin. The stretch sets off local nerve reflexes and gastrin release, and both drive the parietal cells hard. This is the largest phase, producing most of the meal's acid, and it lasts as long as food remains in the stomach.

The **intestinal phase** comes as the chyme begins to pass into the duodenum. At first the arrival of partly digested food briefly encourages further secretion, but the dominant effect is the opposite: as the acidic, fatty chyme fills the duodenum, the small intestine sends nervous and hormonal signals back to the stomach that slow acid production and slow gastric emptying. This protects the intestine from being flooded with acid faster than it can neutralise it. So the three phases switch acid on in anticipation, drive it hard during the meal, and then damp it down as digestion moves on.

Protecting the stomach from its own acid

A strong acid and a protein-digesting enzyme are a threat to the stomach wall itself, which is made of living, protein-rich tissue. The stomach defends itself with a **mucosal barrier**: the mucous cells secrete a thick layer of mucus mixed with bicarbonate that clings to the lining, trapping a neutral, slippery zone right against the cells even while the lumen is strongly acidic. The lining cells are also joined tightly and are replaced quickly if damaged, and a healthy blood flow carries away any acid that leaks through. Disease appears when this defence is overwhelmed or weakened, so that acid and pepsin reach and digest the wall itself. That breakdown of the barrier is the heart of peptic ulcer in Chapter 5, which is why the protective side of the stomach is taught here alongside the aggressive side.

Pepsin and the start of protein digestion

The stomach begins the digestion of **protein**, and it does so with the enzyme **pepsin**. Pepsin is made and stored in an inactive form, **pepsinogen**, by the chief cells. Storing it inactive protects the cells that make it, because an active protein-digesting enzyme would attack the very cell holding it. When pepsinogen meets the acid in the stomach, the acid converts it into active pepsin. Once a little pepsin is formed it activates more pepsinogen, so the process accelerates.

Active pepsin then breaks the long chains of dietary protein into shorter fragments called peptides. It does not finish the job; it makes the first cuts, and the small intestine completes protein digestion later. The key point, and a favourite of examiners, is that pepsin works only in acid: its best activity is at the low pH the parietal cells create, and it stops working when the chyme is neutralised in the small intestine. So acid and pepsin are a team. The acid unfolds the protein and activates the enzyme, and the enzyme makes the cuts. Remove the acid and pepsin cannot work, which is part of why acid-lowering drugs ease the damage in peptic ulcer.

> **Quick-recall box 4.1: The stomach in brief** Parietal cells make HCl (via the proton pump) and intrinsic factor. Chief cells make pepsinogen, which acid turns into pepsin. Acid is driven by three signals: vagus (parasympathetic), gastrin (hormone) and histamine (local). Pepsin starts protein digestion and works only in acid. Chyme leaves through the pyloric sphincter.

4.5 The small intestine

The **small intestine** is the longest part of the gut, a coiled tube about five to six metres long, and it is where most digestion is completed and almost all absorption happens. It is narrow (hence “small”) but very long, and it has three parts in order: the **duodenum**, the short first

part that receives chyme from the stomach and secretions from the pancreas and liver; the **jejunum**, the middle part; and the **ileum**, the last part that joins the large intestine.

Built for absorption

The small intestine has to absorb the nutrients from an entire meal, and its structure is shaped entirely around that task. Its inner surface is enlarged enormously in three nested ways. The lining is thrown into circular folds; the folds are covered in millions of tiny finger-like projections called **villi**; and each cell on a villus carries thousands of even smaller projections called **microvilli**, forming a brush border. Together these multiply the surface area many hundred-fold, turning a tube a few metres long into an absorbing surface of around two hundred square metres. Inside each villus is a network of blood capillaries and a small lymph vessel called a lacteal, ready to carry away whatever is absorbed. This is the clearest example in the book of structure serving function: the job is absorption, so every feature multiplies the surface that absorbs.

Between the villi the lining dips into small pits called crypts, and these crypts and the cells of the wall secrete the intestinal juice, a watery fluid that keeps the contents fluid and carries the brush-border enzymes that finish digestion. In the first part of the duodenum, special glands also secrete an alkaline mucus that helps protect the duodenal lining from the acid arriving from the stomach, the same defensive idea seen in the stomach itself. The lining cells of the small intestine are replaced every few days, one of the fastest turnovers in the body, which is why the gut is one of the first tissues harmed by treatments that stop cells dividing, such as some anticancer drugs and radiation. The structure of the absorbing surface, then, comes at the cost of constant rebuilding, and that cost has direct consequences in therapy.

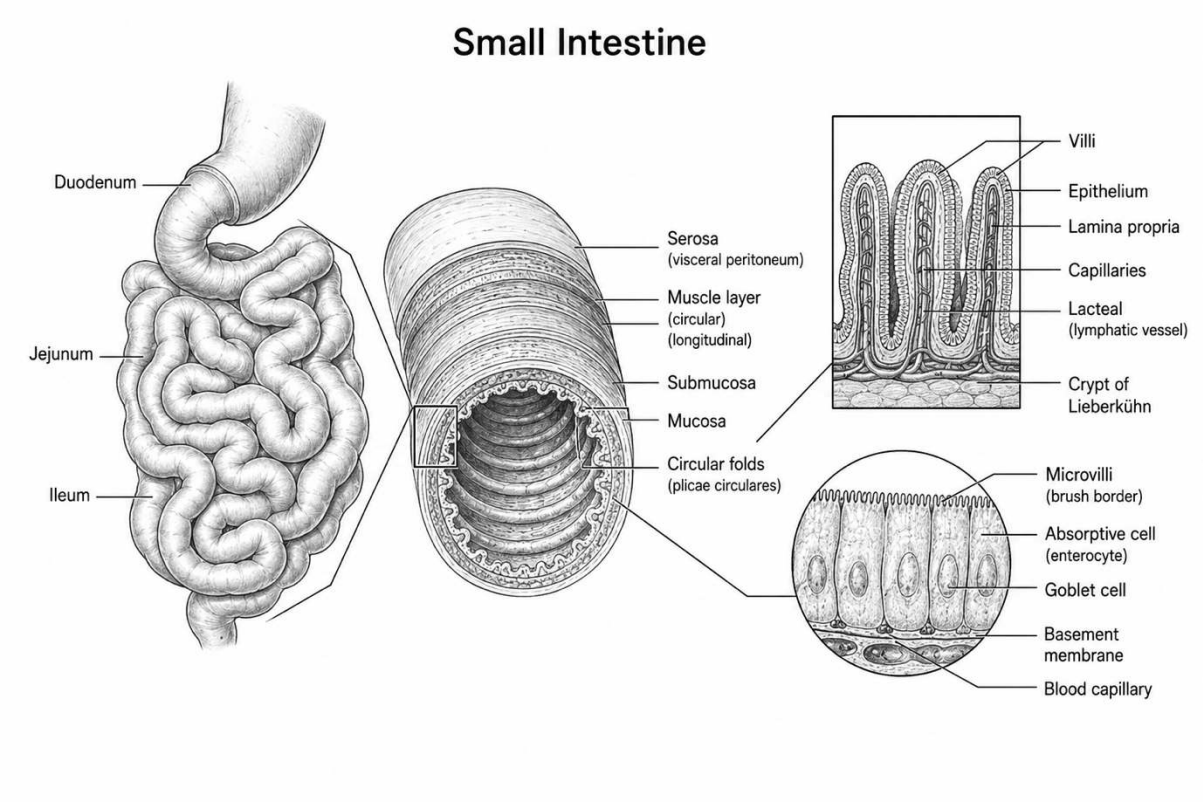


Figure 4.4 The small intestine

Functions

The small intestine completes digestion and carries out absorption. Into the duodenum pour bile from the liver and enzyme-rich juice from the pancreas, along with the intestine's own enzymes from the brush border, and together these finish breaking carbohydrates, proteins and fats into their absorbable units. The intestine then absorbs those units, along with water, vitamins and minerals, across its vast surface into the blood and lymph. It also keeps the contents moving and mixing through its muscle layer. By the time the residue leaves the small intestine, the useful nutrients have largely been taken up, and what remains is mostly water and indigestible material.

Two intestinal hormones that run the pancreas and gallbladder

The small intestine does not only receive the secretions of the pancreas and liver; it calls for them, and it does so with two hormones that are worth knowing by name because they show how neatly the system is matched to its load. When acidic chyme enters the duodenum, the intestinal wall releases **secretin**, which travels in the blood to the pancreas and makes it pour out bicarbonate-rich juice to neutralise the acid. When fatty and protein-rich chyme enters, the wall releases **cholecystokinin (CCK)**, which does two things: it makes the pancreas release its digestive enzymes, and it makes the gallbladder contract and squeeze bile into the

duodenum, right when fat is present and bile is needed. So the arrival of acid calls for neutraliser, and the arrival of fat calls for bile and enzymes. The supply is summoned by the demand, which is the homeostasis throughline working at the level of a single meal.

How absorption actually happens

Absorption is not a single process. Glucose and amino acids are taken across the intestinal lining cells by **active transport**, using carrier proteins and energy, often coupled to the movement of sodium, because these nutrients must be moved even against their concentration gradient to absorb them fully. Fatty acids and glycerol, being fat-soluble, pass more freely into the lining cells, are reassembled into fats inside them, and leave mainly through the lacteals into the lymph. Water follows the absorbed salts and nutrients by **osmosis**, never pumped directly but drawn along after them. Vitamins are absorbed according to their nature: the fat-soluble vitamins (A, D, E and K) ride along with the absorbed fat and so depend on bile, while most water-soluble vitamins are absorbed directly, with vitamin B12 the special case that needs the intrinsic factor made back in the stomach. This is why disease of the stomach can cause a vitamin deficiency felt far down the line.

4.6 The large intestine

The **large intestine** is the final part of the tube, about 1.5 metres long, wider than the small intestine but much shorter. It runs from the end of the ileum as the caecum (with its attached appendix), continues as the colon (ascending, transverse, descending and sigmoid parts), and ends in the rectum and anal canal. Little digestion happens here; its work is to process the residue.

> **Quick-recall box 4.2: Small versus large intestine** Small intestine (5 to 6 m, narrow): completes digestion and absorbs nutrients; surface enlarged by folds, villi and microvilli; three parts (duodenum, jejunum, ileum). Large intestine (1.5 m, wide): absorbs water and salts to form faeces; houses gut flora that make vitamin K; stores and expels waste. Rule of thumb: small absorbs food, large absorbs water.

The large intestine has three main functions. First and most important, it **absorbs water** and salts from the watery residue passed on by the small intestine, turning a liquid into semi-solid **faeces**. This water reclamation is why disorders of the large intestine cause diarrhoea (too little water absorbed) or constipation (too much). Second, it houses a huge population of helpful bacteria, the **gut flora**, that feed on the residue and make some vitamins, including vitamin K, which the body absorbs. Third, it stores the faeces until they are passed out through the rectum and anus in defaecation. A simple way to hold the contrast: the small intestine absorbs nutrients, the large intestine absorbs water.

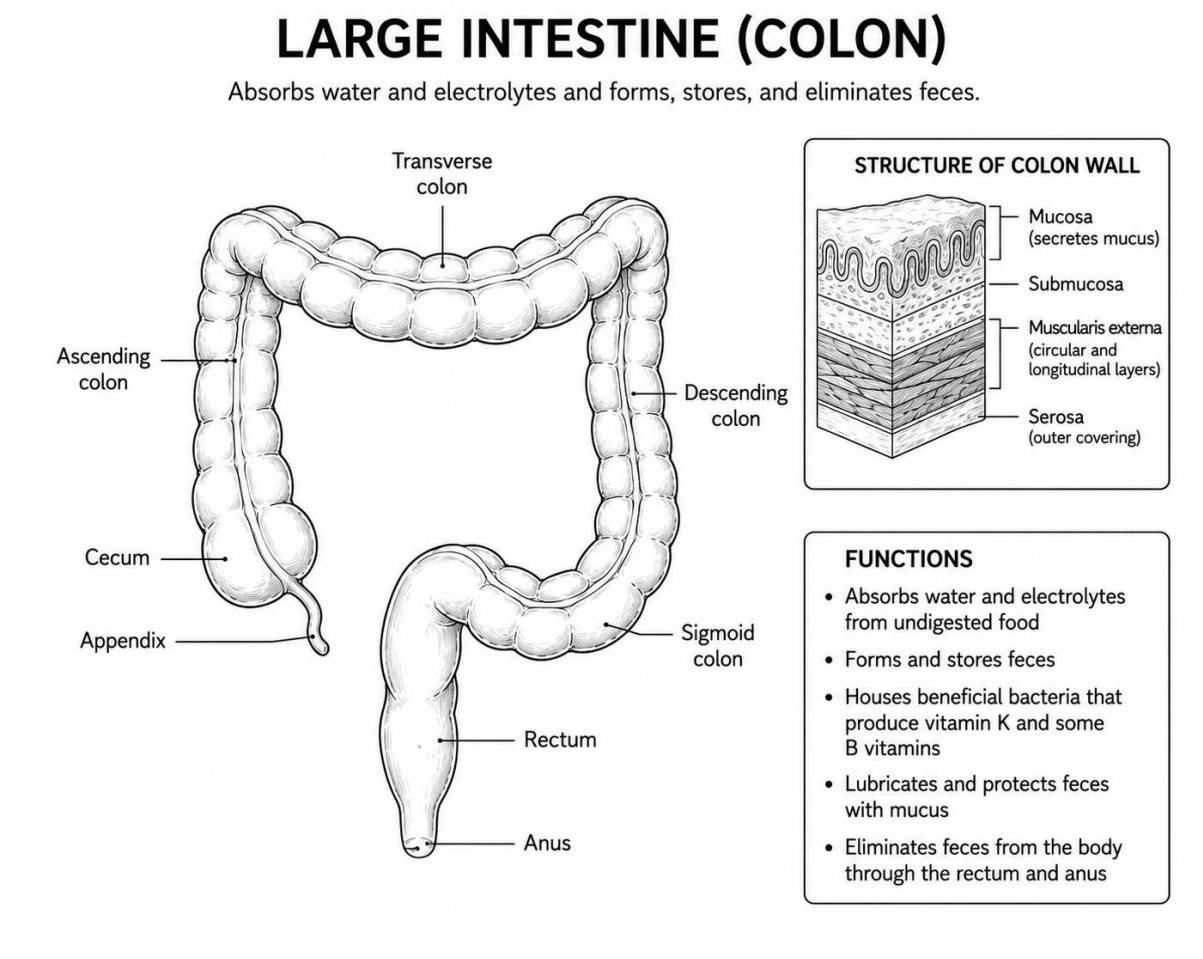


Figure 4.5 The large intestine

Defaecation itself is a reflex worth a sentence, because it connects back to Chapter 2. When faeces fill and stretch the rectum, sensory signals trigger a reflex, partly through the spinal cord, that relaxes the internal anal sphincter, while the external sphincter, being under voluntary control, can hold or release. So the large intestine ends in the same partnership of reflex and voluntary control seen in the nervous unit. The gut flora deserve a closing note too: this huge bacterial population is mostly helpful, and disturbing it, for example with a course of antibiotics, can upset the balance and cause diarrhoea, a fact a pharmacist meets often.

4.7 The accessory organs

Three organs sit outside the gut tube and pour secretions into it. They never see the food directly, but digestion cannot be completed without them.

The salivary glands

The three pairs of **salivary glands**, introduced in section 4.3, secrete saliva into the mouth. Beyond moistening and tasting food, saliva starts carbohydrate digestion with salivary

amylase, which breaks starch into smaller sugars, and it contains substances that protect the mouth against bacteria. Saliva is watery and slightly alkaline, and its flow rises sharply at the sight or smell of food, again through parasympathetic stimulation, mirroring the cephalic control of the stomach. The three pairs of glands differ a little: the parotid glands make a thin, enzyme-rich fluid, while the submandibular and sublingual glands add more mucus. A dry mouth, whether from fear, dehydration or as a side effect of certain drugs, shows how much the nervous system controls this flow, and it is more than an inconvenience, because saliva also protects the teeth and mouth, so a lasting dry mouth raises the risk of dental decay. This is a small but real example of how a drug's effect on one part of the autonomic system shows up as a problem somewhere quite different.

The pancreas

The **pancreas** is a soft gland lying behind the stomach, and it has two quite different jobs that the syllabus expects you to separate. Its **exocrine** part, the larger one, makes **pancreatic juice**, a fluid rich in digestive enzymes and bicarbonate that drains through a duct into the duodenum. The enzymes are a complete digestive toolkit: pancreatic amylase for carbohydrate, lipase for fat, and protein-digesting enzymes (trypsin and others, secreted inactive and activated in the intestine, the same safety trick as pepsinogen). The bicarbonate neutralises the acid chyme arriving from the stomach, raising the pH so the pancreatic enzymes, which work best in mild alkali, can act. So the pancreas both digests and neutralises.

The pancreas also has an **endocrine** part, small clusters of cells called the islets of Langerhans, which make the hormones insulin and glucagon that control blood glucose. That endocrine role belongs to the endocrine system and is taken up fully in Chapters 8 and 9; it is flagged here only so the two functions of the one organ are not confused.

The liver

The **liver** is the largest internal organ, sitting in the upper right of the abdomen, and it is the body's chemical factory, with a long list of jobs reaching far beyond digestion. In digestion its key product is **bile**, a greenish fluid made continuously by the liver, stored and concentrated in the **gallbladder**, and released into the duodenum when fatty food arrives. Bile contains **bile salts** that act on fat the way detergent acts on grease: they break large fat droplets into many tiny ones, a process called emulsification, vastly increasing the surface on which the fat-digesting enzyme lipase can work. Bile does not contain digestive enzymes; it prepares the fat for the enzymes. Bile also carries away a waste pigment called bilirubin, formed from worn-out red blood cells, and it is the build-up of this pigment that causes the yellow colour of jaundice in Chapter 5.

Beyond bile, the liver receives all the nutrient-rich blood draining from the gut and processes it. This delivery is no accident of plumbing. The blood leaving the stomach and intestines does not return straight to the heart; it is collected into the **hepatic portal vein** and carried first to the liver, an arrangement called the **hepatic portal system**. Because of it, every nutrient and every swallowed drug absorbed from the gut passes through the liver before reaching the rest of the body, so the liver gets first refusal on everything absorbed. It uses that position to keep the blood steady and safe: it stores glucose as glycogen and releases it to hold blood sugar level, builds blood proteins such as albumin and the clotting factors, stores vitamins and iron, and breaks down toxins, alcohol and most drugs.

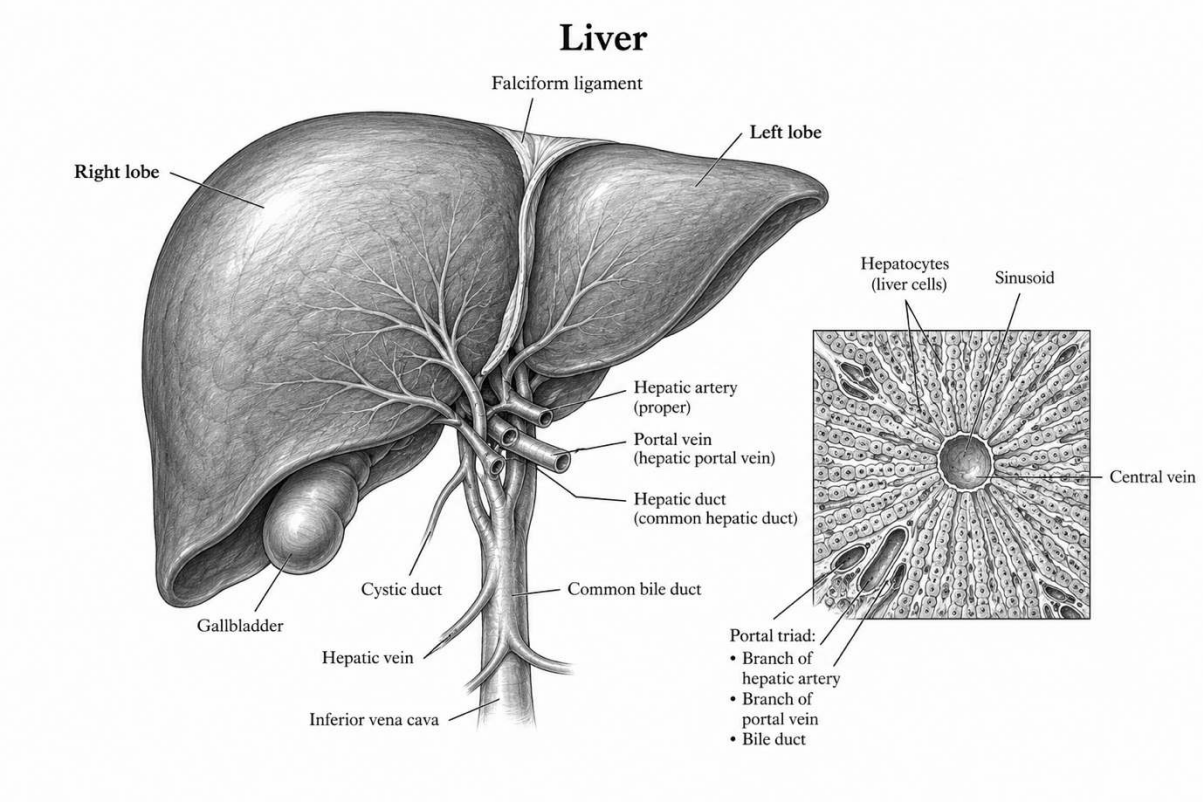


Figure 4.6 The liver

This first-pass position is why the liver matters so much to a pharmacist. A drug swallowed and absorbed from the gut passes first through the liver, which may inactivate a large part of it before it ever reaches the rest of the body, an effect called **first-pass metabolism**. It is the reason some drugs work poorly when swallowed and must be given another way, and the reason liver disease can make ordinary drug doses dangerous. The anatomy of the portal system thus becomes a rule of dosing. Table 4.1 brings together the main digestive secretions and what each does.

Table 4.1: The main digestive secretions

Secretion	Source	Key contents	Main action
Saliva	Salivary glands	Salivary amylase, mucus	Moistens food; begins starch digestion
Gastric juice	Stomach (gastric glands)	HCl, pepsinogen, intrinsic factor, mucus	Acid kills microbes, activates pepsin; pepsin starts protein digestion
Pancreatic juice	Pancreas (exocrine)	Amylase, lipase, protein enzymes, bicarbonate	Digests all three nutrients; neutralises acid chyme
Bile	Liver (stored in gallbladder)	Bile salts, bilirubin	Emulsifies fat; carries away bilirubin
Intestinal (brush border) enzymes	Small intestine lining	Maltase, peptidases, etc.	Complete digestion of sugars and peptides

4.8 Movements of the gastrointestinal tract

The gut is a muscular tube, and its smooth muscle produces two kinds of movement that the syllabus names. **Peristalsis** is the propulsive movement: a wave of contraction behind the contents and relaxation ahead pushes the food forward along the tract, from the oesophagus to the large intestine. It is what moves the bolus, the chyme and the residue along the line. **Segmentation** is the mixing movement, seen mainly in the small intestine: rings of muscle contract at intervals and then relax while neighbouring rings contract, chopping and mixing the contents back and forth without moving them far, so the chyme is thoroughly mixed with the digestive juices and brought into contact with the absorbing surface. Peristalsis moves food along; segmentation mixes it in place. Both are driven by the gut's smooth muscle and coordinated by the enteric nervous system, with the parasympathetic system speeding them and the sympathetic slowing them.

4.9 Digestion and absorption of nutrients

With the organs in place, the whole process can be drawn together for each of the three main food types. The principle is always the same: a large molecule is cut into its absorbable units by specific enzymes, and the units are taken up across the small-intestinal wall.

Carbohydrates start mostly as starch, a long chain of glucose units, with smaller amounts of the sugars in milk and fruit. Salivary amylase begins splitting the starch in the mouth, though it is soon stopped by the stomach acid; pancreatic amylase takes over in the small intestine

and breaks the chains into short pieces and double sugars; and the brush-border enzymes make the final cuts into single sugars, mainly glucose along with some fructose and galactose. Only single sugars can be absorbed, which is the point of the last step. The glucose is taken up by active transport, carried in the portal blood to the liver, and either used at once or stored as glycogen. A common disorder makes the rule clear: people who lack the brush-border enzyme for milk sugar cannot split it, so it passes undigested into the large intestine where bacteria ferment it, causing the wind and diarrhoea of lactose intolerance.

Proteins are long chains of amino acids folded into shape. The acid in the stomach first unfolds them so the enzymes can reach the chain, then pepsin makes the first cuts into shorter peptides. In the small intestine the pancreatic protein-digesting enzymes, chiefly trypsin and its partners, cut the peptides into still shorter pieces, and the brush-border peptidases make the final cuts into single amino acids. Only then can they be absorbed, taken up by active transport into the portal blood and carried to the liver, which uses them to build the body's own proteins. The staged hand-over, acid and pepsin in the stomach, pancreatic enzymes and brush-border enzymes in the intestine, is the same pattern seen for carbohydrate, and it is worth noticing as a general rule: digestion is finished in the small intestine, whatever the nutrient.

Fats are the special case, because fat does not dissolve in water and the digestive juices are watery. This is where bile earns its place: bile salts emulsify the large fat droplets into tiny ones, and pancreatic lipase then breaks the fats into fatty acids and glycerol. These absorbed fat products are mostly carried away not by the blood capillaries but by the lymph vessel (the lacteal) in each villus, eventually reaching the bloodstream. The need to emulsify fat first is why people who cannot make or release bile struggle to digest fatty meals, and why their stools may be pale and greasy, since undigested fat passes straight through. This also explains a clinical link worth carrying to Chapter 5: a gallstone blocking the bile duct stops bile reaching the gut, so fat is poorly digested and the fat-soluble vitamins are poorly absorbed, while the trapped bile pigment backs up into the blood and yellows the skin.

Across all three, the small intestine is the site where digestion finishes and absorption happens, water follows the absorbed nutrients by osmosis, and the liver receives the products first. Figure 4.7 summarises the digestion of the three nutrients as a single chart.

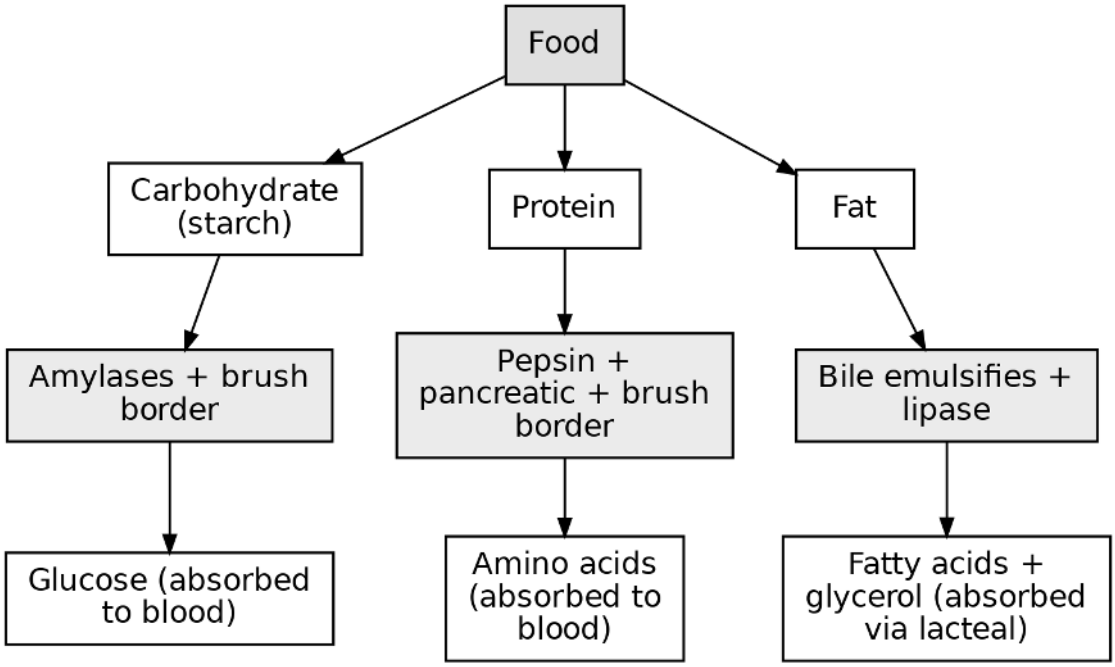


Figure 4.7 *Digestion and absorption of the three nutrients.*

Why this system matters to a pharmacist

This same tract is the road most medicines travel into the body, so its features are not only exam facts but the things that decide whether a tablet works. Three points carry straight into pharmacy. The strong gastric acid that digests food also attacks some drugs, so a medicine that would be destroyed by acid is given a special coating that survives the stomach and dissolves only in the gentler small intestine. The vast absorbing surface of the small intestine, built from villi and microvilli, is where most oral drugs are taken up, which is why the small intestine, not the stomach, is the main site of drug absorption, and why anything that speeds or slows gastric emptying changes how fast a drug starts to act. And the hepatic portal system, which sends absorbed material to the liver first, means a drug can be largely broken down by first-pass metabolism before it reaches its target, so the swallowed dose must allow for what the liver removes. The physiology of digestion, learned for its own sake, turns out to be the physiology of how oral medicines behave, which is a good reason for a pharmacy student to learn it well rather than by rote.

4.10 Chapter summary

The gastrointestinal system is a long muscular tube, the alimentary canal, that takes large food molecules apart and absorbs the pieces, helped by three accessory organs. Its wall has four layers (mucosa, submucosa, muscle and serosa) along its length, and it is controlled by its own enteric nervous system together with the autonomic supply, the parasympathetic vagus generally driving digestion. Food is chewed and mixed with saliva in the mouth, where

salivary amylase begins starch digestion, and is carried by peristalsis down the oesophagus to the stomach. The stomach stores and churns food into acidic chyme; its parietal cells make hydrochloric acid through the proton pump, regulated by three signals working together, the parasympathetic vagus nerve, the hormone gastrin and local histamine, and its chief cells make pepsinogen, which the acid turns into pepsin to begin protein digestion, an enzyme that works only in acid.

The small intestine, vastly enlarged in surface by folds, villi and microvilli, completes digestion using pancreatic and brush-border enzymes and bile, and absorbs almost all the nutrients and most of the water. The large intestine reclaims the remaining water to form faeces, houses helpful bacteria that make some vitamins, and stores waste until it is passed. The accessory organs each add something essential: the salivary glands start carbohydrate digestion, the pancreas supplies a full set of digestive enzymes and the bicarbonate that neutralises stomach acid, and the liver makes bile to emulsify fat, processes the absorbed nutrients and breaks down drugs and toxins. The gut moves its contents by peristalsis and mixes them by segmentation. Carbohydrates end as glucose, proteins as amino acids, and fats as fatty acids and glycerol, all absorbed in the small intestine and delivered first to the liver. With the healthy, working system now understood from one end to the other, Chapter 5 turns to what goes wrong with it, taking the common diseases of the gut and the liver in turn.

4.11 Self-assessment

A. Multiple-choice questions

1. The cells of the stomach that secrete hydrochloric acid are the:
   (a) chief cells (b) parietal cells (c) mucous cells (d) goblet cells. Answer: (b).
2. Pepsinogen is converted to active pepsin by:
   (a) bile (b) gastric acid (c) bicarbonate (d) amylase. Answer: (b).
3. The main parasympathetic nerve that stimulates gastric acid secretion is the:
   (a) phrenic nerve (b) vagus nerve (c) splanchnic nerve (d) optic nerve. Answer: (b).
4. Most absorption of nutrients takes place in the:
   (a) stomach (b) small intestine (c) large intestine (d) oesophagus. Answer: (b).
5. The chief role of the large intestine is to absorb:
   (a) amino acids (b) glucose (c) water and salts (d) fatty acids. Answer: (c).
6. Bile is produced by the ____ and stored in the ____:
   (a) gallbladder; liver (b) liver; gallbladder (c) pancreas; duodenum (d) stomach; pylorus. Answer: (b).
7. The enzyme that digests fat is:

(a) amylase (b) pepsin (c) lipase (d) trypsin. Answer: (c).

8. The proton pump that secretes acid is found in the membrane of the:

(a) chief cell (b) parietal cell (c) mucous cell (d) islet cell. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Name the four layers of the gut wall from inside to outside and give one function of the mucosa. From inside to outside the layers are the mucosa, the submucosa, the muscularis (muscle layer) and the serosa. The mucosa lines the tube and secretes mucus, enzymes and hormones, and in the small intestine it absorbs the digested nutrients.

2. Explain how gastric acid secretion is regulated through the parasympathetic nervous system. The parasympathetic vagus nerve stimulates acid secretion. The sight, smell, taste or thought of food makes the brain send signals down the vagus to the stomach, which stimulates the parietal cells to secrete acid directly and by releasing gastrin and histamine. This is the cephalic phase, and cutting the vagus reduces acid output, showing its central role. *(High-yield.)*

3. Describe the role of pepsin in protein digestion and explain why it works only in acid. Pepsin, made from pepsinogen by the action of gastric acid, begins protein digestion by breaking long protein chains into shorter peptides. It works best at the low pH the parietal cells create and becomes inactive when the chyme is neutralised in the small intestine, so acid is needed both to activate it and to provide its working conditions.

4. How is the small intestine adapted for absorption? Its inner surface is enlarged in three nested ways: circular folds, finger-like villi covering the folds, and microvilli (a brush border) on each cell, together multiplying the surface area hundreds of times. Each villus contains blood capillaries and a lacteal to carry away absorbed nutrients, and the wall is thin, so absorption is rapid.

5. State the functions of bile and explain why it is needed to digest fat. Bile, made by the liver and stored in the gallbladder, contains bile salts that emulsify large fat droplets into many tiny ones, greatly increasing the surface on which pancreatic lipase can act. It also carries away the waste pigment bilirubin. Because fat does not dissolve in the watery digestive juices, emulsification by bile is needed before the enzyme can digest it.

6. Distinguish between peristalsis and segmentation. Peristalsis is a propulsive movement, a wave of contraction behind the contents and relaxation ahead that pushes food forward along the tract. Segmentation is a mixing movement, mainly in the small intestine, where rings of muscle contract and relax in turn to chop and mix the contents without moving them far.

C. Long-answer questions (10 marks)

1. Describe the structure and functions of the stomach, with special reference to acid production and its regulation. A full answer covers the four regions of the stomach and its thick three-layered muscle; the gastric glands and their parietal, chief and mucous cells; the four functions (storage, churning into chyme, protein digestion, controlled emptying); acid production by the parietal cells through the proton pump; the regulation of acid by the vagus (parasympathetic), gastrin and histamine acting together; and pepsin's role in starting protein digestion. A flowchart of acid control (Figure 4.1) should be included. *(High-yield.)*

2. Describe the functions of the liver and pancreas in digestion. A full answer covers the pancreas as an exocrine gland producing pancreatic juice (amylase, lipase, protein-digesting enzymes and bicarbonate to neutralise acid) with a brief note that its endocrine islets make insulin and glucagon; and the liver producing bile (bile salts that emulsify fat, plus bilirubin), processing absorbed nutrients, storing glucose as glycogen, and breaking down toxins and drugs.

3. Trace the digestion and absorption of carbohydrates, proteins and fats along the gastrointestinal tract. A full answer follows each nutrient: carbohydrate from salivary amylase through pancreatic amylase and brush-border enzymes to glucose; protein from pepsin in the acid stomach through pancreatic enzymes and brush-border enzymes to amino acids; and fat emulsified by bile and digested by pancreatic lipase to fatty acids and glycerol, absorbed via the lacteals. It should state that absorption occurs in the small intestine and the products reach the liver first.

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Chapter 5: Pathophysiology of the Gastrointestinal System

Learning outcomes

After working through this chapter the student will be able to:

1. Describe the pathophysiology, types and features of inflammatory bowel disease.
2. Explain how a peptic ulcer forms as an imbalance between aggressive and defensive factors.
3. Classify jaundice into its three types and explain the cause of each.
4. Describe the types, spread and outcomes of viral hepatitis.
5. Outline the cause, features and complications of typhoid fever.
6. Distinguish alcoholic from non-alcoholic fatty liver disease and describe their progression.

5.1 Reading the signs

Yellow eyes are hard to miss. A patient whose skin and the whites of the eyes have turned yellow is showing, on the outside, that something has gone wrong deep inside, with the liver or the flow of bile. Much of the gastrointestinal system is hidden, so disease often announces itself through signs like this one: a yellow tinge, a burning pain after meals, blood in the stool, an unexplained fever. This chapter takes the diseases the syllabus lists and, for each, works back from the signs to the broken mechanism, using the healthy anatomy and physiology built in Chapter 4.

The thread that ties the chapter together is the one from the last chapter inverted. Chapter 4 showed a system beautifully matched to its job: a protective mucus barrier holding off the acid, a liver processing everything absorbed, bile carrying away waste pigment. Each disease here is one of those arrangements failing. The acid overwhelms the barrier and an ulcer forms. The liver is inflamed and cannot clear bilirubin, so jaundice appears. The pigment's exit is blocked and it backs up into the blood. Keep the healthy version in mind as each disease is described, because the disease is always the healthy mechanism gone wrong, and naming the broken part is half the answer an examiner wants. Table 5.1 collects the diseases for revision.

Table 5.1: Gastrointestinal diseases at a glance

Disease	Core problem	Key feature
Inflammatory bowel disease	Immune system attacks the gut	Chronic diarrhoea, abdominal pain (relapsing)
Peptic ulcer	Acid/pepsin overwhelm the mucosal defence	Burning upper abdominal pain
Jaundice	Bilirubin builds up in the blood	Yellow skin and eyes
Hepatitis	Virus inflames the liver	Tiredness, nausea, jaundice
Typhoid	Salmonella Typhi spreads through the body	Stepwise rising fever
Fatty liver disease	Fat builds up in liver cells	Often silent until cirrhosis

5.2 Inflammatory bowel disease

Inflammatory bowel disease (IBD) is a group of chronic disorders in which the gut becomes inflamed for long periods, with no single infection to blame. It is not the same as a passing bout of gastroenteritis; it is a long-running inflammation that flares and settles over years. The two main forms are **ulcerative colitis** and **Crohn's disease**, and telling them apart is a classic exam task.

The cause is not fully known, but it is understood as an over-reaction of the gut's own immune system. In a person with the right genetic background, the immune system seems to react abnormally to the normal gut bacteria, attacking the gut wall as though it were a threat. The result is chronic inflammation that damages the lining and causes the symptoms. Smoking, diet and the gut flora all play a part in shaping who is affected and how badly.

The two forms differ in where and how they damage the gut, and the differences are worth learning side by side, as in Table 5.2. **Ulcerative colitis** is limited to the large intestine, affecting the rectum and colon. The inflammation is continuous, spreading upward from the rectum without gaps, and it is shallow, involving only the inner lining (the mucosa). Its main symptom is bloody diarrhoea, often with mucus, along with cramping lower abdominal pain and an urgent need to pass stool. **Crohn's disease** can affect any part of the gastrointestinal tract, from the mouth to the anus, though it most often strikes the last part of the small intestine and the start of the large intestine. Its inflammation is patchy, with healthy stretches between diseased ones (so-called skip lesions), and it is deep, passing through the whole thickness of the gut wall. This depth is why Crohn's disease tends to cause complications such as narrowing of the bowel, and abnormal channels (fistulae) that burrow between loops

of gut or to the skin. Its symptoms include abdominal pain, diarrhoea (less often bloody than in colitis), weight loss and tiredness.

Table 5.2: Ulcerative colitis versus Crohn's disease

Feature	Ulcerative colitis	Crohn's disease
Site	Colon and rectum only	Any part, mouth to anus
Pattern	Continuous (no gaps)	Patchy (skip lesions)
Depth	Mucosa only (shallow)	Full thickness of wall
Typical stool	Bloody diarrhoea with mucus	Diarrhoea, less often bloody
Complications	Bowel cancer risk (long-standing)	Strictures and fistulae

A simple memory aid keeps the two apart. Ulcerative colitis is the "continuous, colon-only, mucosa-deep, bloody" disease; Crohn's is the "patchy, anywhere, full-thickness" disease. The depth of the inflammation is the key that unlocks the rest: because colitis is shallow it bleeds freely into the stool, while because Crohn's is deep it burrows to form fistulae and scars to form strictures. Both diseases can also show signs outside the gut, such as joint pains and eye or skin problems, a reminder that the immune over-reaction is a whole-body process and not only a bowel one. Long-standing ulcerative colitis also carries a raised risk of bowel cancer, which is why such patients are watched with regular checks.

Both forms run a relapsing course of flares and remissions, and both are treated by calming the overactive immune response. Treatment is stepped: anti-inflammatory drugs that act on the bowel for milder disease, then immune-suppressing drugs and the newer biological agents that block specific parts of the immune reaction for more severe disease, with surgery kept for complications such as a stricture or a fistula. Because the inflammation is long-standing, long-term care and patient support matter as much as the drugs, and a pharmacist has a real part in helping patients keep to treatment and manage flares. The contrast with the next disease is worth noting: inflammatory bowel disease is the gut attacked by its own immune system, whereas a peptic ulcer is the gut attacked by its own acid.

5.3 Peptic ulcer

A **peptic ulcer** is a break or sore in the lining of the gut where it is exposed to acid and pepsin, most often in the stomach (a gastric ulcer) or the first part of the duodenum (a duodenal ulcer). The name peptic points to the cause: the lining is being digested by the very acid and pepsin that Chapter 4 described as tools for digesting food. The disease is the clearest possible example of a protective arrangement failing.

The best way to understand a peptic ulcer is as an **imbalance between aggressive and defensive factors**, and this framing is worth stating plainly because it organises the whole topic. On one side are the aggressive factors that attack the lining: gastric acid and pepsin. On the other side are the defensive factors that protect it: the mucus and bicarbonate barrier, the healthy blood flow, and the quick repair of the lining cells, all met in Chapter 4. As long as defence matches attack, the lining stays intact. An ulcer forms when the balance tips, either because attack rises or because defence falls. Figure 5.1 sets this balance out.

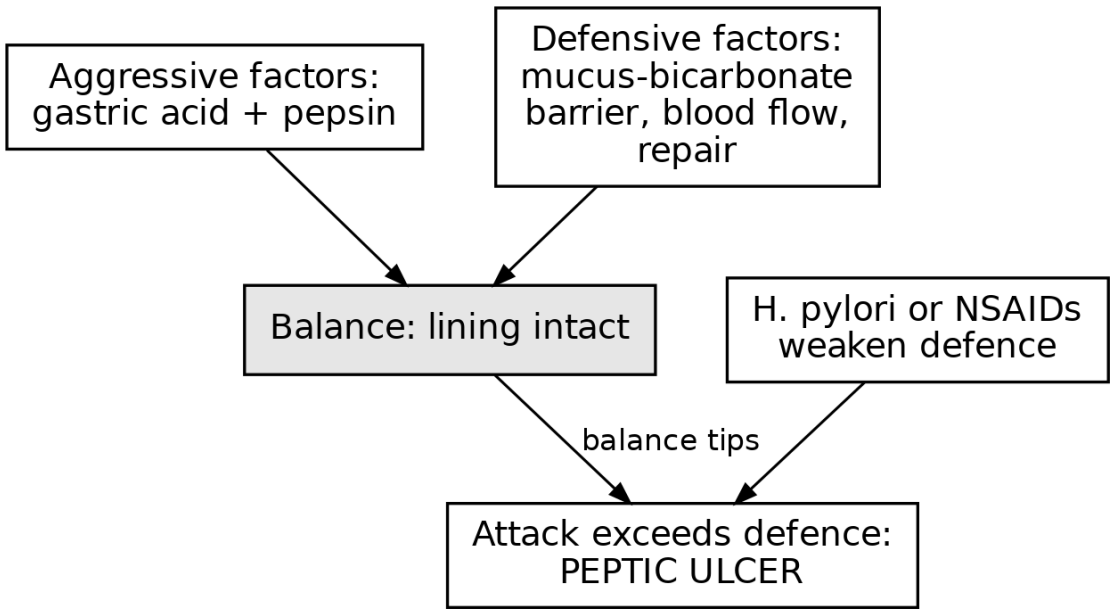


Figure 5.1 *Peptic ulcer as a balance of aggressive and defensive factors.*

Two causes account for most ulcers, and each tips the balance in a different direction. The first and most important is infection with a bacterium called **Helicobacter pylori**, which is able to live in the acid of the stomach. It damages the protective mucus layer and provokes inflammation, weakening the defence so that acid and pepsin reach the wall. The discovery that a bacterium, rather than stress or spicy food alone, causes most ulcers changed their treatment entirely. The second major cause is the regular use of **non-steroidal anti-inflammatory drugs (NSAIDs)**, the common painkillers such as aspirin and ibuprofen. These drugs reduce the substances that maintain the protective mucus and blood flow, again weakening the defence. Excess acid, smoking and severe stress add to the risk.

The classic symptom is a burning or gnawing pain in the upper abdomen, often related to meals, and the timing can hint at the site: a duodenal ulcer often hurts when the stomach is empty and eases with food, while a gastric ulcer may be made worse by eating. Other features include nausea, bloating and, over time, weight loss. The serious dangers come when an ulcer eats deeper. It can erode a blood vessel and **bleed**, showing as blood vomited up or as black, tarry stools (the colour of digested blood), and a large bleed can be life-threatening. It can

perforate right through the wall, spilling gut contents into the abdomen and causing sudden severe pain, a surgical emergency. And a long-standing gastric ulcer can slowly narrow the stomach outlet or, rarely, turn malignant, which is why gastric ulcers are checked more carefully than duodenal ones.

Treatment follows straight from the mechanism, and it is worth setting out because peptic ulcer is one of pharmacy's great success stories. Acid is reduced with the **proton-pump inhibitors** that switch off the proton pump from Chapter 4, the most effective acid-lowering drugs, and an older group, the H2-receptor blockers, lowers acid by blocking the histamine signal also met in Chapter 4. If Helicobacter pylori is present it is cleared with a combination of antibiotics together with an acid-lowering drug, a short course that cures the infection and stops the ulcer returning. Where NSAIDs are the cause, they are stopped where possible, or a protective drug is added. Restore the balance, by lowering attack or removing the cause that weakened defence, and the ulcer heals. The shift from treating ulcers as a lifelong acid problem to curing many of them as an infection is a clear example of how understanding a mechanism transforms treatment.

5.4 Jaundice

Jaundice is the yellow discoloration of the skin and the whites of the eyes caused by a build-up of **bilirubin** in the blood. Bilirubin, met in Chapter 4, is the yellow pigment formed when worn-out red blood cells are broken down; normally the liver takes it up, changes it into a form that dissolves in water, and sends it out in the bile to leave the body in the faeces. Jaundice appears whenever this pathway is overwhelmed or blocked, so bilirubin backs up into the blood and stains the tissues. Because the pathway has three stages, before the liver, in the liver, and after the liver, jaundice is classified into three matching types, shown in Figure 5.2. Learning the three is the heart of this topic, and the trick is to ask one question for any patient: is the problem in the supply of bilirubin, in the liver that processes it, or in the drainage that removes it. The answer places the jaundice in one of the three groups and points to its cause.

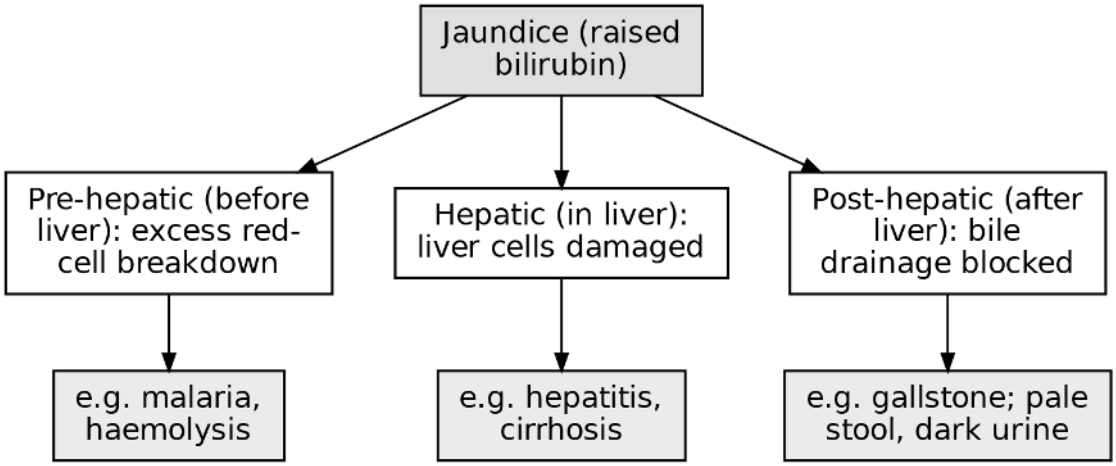


Figure 5.2 *The three types of jaundice.*

Pre-hepatic (haemolytic) jaundice arises before the liver, when red blood cells are broken down faster than normal, so much bilirubin is made that even a healthy liver cannot keep up. The liver is working fine; it is simply overwhelmed by the load. This happens in conditions where red cells are destroyed too quickly, such as certain inherited blood disorders and malaria.

Hepatic (hepatocellular) jaundice arises in the liver itself, when the liver cells are damaged and cannot process bilirubin properly. The fault is in the factory, not the supply or the exit. This is the jaundice of liver diseases such as hepatitis and cirrhosis, where the inflamed or scarred liver cannot take up and convert bilirubin as it should.

Post-hepatic (obstructive) jaundice arises after the liver, when the bile cannot drain because the duct carrying it to the gut is blocked, for example by a gallstone or a tumour. The liver makes and processes the bilirubin normally, but with the exit blocked it cannot leave, so it backs up into the blood. A useful clue points to this type: because the bile that colours the stool cannot reach the gut, the stools become pale, while the bilirubin spilling into the urine through the kidneys makes it dark. Recognising the three types matters because their treatment is quite different, aimed in turn at the blood, the liver or the blockage.

> **Quick-recall box 5.1: The three jaundices** Pre-hepatic: too much bilirubin made (red cells destroyed); liver overwhelmed. Hepatic: liver cells damaged and cannot process bilirubin (hepatitis, cirrhosis). Post-hepatic: bile cannot drain (blocked duct, gallstone); pale stools, dark urine. Before, in, or after the liver: that is the whole classification.

5.5 Hepatitis

Hepatitis means inflammation of the liver. It has several causes, including alcohol, drugs and toxins, but the syllabus centres on **viral hepatitis**, inflammation caused by viruses that specifically attack the liver. There are five main hepatitis viruses, named A to E, and the most useful way to learn them is to group them by how they spread, because the route of spread decides how serious they tend to be. Table 5.3 sets them out together.

Table 5.3: The five hepatitis viruses

Virus	Spread	Course	Vaccine
Hepatitis A	Faecal-oral (food, water)	Acute, self-limiting	Yes
Hepatitis B	Blood and body fluids	Can become chronic; cirrhosis, cancer	Yes
Hepatitis C	Blood (needles, transfusion)	Often chronic; cirrhosis, cancer	No
Hepatitis D	Blood (only with hepatitis B)	Worsens hepatitis B	Via hepatitis B vaccine
Hepatitis E	Faecal-oral (water)	Acute; dangerous in pregnancy	Limited availability

Two of them, **hepatitis A and hepatitis E**, spread by the **faecal-oral route**, through food or water contaminated with infected faeces. They cause a sudden (acute) illness that, in most people, settles on its own within a few weeks and does not become long-term. They are diseases of poor sanitation, which makes them common where clean water is scarce, and hepatitis E is particularly dangerous in pregnancy.

The other three, **hepatitis B, C and D**, spread mainly through **blood and body fluids**, through infected blood, shared needles, unsafe injections, and from mother to baby, with B and C also spread sexually. Their importance is that they can become **chronic**, a long-term infection lasting years, quietly inflaming the liver. Over time that chronic inflammation can scar the liver into **cirrhosis** and can lead to liver cancer, so hepatitis B and C are major causes of serious liver disease worldwide. Hepatitis D is unusual in that it can only infect a person who already carries hepatitis B.

Whatever the virus, the features of an acute attack come from the inflamed liver: tiredness, loss of appetite, nausea, discomfort over the liver, and jaundice of the hepatic type from section 5.4. Often the urine darkens and the stools pale as the inflamed liver handles bilirubin

poorly. Many infections, especially in children, are mild or even silent, which is part of why the blood-borne viruses spread so widely: a person can carry and pass on hepatitis B or C for years without feeling ill, while the virus quietly damages the liver. This silent chronic phase is the dangerous one, because by the time symptoms of cirrhosis appear the damage is far advanced.

The crucial public-health point is prevention. There is an effective **vaccine against hepatitis B** (which also protects against D), and one against hepatitis A, while clean water and safe injection practice prevent the others. For a pharmacist, hepatitis matters twice over: as a disease to help prevent through vaccination, and as a reason for caution, since a damaged liver breaks down drugs poorly and ordinary doses can become harmful, the first-pass point from Chapter 4 turned into a warning.

5.6 Typhoid

Typhoid fever, also called enteric fever, is a serious infection caused by the bacterium **Salmonella Typhi**. Like hepatitis A, it spreads by the **faecal-oral route**, through food and water contaminated with the faeces of an infected person, so it too is a disease of poor sanitation and unsafe water, and it remains common in many parts of the world including India.

After the bacteria are swallowed, they survive the stomach, invade the wall of the small intestine, and spread through the body in the blood, which is why typhoid is a whole-body illness and not merely a gut upset. The illness builds up over a week or more, and its hallmark is a **stepwise rising fever** that climbs higher each day, together with headache, weakness, abdominal pain, and often constipation early followed by diarrhoea. A faint rash of pink spots, called rose spots, may appear on the trunk, and the spleen and liver may enlarge. The dangerous complication is in the gut itself: the infected patches of the intestinal wall can ulcerate and, in severe cases, bleed or perforate, which is life-threatening.

A particular danger is the symptomless carrier: some people recover from the illness but continue to harbour the bacteria in the gallbladder and shed them in their faeces for months or years, silently infecting others if they handle food. This is why food handlers who have had typhoid are followed up carefully.

Typhoid is diagnosed by growing the bacterium from a blood sample and is treated with **antibiotics**, though resistance to common antibiotics is a growing problem that a pharmacist should be aware of, since strains resistant to several drugs now circulate and make the choice of antibiotic harder. As with the faecal-oral hepatitis viruses, prevention rests on clean water, safe food and good sanitation, and a **vaccine** is available for those at risk. The recurring

lesson across typhoid and hepatitis A and E is plain: the faecal-oral diseases are diseases of sanitation, and clean water prevents them all.

5.7 Alcoholic and non-alcoholic fatty liver disease

The last two conditions are best taken together, because they are the same kind of damage from two different causes. In both, fat builds up inside the liver cells, a state called **fatty liver (steatosis)**, and in both, that fatty liver can progress through inflammation to scarring if the cause continues. The difference is in the trigger.

Alcoholic liver disease is caused by drinking too much alcohol over a long time. The liver, which breaks down most of the alcohol a person drinks (the detoxifying role from Chapter 4), is damaged by the by-products of that breakdown. The damage runs through a recognised sequence. First comes **fatty liver**, the build-up of fat in the liver cells, which is reversible if the person stops drinking. If drinking continues it can progress to **alcoholic hepatitis**, an inflammation of the liver, and finally to **cirrhosis**, in which the liver is permanently scarred, hard and shrunken, and large parts of it no longer work. Cirrhosis is the dangerous end point: a scarred liver cannot do its many jobs, so it fails to process bilirubin (causing jaundice), fails to make blood proteins, and lets toxins build up, and the scarring obstructs the blood flowing through the liver.

Non-alcoholic fatty liver disease (NAFLD) is the same fat build-up and the same possible progression, but in people who drink little or no alcohol. Its causes are the conditions of the modern metabolic syndrome: obesity, type 2 diabetes, high blood fats and a sedentary life. It has become very common as these conditions have spread, and it runs a similar course, from simple fatty liver, through an inflamed form (non-alcoholic steatohepatitis), to cirrhosis in some people. Because it usually causes few symptoms until late, it is often found by chance on a blood test or scan.

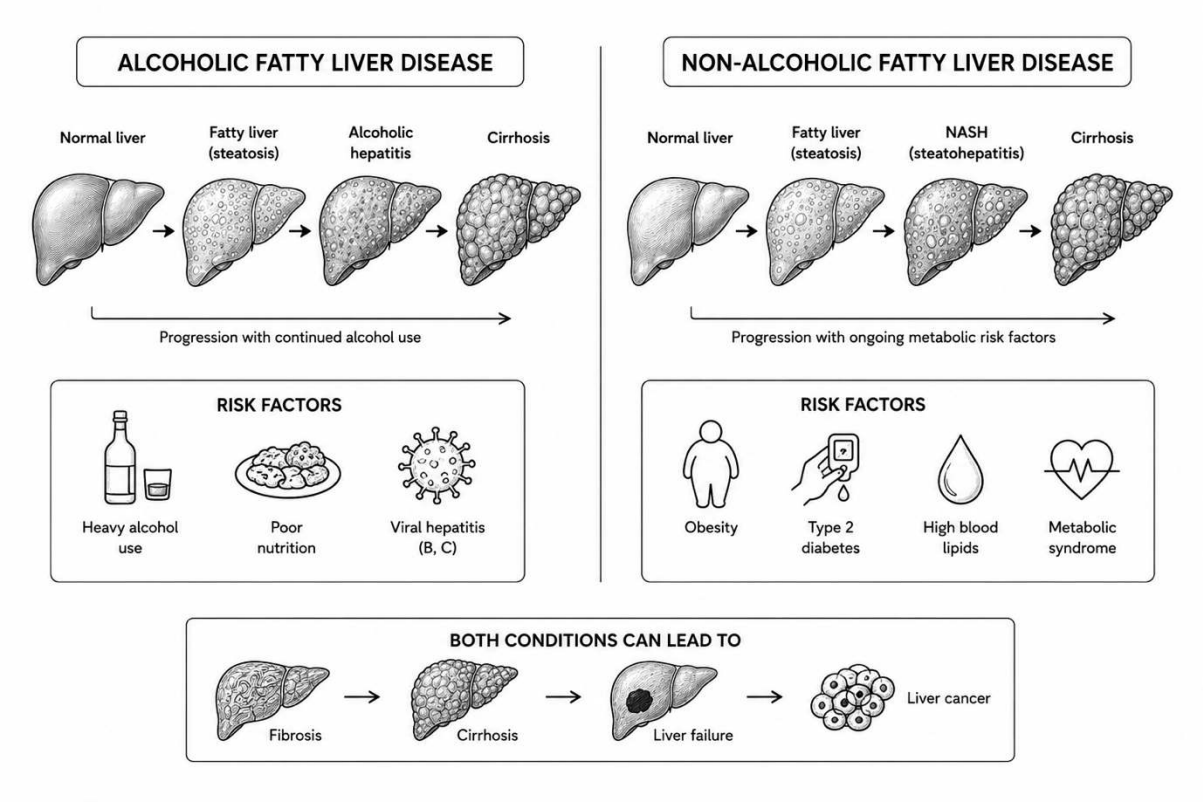


Figure 5.3 Alcoholic and Non-alcoholic fatty liver disease

It is worth pausing on why cirrhosis is so serious, because it is the common end point of several diseases in this chapter. A cirrhotic liver is scarred and hard, and the scarring does two kinds of harm. It destroys working liver tissue, so the liver fails at its jobs: jaundice appears as bilirubin is not cleared, bruising and bleeding follow as clotting proteins are not made, fluid collects in the abdomen as blood proteins fall, and toxins build up and affect the brain. And the scarring physically obstructs the blood trying to flow through the liver from the gut, the portal blood from Chapter 4, so pressure rises behind the block and the blood is forced through swollen veins that can rupture and bleed. So cirrhosis is both a failure of function and a blockage of flow, and it can lead on to liver cancer. Once established it cannot be undone, which is the whole reason the earlier, reversible stages matter so much.

The treatment of both turns on removing the cause. For alcoholic liver disease that means stopping alcohol, which can reverse the early fatty stage. For non-alcoholic fatty liver disease it means treating the underlying problems: losing weight, controlling diabetes and blood fats, and exercising. The shared lesson is that the early, fatty stage of both diseases is reversible, and the damage becomes permanent only if the cause is allowed to continue, which is why early recognition and a change of habits matter so much.

5.8 Chapter summary

The diseases of the gastrointestinal system are the healthy mechanisms of Chapter 4 failing. Inflammatory bowel disease is a chronic, immune-driven inflammation of the gut in two forms: ulcerative colitis, which is continuous, shallow and confined to the colon and rectum with bloody diarrhoea, and Crohn's disease, which is patchy, deep and able to affect any part of the gut from mouth to anus, with a tendency to strictures and fistulae. A peptic ulcer is a break in the acid-exposed lining of the stomach or duodenum, best understood as an imbalance between the aggressive factors (acid and pepsin) and the defensive factors (mucus, bicarbonate, blood flow and repair); its main causes, Helicobacter pylori infection and NSAID use, both weaken the defence, and treatment lowers acid with proton-pump inhibitors and clears the bacterium with antibiotics.

Jaundice is a yellowing of the skin and eyes from a build-up of bilirubin, classified by where the pathway fails: pre-hepatic (too much bilirubin made by excess red-cell breakdown), hepatic (liver cells damaged), and post-hepatic (bile drainage blocked, with pale stools and dark urine). Hepatitis is inflammation of the liver, most importantly viral; hepatitis A and E spread by the faecal-oral route and cause an acute, self-limiting illness, while hepatitis B, C and D spread through blood and body fluids and can become chronic, leading to cirrhosis and liver cancer, with vaccines available against A and B. Typhoid fever is a faecal-oral infection by Salmonella Typhi that spreads through the body, causing a stepwise fever and the danger of intestinal perforation, treated with antibiotics and prevented by sanitation and vaccine. Finally, alcoholic and non-alcoholic fatty liver disease are the same progression, fatty liver to inflammation to cirrhosis, from two causes, chronic alcohol and the metabolic syndrome, with the early fatty stage reversible if the cause is removed. Across the unit the message holds: name the broken part of the healthy system, and the disease, its signs and its treatment fall into place. Several of these diseases also share a single preventable thread, clean water and safe food, while others share a single treatable thread, the early reversible stage. Unit III now turns to the systems that bring in oxygen and clear the blood, the respiratory and urinary systems.

5.9 Self-assessment

A. Multiple-choice questions

1. Ulcerative colitis differs from Crohn's disease in that it:
   (a) affects the whole gut (b) is patchy with skip lesions (c) is limited to the colon and rectum (d) goes through the full wall thickness. Answer: (c).
2. The bacterium responsible for most peptic ulcers is:

(a) Salmonella Typhi (b) Helicobacter pylori (c) Escherichia coli (d) Mycobacterium. Answer: (b).

3. Pale stools and dark urine are typical of:
   (a) pre-hepatic jaundice (b) hepatic jaundice (c) post-hepatic (obstructive) jaundice
   (b) haemolytic jaundice. Answer: (c).
4. Which hepatitis viruses spread mainly by the faecal-oral route?
   (a) B and C (b) A and E (c) B and D (d) C and D. Answer: (b).
5. Typhoid fever is caused by:
   (a) a virus (b) Salmonella Typhi (c) Helicobacter pylori (d) a parasite. Answer: (b).
6. The reversible early stage common to both alcoholic and non-alcoholic liver disease is:
   (a) cirrhosis (b) fatty liver (c) liver cancer (d) hepatitis B. Answer: (b).
7. A peptic ulcer is best described as an imbalance between:
   (a) bile and acid (b) aggressive and defensive factors (c) trypsin and amylase (d) flora and acid. Answer: (b).
8. The pigment that builds up in the blood in jaundice is:
   (a) melanin (b) haemoglobin (c) bilirubin (d) bile salt. Answer: (c).

B. Short-answer questions (2–5 marks)

1. Differentiate between ulcerative colitis and Crohn's disease. Ulcerative colitis is limited to the colon and rectum, causes continuous and shallow inflammation of the mucosa only, and presents with bloody diarrhoea. Crohn's disease can affect any part of the gut from mouth to anus, causes patchy (skip lesion) inflammation through the full thickness of the wall, and tends to cause strictures and fistulae, with pain, diarrhoea and weight loss. *(High-yield.)*

2. Explain the pathophysiology of peptic ulcer as a balance of factors. A peptic ulcer forms when the aggressive factors attacking the lining (gastric acid and pepsin) outweigh the defensive factors protecting it (the mucus and bicarbonate barrier, blood flow and cell repair). The main causes, Helicobacter pylori infection and NSAID use, both weaken the defence, so acid and pepsin reach and digest the wall, producing the ulcer.

3. Classify jaundice into its three types with one cause of each. Pre-hepatic (haemolytic) jaundice results from excessive breakdown of red blood cells producing more bilirubin than the liver can handle, as in malaria. Hepatic jaundice results from damage to the liver cells, as in hepatitis. Post-hepatic (obstructive) jaundice results from blocked bile drainage, as from a gallstone. *(High-yield.)*

4. How do the faecal-oral and blood-borne hepatitis viruses differ in spread and outcome? The faecal-oral viruses (hepatitis A and E) spread through contaminated food and water and cause an acute, usually self-limiting illness that does not become chronic. The blood-borne viruses (hepatitis B, C and D) spread through blood and body fluids and can become chronic, leading over years to cirrhosis and liver cancer.

5. Describe the cause, key feature and main danger of typhoid fever. Typhoid fever is caused by Salmonella Typhi, spread by the faecal-oral route. Its key feature is a stepwise rising fever with headache, abdominal pain and sometimes rose spots, because the bacteria spread through the body. Its main danger is ulceration of the intestinal wall, which can bleed or perforate.

6. Why is the early stage of fatty liver disease important to recognise? Because the early fatty liver stage, in both alcoholic and non-alcoholic disease, is reversible if the cause is removed by stopping alcohol or treating obesity and diabetes. If the cause continues, it can progress through inflammation to irreversible cirrhosis, so early recognition allows the damage to be stopped.

C. Long-answer questions (10 marks)

1. Discuss the causes, pathophysiology, clinical features and treatment of peptic ulcer. A full answer defines a peptic ulcer; explains the imbalance between aggressive factors (acid, pepsin) and defensive factors (mucus, bicarbonate, blood flow, repair); details the two main causes, Helicobacter pylori and NSAIDs, and how each weakens defence; describes the burning upper abdominal pain and its relation to meals, and the dangers of bleeding and perforation; and explains treatment by acid suppression with proton-pump inhibitors, antibiotics for Helicobacter pylori, and stopping NSAIDs. A diagram of the aggressive-defensive balance (Figure 5.1) should be included. *(High-yield.)*

2. Classify jaundice and explain the three types in detail. A full answer defines jaundice as yellowing from raised bilirubin; recalls the normal handling of bilirubin by the liver; and explains pre-hepatic jaundice (excess red-cell breakdown overwhelming the liver), hepatic jaundice (damaged liver cells unable to process bilirubin), and post-hepatic jaundice (blocked bile drainage, with pale stools and dark urine), giving a cause for each.

3. Write notes on viral hepatitis and typhoid fever. For viral hepatitis: the five viruses, the faecal-oral group (A and E, acute, self-limiting) versus the blood-borne group (B, C and D, can be chronic, leading to cirrhosis and cancer), the features of an acute attack, and prevention by vaccine and clean water. For typhoid: cause by Salmonella Typhi, faecal-oral

spread, stepwise fever and systemic illness, the danger of intestinal perforation, treatment with antibiotics and prevention by sanitation and vaccine.

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Chapter 6: The Respiratory System: Anatomy, Physiology and Pathophysiology

Learning outcomes

After working through this chapter the student will be able to:

1. Describe the anatomy of the respiratory tract, with special reference to the lungs.
2. Explain the mechanism of breathing and how respiration is regulated.
3. Define the lung volumes and capacities and state their approximate values.
4. Describe how oxygen and carbon dioxide are carried in the blood.
5. Outline the methods of artificial respiration and resuscitation.
6. Explain the pathophysiology of asthma, chronic obstructive pulmonary disease and tuberculosis.

6.1 The body cannot hold its breath

Every cell in the body burns fuel with oxygen and makes carbon dioxide as waste. The body stores plenty of fuel but almost no oxygen, and carbon dioxide is a fast-acting acid that cannot be allowed to build up. So the supply of oxygen and the removal of carbon dioxide must go on without pause, minute by minute, for a lifetime. That is the job of the respiratory system: to bring air to a surface thin enough for oxygen to cross into the blood and carbon dioxide to cross out, and to move air in and out so the surface is always fresh. Stop it for a few minutes and the brain, the most oxygen-hungry organ from Chapter 2, begins to die.

This chapter follows that job in order. First the airway and the lungs, built to carry air down to a vast, thin gas-exchange surface. Then the mechanism that pumps air in and out, and the control that sets its rate. Then the measurement of how much air the lungs move, the carriage of the two gases in the blood, and the emergency methods used when breathing fails. Finally the three diseases the syllabus names, each of which attacks the system at a different point. For a pharmacy student the lungs matter twice: as the site of common diseases treated by inhaled drugs, and as a route by which some drugs and gases enter the body.

6.2 Anatomy of the respiratory system

The respiratory tract is usually divided into an upper and a lower part, and air passes through them in order on its way to the lungs. It is also useful to split the tract by function into a **conducting zone**, the tubes that only carry air, and a **respiratory zone**, the tiny sacs where gas exchange actually happens. Figure 6.1 shows the tract.

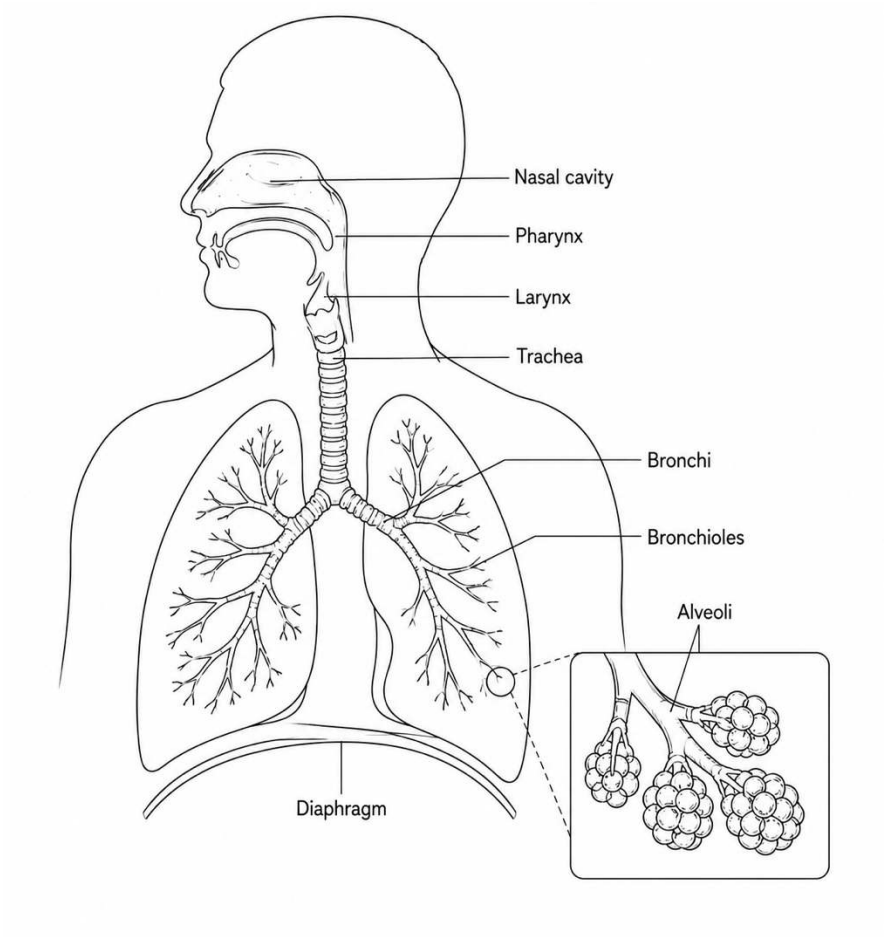


Figure 6.1 *The respiratory tract.*

Air enters through the **nose**, where it is warmed, moistened and filtered of dust by hairs and a sticky mucus lining, so it reaches the lungs clean and at body temperature. This conditioning of the air is the reason nose-breathing is healthier than mouth-breathing: the nose does a job the mouth cannot, delivering air that is warm, damp and clean so the delicate alveoli are not chilled, dried or dirtied. It passes through the **pharynx** (the throat, shared with the digestive tract) and then the **larynx** (the voice box, which also holds the epiglottis that guards the airway during swallowing, met in Chapter 4, and the vocal cords that vibrate to make the voice as air passes over them). From the larynx air enters the **trachea** (the windpipe), a tube held permanently open by C-shaped rings of cartilage so it cannot collapse.

The trachea divides into two **bronchi**, one to each lung, and each bronchus branches again and again into smaller and smaller **bronchioles**, like the branches of an upturned tree. This branching is the conducting zone: it carries air but does not exchange gas. The smallest bronchioles finally open into clusters of tiny air sacs called **alveoli**, and these are the respiratory zone, where the real work is done.

The conducting airways do more than carry air; they clean it. Their lining is covered with a sheet of sticky mucus and with millions of tiny beating hairs called cilia. Dust, smoke particles and bacteria stick to the mucus, and the cilia beat in waves to sweep the dirty mucus steadily up toward the throat, where it is swallowed or coughed out. This **mucociliary escalator** is a constant self-cleaning system, and it matters to disease: cigarette smoke paralyses and destroys the cilia, so the cleaning fails, mucus and dirt collect, and infection follows, which is part of why smokers suffer the chronic cough and infections of COPD later in the chapter.

Special reference to the lungs

The **lungs** are two cone-shaped organs that fill most of the chest, the right with three lobes and the left with two (the left is smaller to make room for the heart). Their substance is mostly air sacs and blood vessels, which makes them light and spongy. Each lung is wrapped in a double membrane, the **pleura**, with a thin film of fluid between its two layers; this fluid lets the lungs slide smoothly against the chest wall as they expand and holds the lungs against the wall so they follow its movements.

The genius of the lung is in the **alveoli**, and they are worth dwelling on because they are where structure serves function most clearly in this chapter. There are hundreds of millions of them, giving a total gas-exchange surface of around seventy square metres, the size of a small room folded into the chest. Each alveolus has an extremely thin wall, just one cell thick, and is wrapped in a dense net of capillaries whose walls are also one cell thick. So oxygen crossing from air to blood has only two thin cell layers to pass, and the distance is tiny. A vast surface and a tiny diffusion distance are exactly what fast gas exchange needs, and that is what the alveoli provide. Anything that thickens this wall or destroys these sacs, as the diseases later in the chapter do, cripples gas exchange.

How gas exchange actually happens

The exchange of gases at the alveolus is pure **diffusion**, the movement of a gas from where it is plentiful to where it is scarce, and no energy is spent on it. Air in the alveolus is rich in oxygen and poor in carbon dioxide; the blood arriving in the capillaries is the opposite, poor in oxygen and rich in carbon dioxide after its trip round the body. So oxygen diffuses from the alveolar air into the blood and carbon dioxide diffuses from the blood into the alveolar air, each moving down its own gradient, until the blood leaving the lung is loaded with oxygen and stripped of carbon dioxide. The same diffusion happens in reverse at the tissues, where the cells are poor in oxygen and rich in carbon dioxide. This is why the thin wall and the large surface matter so much: diffusion is fast only over a short distance and a wide area, and the alveolus is built to give both. It is also why a fluid-filled or thickened alveolar wall,

as in pneumonia or the diseases below, slows the exchange and leaves the blood short of oxygen.

The pleura and why the lungs follow the chest

The double-layered pleura deserves a closer look, because the thin film of fluid between its layers does something subtle and vital. The fluid holds the two layers together the way a film of water holds two glass slides together, easy to slide but hard to pull apart. Through this bond the lung is held against the chest wall and forced to follow its every movement, which is what lets the muscles of the chest expand the lungs at all. If air or fluid gets between the pleural layers and breaks the bond, a condition called pneumothorax, the lung springs back and collapses, and it can no longer be expanded by the chest. This shows, by its failure, why the pleural seal is what makes breathing possible.

6.3 The mechanism of respiration

Breathing moves air in and out of the lungs, and it works by a simple physical rule: air flows from high pressure to low pressure, so to pull air in, the lungs must be made into a low-pressure space, and to push it out, a high-pressure one. The lungs cannot do this themselves, because they have no muscle of their own; they are moved by the muscles around them, chiefly the **diaphragm**, the dome-shaped sheet of muscle below the lungs, and the **intercostal muscles** between the ribs. Figure 6.2 sets out the cycle.

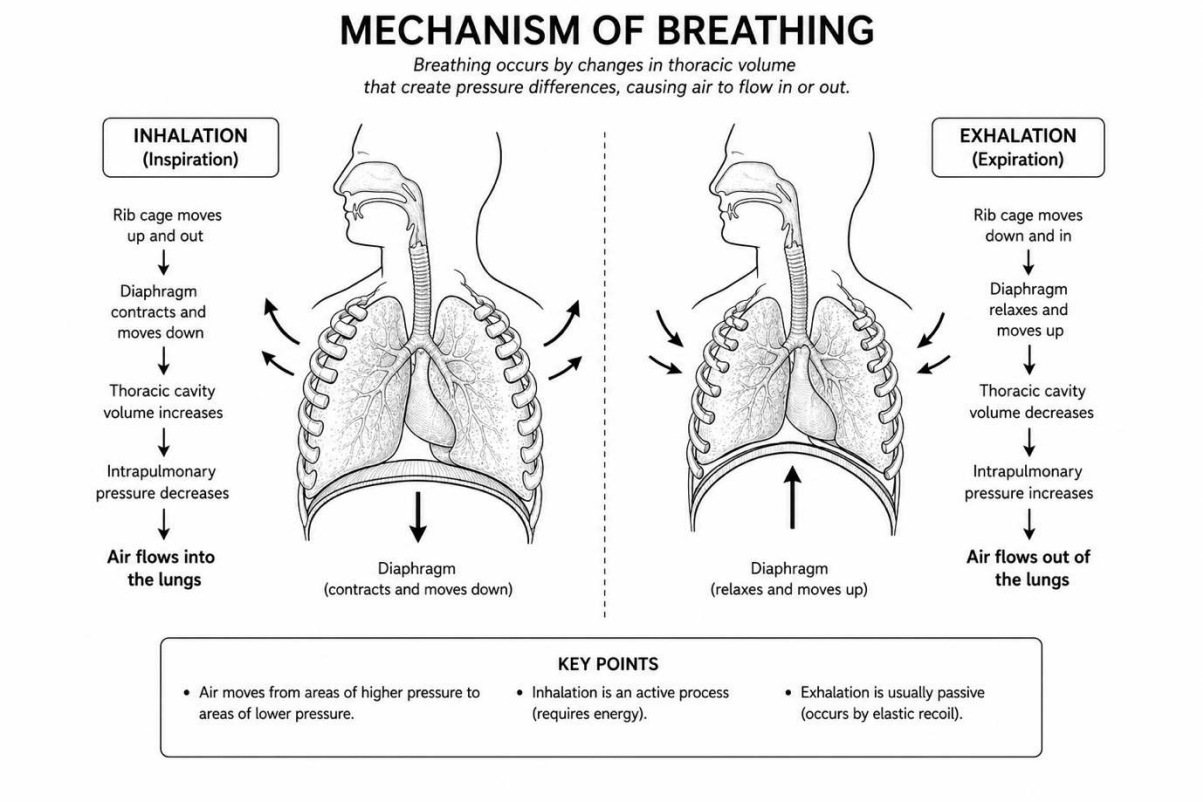


Figure 6.2 *The mechanism of breathing.*

Inspiration (breathing in) is the active phase. The diaphragm contracts and flattens downward, and the external intercostal muscles pull the ribs up and out. Both movements enlarge the chest, and because the lungs are held against the chest wall by the pleura, the lungs enlarge with it. As the lung space grows, the pressure inside it falls below the pressure of the outside air, and air flows in down the pressure difference until the lungs are filled. The key idea is that the chest expands first and the air follows; the lungs do not suck, they are opened.

Expiration (breathing out) at rest is the passive phase. The diaphragm and intercostal muscles simply relax, the chest springs back to its smaller size by its own elasticity, the lung space shrinks, the pressure inside rises above the outside air, and air flows out. Because it relies on elastic recoil rather than muscle work, quiet breathing out costs almost no energy. Only during forceful breathing, as in exercise or disease, do other muscles push the air out actively. This contrast, active in and passive out, is a favourite exam point, and it explains why diseases that destroy the lung's elasticity make breathing out the hard part.

6.4 Regulation of respiration

Breathing must match the body's needs, speeding up during exercise and slowing during rest, and it must do so without conscious thought, since no one could remember to breathe while

asleep. The control sits in the brain stem from Chapter 2. The **respiratory centre**, mainly in the **medulla oblongata** with help from the pons, sets the basic rhythm by sending regular bursts of nerve signals to the breathing muscles, around twelve to sixteen breaths a minute at rest.

What adjusts this rhythm is mostly the level of **carbon dioxide** in the blood, and this is the single most important point in the section. Special sensors called **chemoreceptors**, in the brain stem and in the great arteries, constantly monitor the blood. A rise in carbon dioxide (which makes the blood more acidic) is detected at once and drives the respiratory centre to make breathing deeper and faster, blowing off the excess carbon dioxide and bringing the level back down. A fall in carbon dioxide slows breathing. So it is carbon dioxide, not oxygen, that is the main minute-to-minute driver of breathing, which surprises students but makes sense: carbon dioxide is the fast-rising acid that must be controlled tightly. Oxygen acts as a backup driver, taking over only when its level falls dangerously low. This is the homeostasis throughline again, holding the blood gases and pH steady through a feedback loop.

A few other controls fine-tune the basic rhythm. Breathing is partly under voluntary control, so a person can deliberately hold their breath or breathe faster, though only up to a point: hold your breath and the rising carbon dioxide eventually forces a breath whether you will it or not, which is why a child cannot harm themselves by breath-holding. Stretch sensors in the lungs guard against over-inflation, sending signals that end a breath before the lungs are stretched too far. And protective reflexes such as coughing and sneezing, driven from the brain stem, clear the airway of irritants. The carbon-dioxide point has one important clinical twist worth flagging for later study: in a few patients with severe long-standing lung disease, the body comes to rely on the low-oxygen backup drive instead of carbon dioxide, so giving them too much oxygen carelessly can actually slow their breathing. The detail belongs to pharmacology, but it shows why the control of breathing is not an abstract topic.

The same mechanism explains why certain diseases make breathing harder in opposite ways. When the lungs become stiff or scarred, they are hard to expand, so breathing in takes more effort; when the lungs lose their elastic recoil or the airways are obstructed, the problem is breathing out, because the passive recoil that should empty them is gone or the air is trapped. Holding on to which phase fails, the in or the out, is the quickest way to tell the two great families of lung disease apart, and it is exactly the distinction the diseases in section 6.8 turn on.

> **Quick-recall box 6.1: Breathing in brief** Inspiration is active: diaphragm and external intercostals contract, chest enlarges, lung pressure falls, air flows in.

Expiration at rest is passive: muscles relax, chest recoils, air flows out. The respiratory centre in the medulla sets the rhythm, and rising blood carbon dioxide (sensed by chemoreceptors) is the main driver of faster, deeper breathing.

6.5 Lung volumes and capacities

To measure how well the lungs work, the air they move is divided into named **volumes**, and combinations of these volumes are called **capacities**. They are measured with an instrument called a spirometer, which records the volume of air breathed in and out as the spirogram in Figure 6.3. The standard values below are typical for a healthy young adult and vary with body size, sex and age, so they are learnt as approximate figures.

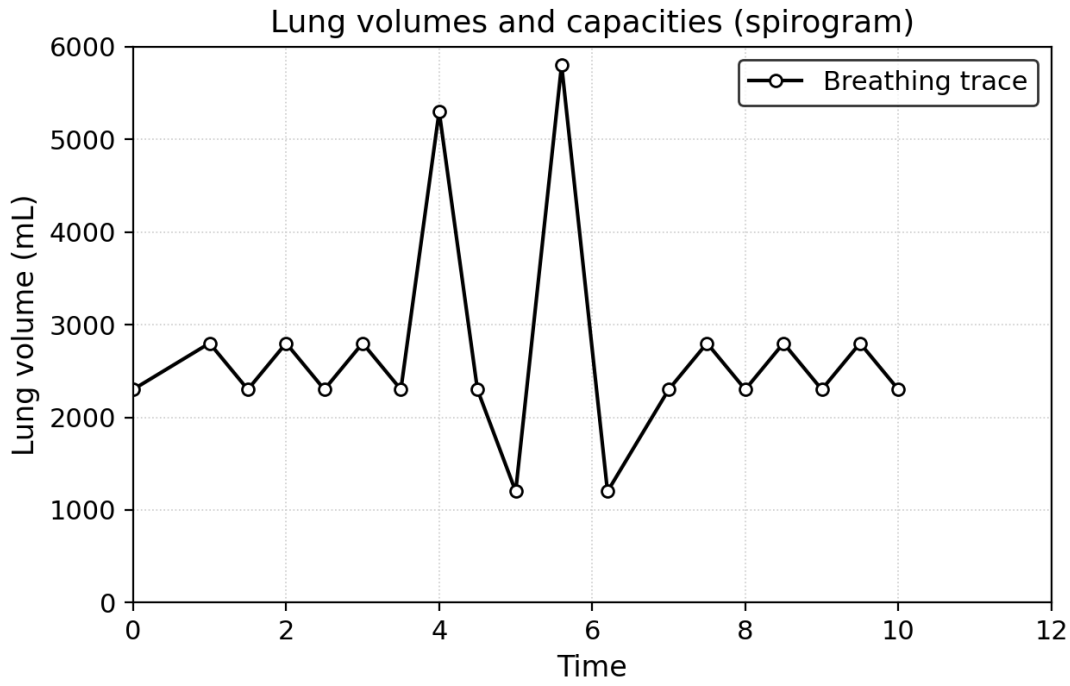


Figure 6.3 *Lung volumes and capacities (spirogram).*

The distinction between a volume and a capacity is simply that a volume is one basic measured amount, while a capacity is two or more volumes added together. Keeping that rule in mind makes the list far easier to learn, because the capacities are then just sums you can work out rather than separate facts to memorise.

The four volumes are:

- **Tidal volume (TV)**, the air moved in or out in one quiet breath, about 500 mL.
- **Inspiratory reserve volume (IRV)**, the extra air that can be breathed in forcefully on top of a tidal breath, about 3000 mL.

- **Expiratory reserve volume (ERV)**, the extra air that can be forced out after a normal breath out, about 1100 mL.
- **Residual volume (RV)**, the air that always stays in the lungs and cannot be breathed out, about 1200 mL, which keeps the alveoli from collapsing.

The capacities are sums of these volumes, and three matter most:

- **Vital capacity (VC)**, the largest volume that can be moved in one breath, from a full breath in to a full breath out. It is TV + IRV + ERV, about 4600 mL, and is a key measure of lung health.
- **Total lung capacity (TLC)**, all the air the lungs can hold, VC + RV, about 5800 mL.
- **Functional residual capacity (FRC)**, the air left after a quiet breath out, ERV + RV, about 2300 mL.

A worked relationship makes these stick. If a person has a tidal volume of 500 mL, an inspiratory reserve of 3000 mL and an expiratory reserve of 1100 mL, their vital capacity is 500 + 3000 + 1100 = 4600 mL. Add the residual volume of 1200 mL and the total lung capacity is 4600 + 1200 = 5800 mL. These sums are exactly the kind of calculation an exam asks, so practise adding the volumes rather than memorising the capacities alone. The clinical value is that diseases change these numbers in tell-tale ways: vital capacity falls when the lungs are stiff or scarred, and the air trapped in the lungs (residual volume) rises when airways are obstructed, as in the diseases below.

6.6 Transport of respiratory gases

Once oxygen has crossed into the blood at the alveoli, it must be carried to the tissues, and carbon dioxide must be carried back. The two gases travel in quite different ways.

Oxygen is carried almost entirely bound to **haemoglobin**, the red pigment in red blood cells, as a loose compound called oxyhaemoglobin. Only a tiny amount dissolves in the plasma, because oxygen does not dissolve well in water; haemoglobin is what lets blood carry enough. The binding is reversible and depends on the oxygen level: where oxygen is plentiful, as in the lungs, haemoglobin picks it up and becomes nearly fully loaded; where oxygen is scarce, as in the working tissues, haemoglobin releases it. This relationship, plotted as the **oxygen dissociation curve** in Figure 6.4, has a characteristic S-shape, and its shape is clever: it is flat at the top, so haemoglobin stays well loaded even if lung oxygen drops a little, and steep in the middle, so a small fall in tissue oxygen unloads a lot where it is needed. Conditions in active tissue, more carbon dioxide, more acid and more warmth, shift the curve so that haemoglobin gives up still more oxygen exactly where activity is greatest. This shift, driven mainly by the rise in carbon dioxide and acid, is a neat piece of automatic matching:

the hardest-working tissues, which make the most carbon dioxide, are the ones to which haemoglobin surrenders the most oxygen.

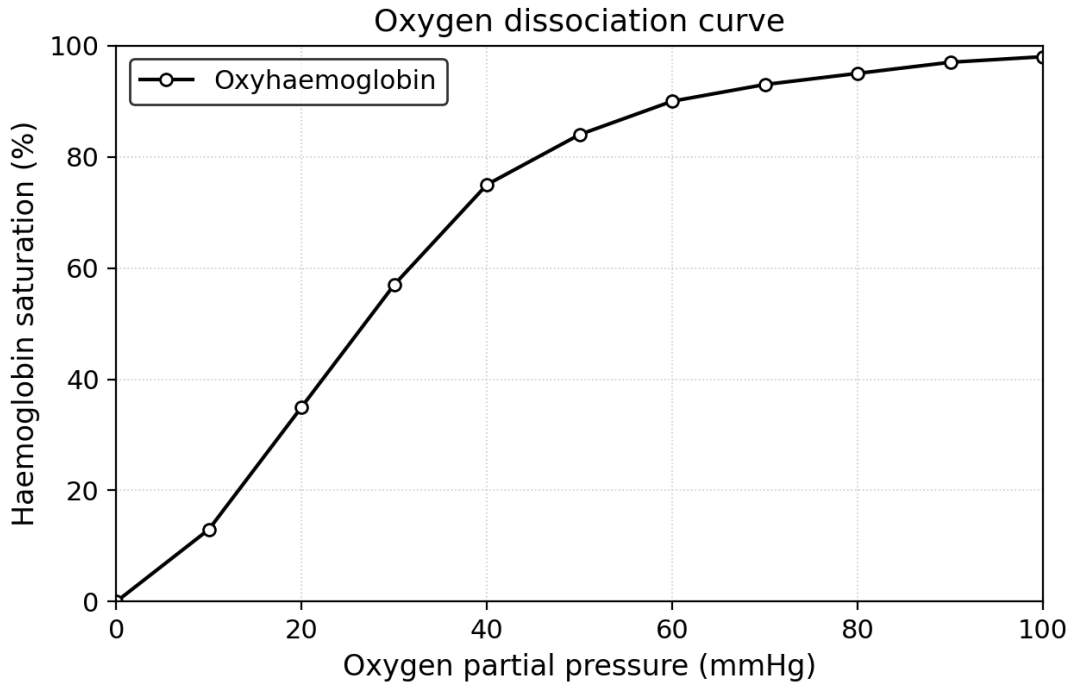


Figure 6.4 *The oxygen dissociation curve.*

The reliance on haemoglobin also explains a deadly poison. Carbon monoxide, the gas in smoke and faulty heaters, binds to haemoglobin far more tightly than oxygen does and in the same place, so it takes the seats meant for oxygen and will not let go. A person breathing carbon monoxide can have plenty of air yet starve of oxygen, because the haemoglobin is blocked, and they may not feel short of breath because the carbon dioxide that drives breathing is still being cleared. This is why carbon monoxide poisoning is so dangerous and so easily missed, and it is a direct consequence of how oxygen is carried.

Carbon dioxide is carried three ways at once. Most of it (around seventy percent) travels as **bicarbonate** dissolved in the plasma, formed when carbon dioxide reacts with water in the red cells and is released back to gas in the lungs. Some is carried bound to haemoglobin (as carbaminohaemoglobin), and a smaller part is simply dissolved in the plasma. The bicarbonate route matters beyond the lung, because it links breathing to the body’s acid balance: carbon dioxide is an acid in the blood, so breathing it off helps control blood pH, a connection picked up in the urinary chapter where the kidney handles the same balance from the other side.

6.7 Artificial respiration and resuscitation

When breathing stops, whether from drowning, electric shock, drug overdose or cardiac arrest, the body's oxygen runs out within minutes and the brain is damaged soon after. **Artificial respiration** is any method of forcing air in and out of the lungs of a person who cannot breathe, to keep oxygen reaching the blood until normal breathing returns or help arrives. The simplest is **mouth-to-mouth (rescue) breathing**, in which the rescuer blows their own exhaled air, which still holds enough oxygen, into the patient's lungs, making the chest rise; the chest then falls on its own.

When the heart has also stopped, rescue breathing alone is not enough, because the blood is not circulating to carry the oxygen. Then **cardiopulmonary resuscitation (CPR)** is used, combining chest compressions, which pump blood by pressing rhythmically on the breastbone, with rescue breaths, so that oxygenated blood reaches the brain and heart. CPR buys time until a defibrillator or medical team can restart the heart properly, and the current advice for an untrained rescuer is to give chest compressions hard and fast in the centre of the chest, since keeping the blood moving is the most important thing. In hospital, a **mechanical ventilator** takes over breathing entirely, pushing measured volumes of an oxygen-rich mixture into the lungs through a tube, for patients who cannot breathe for themselves. Oxygen itself is also given by mask or nasal tube to patients who are breathing but short of oxygen, which a pharmacist will recognise as a medicine in its own right, prescribed, dosed and not without hazards. The shared principle of all these methods is the same physics as normal breathing from section 6.3: get fresh air to the alveoli and let gas exchange do the rest.

6.8 Pathophysiology of the respiratory system

The syllabus names three diseases, and they damage the system in three different ways. Asthma and chronic obstructive pulmonary disease are **obstructive** diseases, in which air flows out of the lungs poorly, while tuberculosis is an infection that destroys lung tissue. Table 6.1 contrasts the obstructive diseases, and the sections explain each.

Table 6.1: Asthma versus chronic obstructive pulmonary disease

Feature	Asthma	COPD
Obstruction	Reversible (comes and goes)	Largely irreversible (permanent)
Main cause	Allergy, airway hyper-reactivity	Long-term cigarette smoking
Typical age	Often begins in childhood	Older adults (smokers)
Mechanism	Muscle spasm, swelling, mucus	Chronic bronchitis + emphysema
Course	Attacks with normal periods between	Slow, progressive decline

Asthma

Asthma is a chronic inflammatory disease of the airways in which the bronchioles become narrowed in attacks, making it hard to breathe, especially to breathe out. Between attacks the airways may be near normal, which is why asthma is described as reversible airway obstruction. An attack has three parts that narrow the airway together, shown in Figure 6.5: the smooth muscle in the bronchiole walls tightens (bronchoconstriction), the inflamed lining swells, and extra mucus is produced that clogs the narrowed tube. The result is wheezing, coughing, chest tightness and breathlessness.

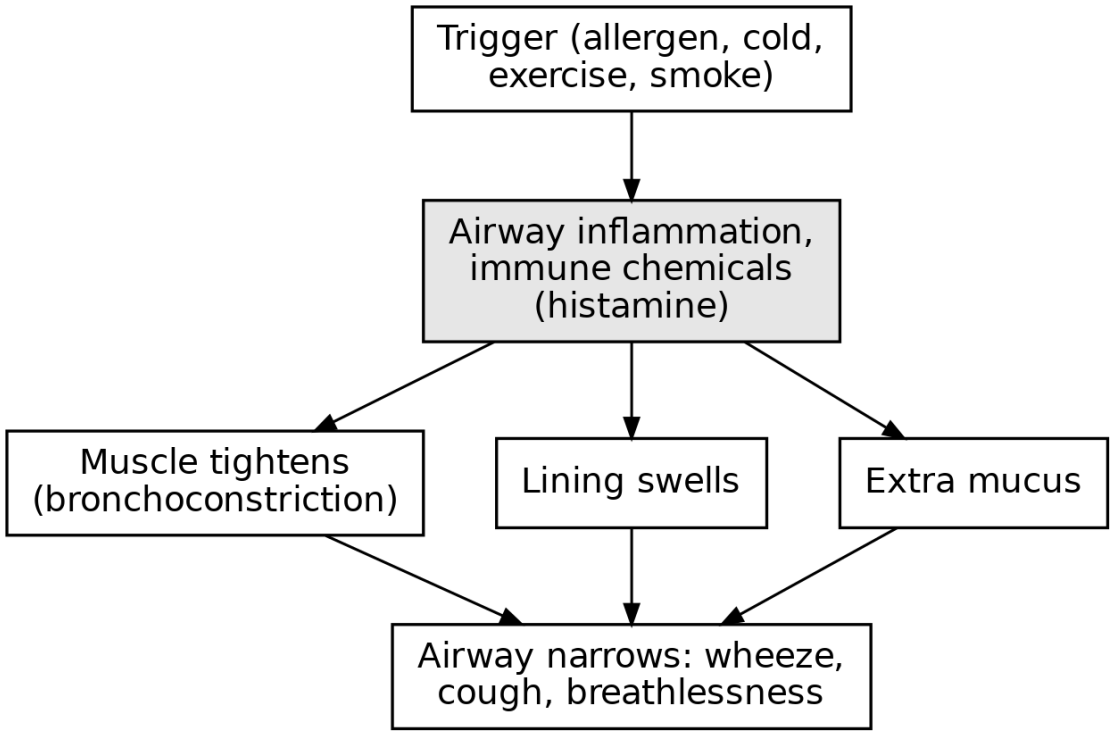


Figure 6.5 *Pathogenesis of an asthma attack.*

The underlying problem is an over-sensitive, inflamed airway that over-reacts to triggers such as allergens (pollen, dust mites), cold air, exercise, smoke or infection. In an allergic attack the immune system, primed against the trigger, releases inflammatory chemicals including histamine that drive the muscle to tighten and the lining to swell. Because so much of asthma is inflammation rather than simple spasm, modern treatment leans on controlling that inflammation for the long term rather than only relieving the spasm of each attack, which is the single biggest change in how asthma has come to be managed. Identifying and avoiding a patient's particular triggers, where possible, is as much a part of care as the medicines themselves. The treatment follows the two parts of the problem and is a model of inhaled therapy: drugs that relax the airway muscle and open it (bronchodilators, used to relieve an attack) and drugs that calm the underlying inflammation (inhaled steroids, used regularly to prevent attacks). Giving these by inhaler delivers them straight to the airway with little reaching the rest of the body, which a pharmacy student should recognise as the reason inhalers are the mainstay of asthma care.

A severe attack that does not respond to the usual reliever, called **status asthmaticus**, is a medical emergency in which the airways close so far that the person cannot move enough air, and it needs urgent hospital treatment with oxygen and strong drugs. It is the reason asthma, though usually controllable, must never be taken lightly. A useful counselling point a pharmacist gives patients is the difference between the two inhalers: the reliever opens the airway quickly during an attack, while the preventer must be used every day even when the

chest feels clear, because it works slowly on the underlying inflammation and not on the spasm. Patients who treat the preventer as an as-needed reliever stay poorly controlled, so explaining the difference is real, useful pharmacy.

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is a long-term, progressive disease in which air flow out of the lungs is permanently obstructed, and unlike asthma it is largely irreversible. Its overwhelming cause is long-term **cigarette smoking**, which is why it is mainly a disease of older smokers. It combines two overlapping conditions. In **chronic bronchitis**, the airways are chronically inflamed and clogged with mucus, giving a long-standing cough with sputum. In **emphysema**, the walls of the alveoli are destroyed, so the many small sacs merge into fewer large ones; this wrecks gas exchange by cutting the surface area, and it destroys the lung's elastic recoil, so the airways collapse on breathing out and air is trapped.

The patient suffers worsening breathlessness, a chronic cough and frequent chest infections, and because gas exchange fails, the blood oxygen falls and carbon dioxide rises in advanced disease. A serious late complication links this chapter back to the circulation. When large areas of lung are destroyed, the blood vessels in them are lost and the oxygen level falls, which makes the remaining lung vessels narrow and raises the pressure the right side of the heart must pump against. Over time the strain enlarges and weakens the right side of the heart, a condition called **cor pulmonale** (right heart failure from lung disease). It is a reminder that the lungs and the heart work as one system, and that a disease of one becomes a disease of the other.

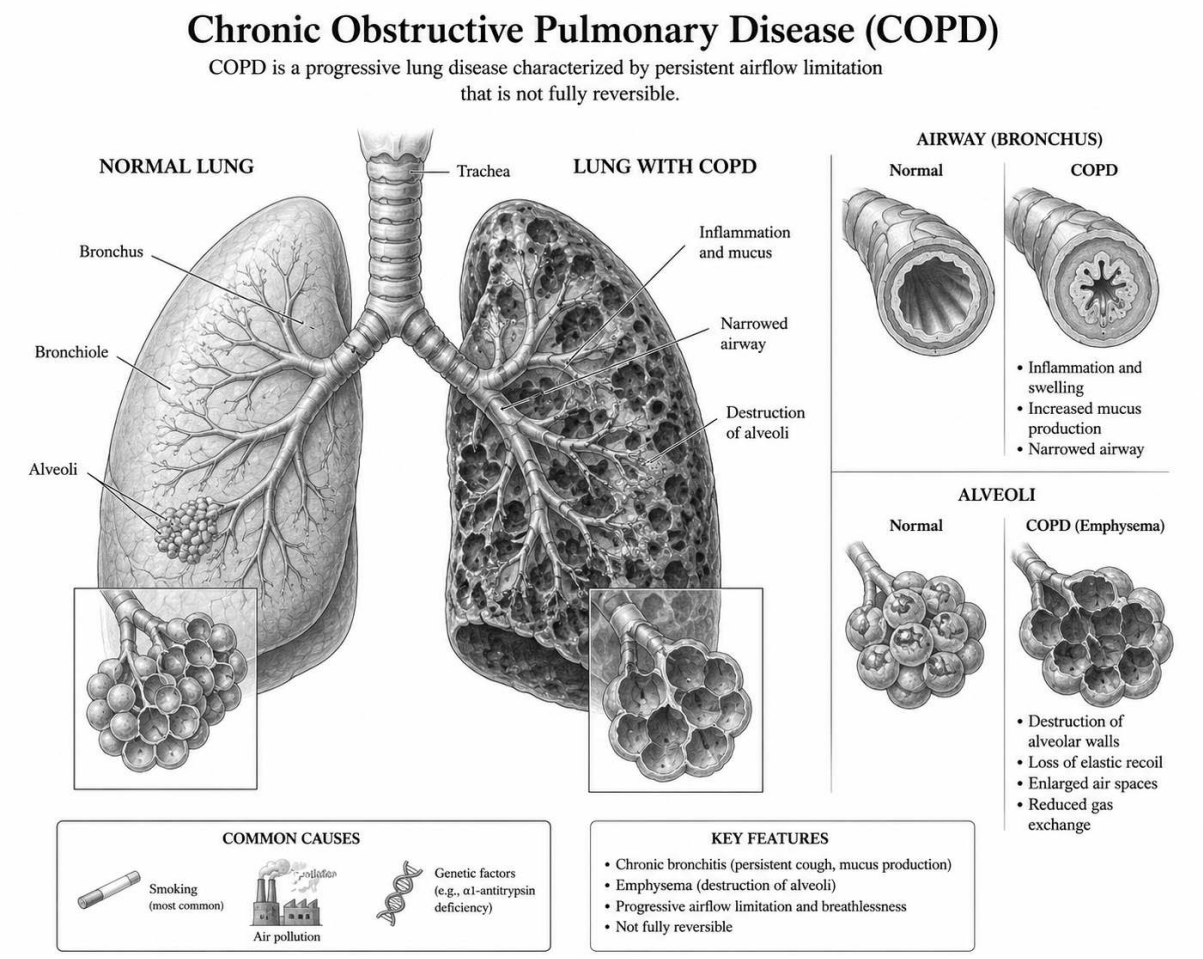


Figure 6.6 Chronic obstructive pulmonary disease

COPD cannot be cured, because the lung destruction is permanent, so treatment aims to relieve symptoms with bronchodilators, prevent and treat chest infections, give oxygen in advanced disease, and above all to stop smoking, which is the one measure that slows the decline. The contrast with asthma is the exam's favourite: asthma is reversible and often allergic; COPD is largely irreversible and usually caused by smoking.

Tuberculosis

Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*, which most often attacks the lungs, though it can affect almost any organ. It spreads through the air, in the tiny droplets coughed out by an infected person, which is why it spreads in crowded, poorly ventilated places and remains a major disease in many countries including India.

The course of TB is unusual and worth understanding. When the bacteria are first inhaled, the body's immune system usually walls them off inside small nodules in the lung, called tubercles, controlling but not always killing them. In many people the infection then stays

latent, shut away and causing no illness, sometimes for years. If the immune system later weakens, for example through malnutrition, HIV infection or old age, the walled-off bacteria can break out and multiply, causing **active TB**. Active disease in the lung gives a long-lasting cough (often with blood in the sputum), fever, night sweats and weight loss, and it slowly destroys lung tissue. Because the bacterium grows slowly and hides inside cells, TB must be treated with a combination of several antibiotics taken together for a long course, usually six months or more. Taking the full course is essential, since stopping early lets the hardier bacteria survive and breed drug-resistant strains, a serious and growing problem that makes TB much harder to treat. This is a point where a pharmacist's role in supporting patients to complete treatment directly affects public health.

Diagnosis and prevention round out the picture. Active lung TB is found by examining the sputum for the bacteria and by a chest X-ray showing the damaged areas, while a skin test can show whether a person has ever been exposed. Prevention rests on the **BCG vaccine**, given in many countries including India to protect children against severe forms of the disease, together with good ventilation, nutrition and the prompt treatment of infectious cases so they stop spreading the bacteria. Because TB so often takes hold when the immune system is weak, it is closely tied to HIV and AIDS, which is why it returns in Chapter 11; a person whose immune defences are failing is exactly the person in whom latent TB breaks out into active disease.

6.9 Chapter summary

The respiratory system supplies oxygen and removes carbon dioxide without pause. Air is warmed and cleaned in the nose, passes through the pharynx, larynx and trachea, and branches through the bronchi and bronchioles (the conducting zone) to reach the alveoli (the respiratory zone), where hundreds of millions of thin-walled sacs wrapped in capillaries give a huge surface and a tiny diffusion distance for gas exchange. Breathing in is active: the diaphragm and external intercostals contract, the chest and lungs enlarge, pressure falls and air flows in; breathing out at rest is passive elastic recoil. The respiratory centre in the medulla sets the rhythm, and rising blood carbon dioxide, sensed by chemoreceptors, is the main driver of faster, deeper breathing.

The air the lungs move is described by volumes (tidal 500 mL, inspiratory reserve 3000 mL, expiratory reserve 1100 mL, residual 1200 mL) and capacities (vital capacity about 4600 mL, total lung capacity about 5800 mL). Oxygen is carried bound to haemoglobin along an S-shaped dissociation curve that loads it in the lungs and unloads it in the tissues, while carbon dioxide travels mostly as bicarbonate, linking breathing to blood pH. When breathing fails, artificial respiration and CPR keep oxygenated blood reaching the brain until help arrives.

The three named diseases each strike differently: asthma is a reversible, often allergic narrowing of the airways by muscle spasm, swelling and mucus; COPD is a largely irreversible obstruction caused by smoking, combining chronic bronchitis and the alveolar destruction of emphysema; and tuberculosis is a slow bacterial infection that walls off and may later reactivate, treated only by a long, complete course of several antibiotics. Across all of it the same theme returns: a thin, wide surface, a steady pump and a tight feedback control, with disease following whenever one of the three is damaged. Chapter 7 turns to the partner system that also cleans the blood and controls its acid balance, working alongside the lungs from the other direction, the urinary system.

6.10 Self-assessment

A. Multiple-choice questions

1. The actual site of gas exchange in the lungs is the:
   (a) trachea (b) bronchioles (c) alveoli (d) larynx. Answer: (c).
2. During quiet inspiration, the diaphragm:
   (a) relaxes and rises (b) contracts and flattens (c) does not move (d) pushes air out. Answer: (b).
3. The main minute-to-minute driver of breathing is the blood level of:
   (a) oxygen (b) carbon dioxide (c) glucose (d) nitrogen. Answer: (b).
4. The volume of air moved in one quiet breath is the:
   (a) vital capacity (b) residual volume (c) tidal volume (d) total lung capacity. Answer: (c).
5. Most oxygen is carried in the blood:
   (a) dissolved in plasma (b) bound to haemoglobin (c) as bicarbonate (d) as carbonic acid. Answer: (b).
6. Most carbon dioxide is carried in the blood as:
   (a) bicarbonate (b) oxyhaemoglobin (c) dissolved gas only (d) carbon monoxide. Answer: (a).
7. The disease in which alveolar walls are destroyed and the lung loses its elastic recoil is:
   (a) asthma (b) emphysema (c) tuberculosis (d) bronchitis. Answer: (b).
8. Tuberculosis is caused by:
   (a) a virus (b) Mycobacterium tuberculosis (c) Helicobacter pylori (d) an allergen. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Explain the mechanism of inspiration. Inspiration is active. The diaphragm contracts and flattens downward while the external intercostal muscles pull the ribs up and out, enlarging the chest. Because the lungs are held to the chest wall by the pleura, they enlarge too; the pressure inside the lungs falls below atmospheric pressure, and air flows in until the lungs are filled. *(High-yield.)*

2. Why is carbon dioxide, rather than oxygen, the main driver of breathing? Chemoreceptors in the brain stem and arteries are most sensitive to carbon dioxide, which is a fast-rising acid that must be controlled tightly. A rise in carbon dioxide drives the respiratory centre to make breathing faster and deeper to blow off the excess, while oxygen acts only as a backup driver when its level falls dangerously low.

3. Define vital capacity and total lung capacity and give their approximate values. Vital capacity is the largest volume of air that can be moved in one breath, from a full inspiration to a full expiration; it equals tidal volume plus inspiratory and expiratory reserve volumes, about 4600 mL. Total lung capacity is all the air the lungs can hold, vital capacity plus residual volume, about 5800 mL.

4. How are oxygen and carbon dioxide carried in the blood? Oxygen is carried almost entirely bound to haemoglobin in red blood cells as oxyhaemoglobin, with a little dissolved in plasma. Carbon dioxide is carried in three ways: mostly as bicarbonate in the plasma, some bound to haemoglobin, and a little dissolved in the plasma.

5. Differentiate between asthma and chronic obstructive pulmonary disease. Asthma is a chronic inflammatory airway disease causing reversible narrowing in attacks by muscle spasm, swelling and mucus, often triggered by allergy. COPD is a largely irreversible, progressive obstruction caused mainly by smoking, combining chronic bronchitis and emphysema (alveolar destruction). Asthma is reversible; COPD is not.

6. Why must tuberculosis be treated with several drugs for a long time? Because Mycobacterium tuberculosis grows slowly and hides inside cells, a long combined course of antibiotics (usually six months or more) is needed to kill it. Several drugs together prevent the survival of resistant bacteria, and stopping early lets resistant strains breed, making the disease much harder to treat.

C. Long-answer questions (10 marks)

1. Describe the anatomy of the respiratory system with special reference to the lungs, and explain the mechanism of breathing. A full answer traces air through the nose, pharynx,

larynx, trachea, bronchi and bronchioles (conducting zone) to the alveoli (respiratory zone); describes the lungs, their lobes and pleura, and the thin alveolar wall with its capillaries giving a huge surface and short diffusion distance; then explains inspiration as active (diaphragm and intercostals contract, chest and lungs expand, pressure falls, air enters) and expiration at rest as passive elastic recoil. A labelled diagram (Figure 6.1) should be included. *(High-yield.)*

2. Describe the lung volumes and capacities and the transport of respiratory gases. A full answer defines the four volumes (tidal, inspiratory reserve, expiratory reserve, residual) with values, and the capacities (vital capacity, total lung capacity, functional residual capacity) as their sums; then explains oxygen transport bound to haemoglobin along the S-shaped dissociation curve and carbon dioxide transport mainly as bicarbonate, with the link to blood pH.

3. Write notes on asthma and tuberculosis. For asthma: a reversible inflammatory airway disease, the three components of narrowing (bronchoconstriction, swelling, mucus), common triggers, and treatment by inhaled bronchodilators and steroids. For tuberculosis: infection by Mycobacterium tuberculosis, airborne spread, the latent and active phases, features of active lung disease (chronic cough, blood in sputum, fever, night sweats, weight loss), and treatment by a long combined antibiotic course with the danger of resistance.

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Chapter 7: The Urinary System: Anatomy, Physiology and Pathophysiology

Learning outcomes

After working through this chapter the student will be able to:

1. Describe the anatomy of the urinary tract, with special reference to the kidney and the nephron.
2. State the functions of the kidney and the urinary tract.
3. Explain how urine is formed by filtration, reabsorption and secretion.
4. Describe the micturition reflex and the role of the kidney in acid–base balance.
5. Explain the renin–angiotensin–aldosterone system and its effect on blood pressure.
6. Describe the pathophysiology of acute and chronic renal failure and of urinary tract infections.

7.1 A hundred and eighty litres in, one and a half out

The two kidneys filter the entire blood supply many times over each day. The fluid they filter out of the blood adds up to around a hundred and eighty litres a day, enough to fill a bathtub, yet a healthy person passes only about one and a half litres of urine in that time. Almost everything filtered, more than ninety-nine percent of the water and all the useful substances, is taken back into the blood, and only the true waste and the right amount of water are let go. That single contrast captures what the kidney does. It does not simply make urine. It processes the blood on a huge scale, reclaiming what the body needs and discarding what it does not, and in doing so it controls the volume, the salt content and the acidity of the blood.

This chapter follows that work. First the anatomy of the urinary tract and the nephron, the tiny filtering unit that does the job. Then how urine is actually formed in three steps, how it is stored and passed, and how the kidney helps control the blood's acidity and, through a hormone system, its pressure. Finally the diseases that follow when the kidney fails or the tract is infected. The urinary system is the partner of the respiratory system from Chapter 6: both clean the blood and both help hold its acid balance steady, one by breathing off carbon dioxide and the other by adjusting the urine. For a pharmacy student the kidney has a special importance, because it is the main route by which most drugs and their breakdown products leave the body, so a failing kidney changes how nearly every medicine must be dosed.

7.2 Anatomy of the urinary system

The urinary system has four parts: two **kidneys** that make the urine, two **ureters** that carry it down, one **urinary bladder** that stores it, and one **urethra** that passes it out. The kidneys are the organs that do the chemical work; the rest is plumbing that collects, stores and releases the finished urine.

The **kidneys** are two bean-shaped organs, each about the size of a fist, lying against the back wall of the abdomen, one on each side of the spine. Cut a kidney in half and three regions appear: an outer **cortex**, an inner **medulla** arranged in cone-shaped pyramids, and a central space, the **renal pelvis**, that funnels the finished urine into the ureter. Each kidney receives a rich blood supply through the renal artery, which makes sense given that its job is to process blood; in fact the kidneys receive around a fifth of the blood the heart pumps, far more than their size would suggest, because they are filtering it rather than merely feeding themselves.

From the renal pelvis the urine drains into the **ureter**, a muscular tube that carries it down to the bladder by peristalsis, the same wave-like contraction seen in the gut in Chapter 4. The **urinary bladder** is a muscular bag that stores the urine until it is convenient to pass it, expanding as it fills. The **urethra** is the tube that carries urine from the bladder out of the body, and it is guarded by sphincters that keep it closed until release. The urethra is short in the female and longer in the male, a small anatomical fact with a real consequence taken up in the section on infection.

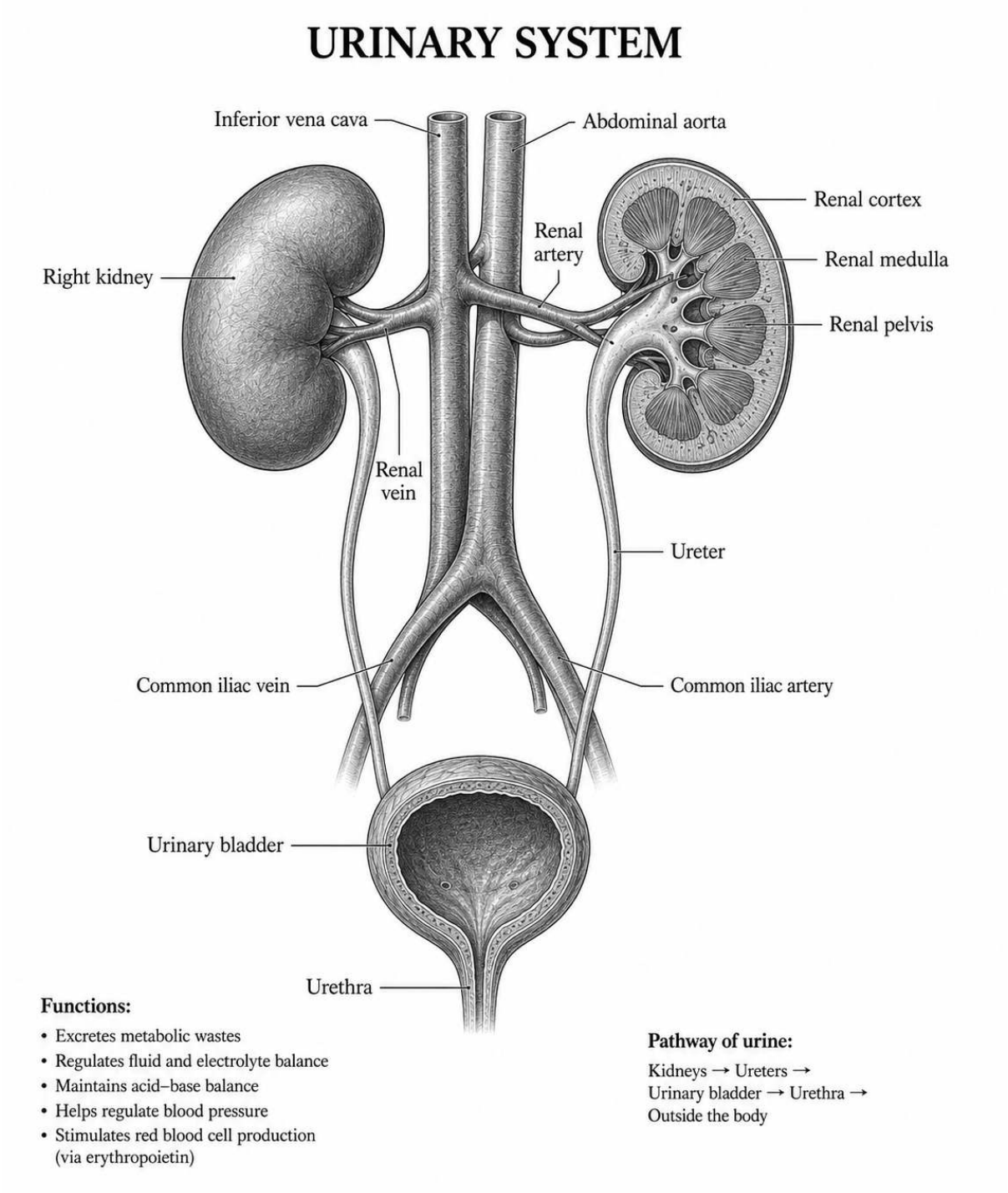


Figure 7.1 The urinary system

Special reference to the nephron

The working unit of the kidney is the **nephron**, and there are about a million of them in each kidney. Every drop of urine is made by these tiny units working in parallel, so understanding one nephron is understanding the kidney. A nephron has two linked parts, a filter and a long tubule, shown in Figure 7.2.

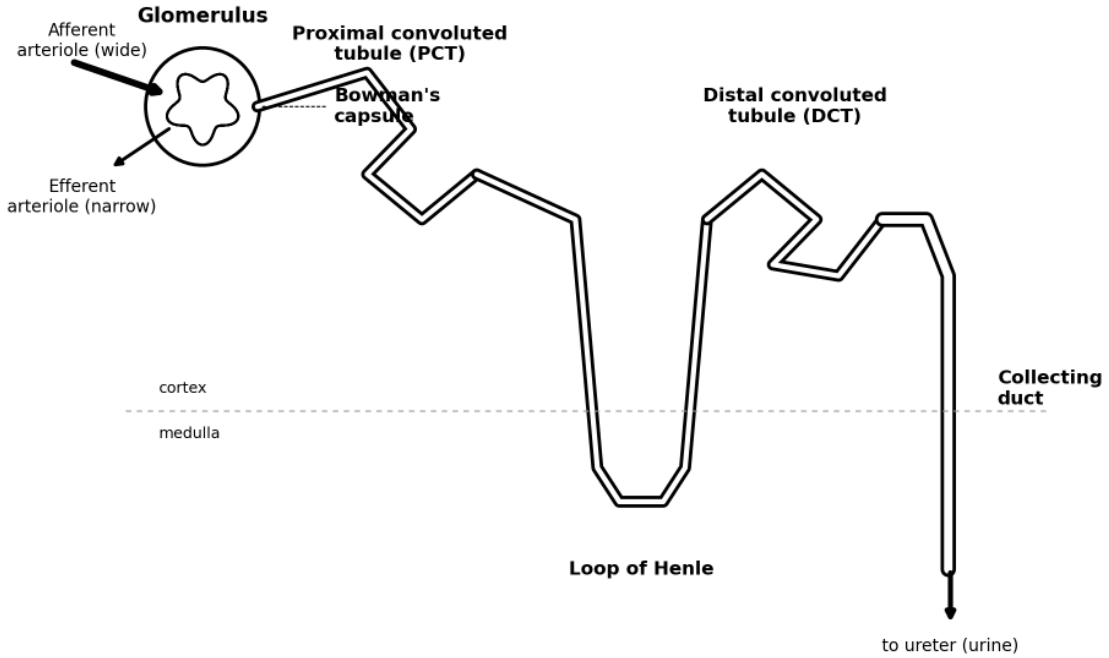


Figure 7.2 *Structure of a nephron.*

The filter is the **glomerulus**, a tight knot of capillaries sitting inside a cup-shaped **Bowman's capsule**. Blood enters the glomerulus under pressure, and that pressure squeezes a watery fluid out of the blood through the thin capillary walls into the capsule. This is the first step of urine formation, and the structure is built for it: a high-pressure tuft of leaky capillaries wrapped in a collecting cup.

The high pressure inside the glomerulus is itself a clever piece of plumbing worth a sentence. Blood arrives through a wider vessel (the afferent arteriole) and leaves through a narrower one (the efferent arteriole), and the narrow exit dams the blood back and keeps the pressure inside the glomerulus high, which is what drives filtration. By adjusting the width of these two vessels the kidney can raise or lower the filtration pressure to keep the filtration rate steady even when the body's blood pressure wanders, an example of the kidney protecting its own function. After leaving the glomerulus the blood does not return to the general circulation at once; it runs on into a second network, the peritubular capillaries, that wraps closely around the tubule, perfectly placed to take back whatever the tubule reabsorbs in the next stage.

The tubule is a long, winding tube that leads away from Bowman's capsule, and the filtered fluid travels along it being processed. It has named regions in order: the **proximal convoluted tubule**, then the **loop of Henle** that dips down into the medulla and back, then the **distal convoluted tubule**, which empties into a **collecting duct** shared by many

nephrons. As the fluid runs along this tubule, the useful substances are taken back into the surrounding blood and the final adjustments are made, turning the large volume of filtrate into the small volume of urine. The tubule is long and winding for a reason: reabsorption takes place across its wall, so a long tube gives the time and surface to reclaim almost everything worth keeping. Structure serves function once again.

7.3 Functions of the kidney

Before tracing urine formation, it helps to list what the kidney achieves, because urine is only the visible product of several deeper jobs. The kidney:

- **Removes waste.** It clears the nitrogen wastes from protein breakdown, chiefly urea, along with other waste and excess substances, in the urine.
- **Controls water balance.** It adjusts how much water is kept or lost, so the body's water content and blood volume stay steady.
- **Controls salt and electrolyte balance.** It keeps the levels of sodium, potassium and other ions in the right range.
- **Controls acid–base balance.** It adjusts the acidity of the blood by altering what it excretes, working alongside the lungs.
- **Helps control blood pressure**, both through water and salt balance and through the renin–angiotensin–aldosterone system described below.
- **Has hormonal roles**, including making a hormone that drives red blood cell production and activating vitamin D.

Two of these hormonal roles deserve a closer word, because they explain symptoms of kidney failure that seem at first to have nothing to do with the kidney. The kidney makes a hormone called erythropoietin that tells the bone marrow to make red blood cells; when the kidney fails this signal is lost, the marrow makes too few cells, and the patient becomes anaemic. The kidney also carries out the final step that turns vitamin D into its active form, the form needed to absorb calcium and keep bones strong; when the kidney fails this activation is lost and the bones weaken. So a failing kidney causes anaemia and bone disease, and both trace back to these quiet hormonal jobs rather than to the filtering of waste.

Most of these come down to one idea: the kidney keeps the internal fluid of the body constant, which is the homeostasis throughline at its clearest. Urine is simply what is left after the kidney has finished holding the blood steady.

7.4 Physiology of urine formation

Urine is formed in three steps as the blood is processed through the nephron: filtration, reabsorption and secretion. Following the fluid through these three, shown in Figure 7.3, is the heart of this chapter.

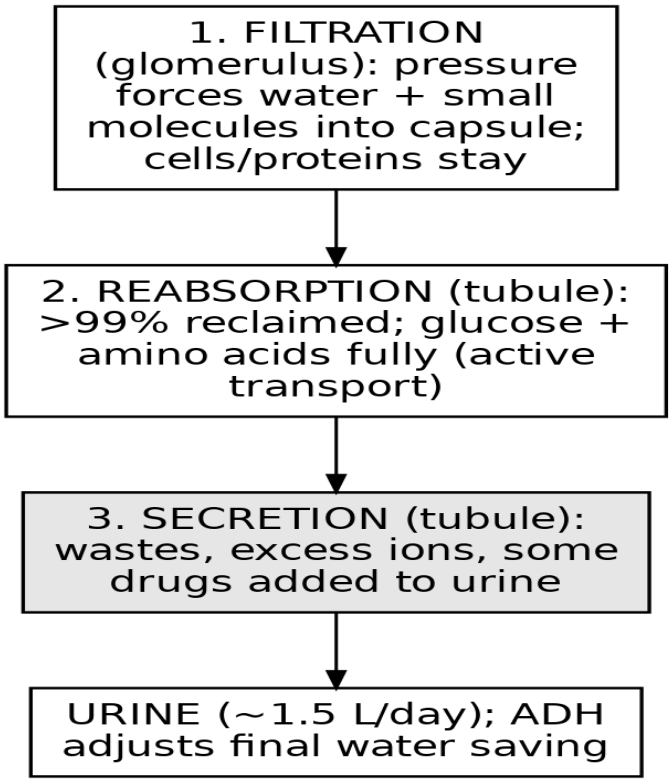


Figure 7.3 *The three steps of urine formation.*

Step 1: Glomerular filtration. Blood under pressure reaches the glomerulus, and the pressure forces water and small dissolved substances out through the capillary walls into Bowman's capsule. Small molecules pass easily: water, glucose, amino acids, salts and the waste urea all cross into the filtrate. Large things stay behind in the blood: the blood cells and the plasma proteins are too big to pass, so they remain in the circulation. The fluid now in the capsule, called the filtrate, is therefore like blood plasma but without its proteins and cells. The total volume filtered by all the nephrons in a minute is the **glomerular filtration rate (GFR)**, about 125 mL per minute in a healthy adult, which works out to roughly 180 litres a day. To see where that large daily figure comes from, multiply the rate by the minutes in a day: 125 mL per minute times 1440 minutes is about 180000 mL, or 180 litres, the bathtub of filtrate from the start of the chapter. The GFR is the single most useful measure of kidney health, and it falls steadily as the kidney fails, which is why it is the number doctors track to judge how far chronic kidney disease has progressed.

Step 2: Tubular reabsorption. If the body simply passed all 180 litres of filtrate, it would lose all its water, sugar and salt within an hour. So as the filtrate flows along the tubule, almost everything useful is reabsorbed back into the blood in the capillaries wrapped around the tubule. The work is shared along the tubule's length. The proximal convoluted tubule does the bulk of it, reclaiming most of the water and salt and all of the glucose and amino acids; the loop of Henle sets up the conditions that let the kidney concentrate the urine; and the distal tubule and collecting duct make the fine, adjustable final reabsorption under hormonal control. Glucose and amino acids are reabsorbed completely, by active transport, so that none is normally lost in the urine. This last point has a neat clinical echo: there is a limit to how much glucose the tubule can reabsorb, so when blood glucose is very high, as in uncontrolled diabetes, the excess spills into the urine, which is why sugar in the urine is a classic sign of diabetes in Chapter 9. Most of the water and salt is reabsorbed too. This is why more than ninety-nine percent of the filtrate is reclaimed and only a small, concentrated remainder becomes urine. Reabsorption is selective: the body keeps what it needs and lets the rest go.

Step 3: Tubular secretion. In the last part of the tubule the process runs in reverse for a few substances: certain wastes, excess ions such as hydrogen and potassium, and some drugs are actively moved from the blood into the tubule to be added to the urine. Secretion is the kidney's way of getting rid of things faster than filtration alone would manage, and it is part of how the kidney fine-tunes the blood's acidity and clears many drugs.

What leaves the collecting ducts after these three steps is **urine**: water with the dissolved wastes, chiefly urea, and whatever salts the body needed to lose, concentrated down to about a litre and a half a day. The exact amount of water saved or lost is adjusted at the end of the tubule by **antidiuretic hormone (ADH)**, a hormone from the brain that makes the collecting ducts reabsorb more water when the body is short of it, producing a smaller volume of concentrated urine. When you are dehydrated, ADH rises and the urine is dark and scant; when you drink plenty, ADH falls and the urine is pale and copious. This is the body holding its water steady, nephron by nephron.

> **Quick-recall box 7.1: Urine formation in three steps** Filtration (glomerulus): pressure forces water and small molecules into Bowman's capsule; cells and proteins stay in blood. GFR about 125 mL/min. Reabsorption (tubule): more than 99 percent reclaimed, glucose and amino acids fully, by active transport. Secretion (tubule): wastes, excess ions and some drugs added from blood to urine. ADH adjusts final water saving.

7.5 Micturition

The urine made by the kidneys drains continuously down the ureters into the bladder, which stores it until it is convenient to empty. The act of passing urine is called **micturition**, and it is controlled by a reflex with a layer of voluntary override, much like defaecation in Chapter 4.

As the bladder fills and its wall is stretched, stretch sensors send signals to the spinal cord, which triggers the **micturition reflex**: the bladder muscle contracts and the internal sphincter relaxes, ready to empty the bladder. In an infant this reflex empties the bladder automatically. As a child grows, the brain learns to control the external sphincter, which is under voluntary command, so an adult can hold on until a suitable time and then consciously relax the external sphincter to let the reflex complete. So micturition is a spinal reflex that the brain can postpone, the same partnership of automatic and voluntary control seen elsewhere in the book. Damage to the spinal cord can break the voluntary control while leaving the reflex, which is why bladder problems are common after spinal injury.

> **Quick-recall box 7.2: When the kidney fails** Acute renal failure: sudden, often reversible; causes are pre-renal (low blood flow), renal (tissue damage) or post-renal (blocked outflow). Chronic renal failure: slow, irreversible; commonest causes diabetes and high blood pressure; ends in dialysis or transplant. Both raise blood urea, upset fluid and salt, and make the blood acidic; chronic failure also causes anaemia (no erythropoietin) and weak bones (no active vitamin D).

A closing point ties the kidney back to pharmacy and is worth fixing firmly. Because the kidney is the main exit route for most drugs and their breakdown products, a kidney that filters and secretes poorly clears those drugs slowly, so they linger and build up in the blood. A dose that is safe for a healthy person can become an overdose in someone with renal failure. This is why drug doses are routinely reduced, or the drug avoided, when kidney function is low, and why the glomerular filtration rate from section 7.4 is checked before prescribing many medicines. The anatomy and physiology of this chapter are, for a pharmacist, the rules that keep a patient with weak kidneys safe.

7.6 The kidney and acid–base balance

The blood must be kept very close to a steady acidity, a pH of about 7.35 to 7.45, because the body's enzymes work only within that narrow band. Two organs guard this balance, and the kidney is the second of them. The lungs, from Chapter 6, handle the fast part by breathing off carbon dioxide, which is an acid in the blood. The kidney handles the slower, longer-term part by adjusting what it excretes.

The kidney controls acidity in two linked ways. When the blood is too acidic, the kidney **excretes more hydrogen ions** into the urine by tubular secretion, removing acid from the body, and at the same time it **reabsorbs and makes more bicarbonate**, the main base that neutralises acid, returning it to the blood. When the blood is too alkaline, it does the reverse, keeping more hydrogen and letting bicarbonate go. So the kidney can shift the balance in either direction by choosing what to keep and what to dump in the urine. The two organs together make a robust system: the lungs adjust acidity within minutes, the kidney within hours to days, and between them they hold the blood pH in its narrow safe range. When the kidney fails, this control is lost, and the blood becomes dangerously acidic, one of the serious consequences of renal failure below.

The partnership also explains how the body compensates when one side is disturbed. If a lung disease lets carbon dioxide build up and the blood turn acidic, the kidney responds over the following days by holding on to more bicarbonate, pushing the pH back toward normal. If instead the body becomes too acidic for a metabolic reason, the lungs respond within minutes by breathing faster to blow off carbon dioxide. Each organ can partly cover for a problem in the other, which is why a single disturbance rarely pushes the pH straight out of its safe range. This is the clearest example in the book of two systems sharing one homeostatic job, and it is the reason the respiratory and urinary chapters sit side by side in this unit.

7.7 The renin–angiotensin–aldosterone system

The kidney is central to controlling **blood pressure**, and the main tool it uses is a hormone chain called the **renin–angiotensin–aldosterone system (RAAS)**. It is worth learning carefully, because it is one of the most important drug targets in all of medicine: several of the most common blood-pressure drugs act on this very system. Figure 7.4 sets out the chain.

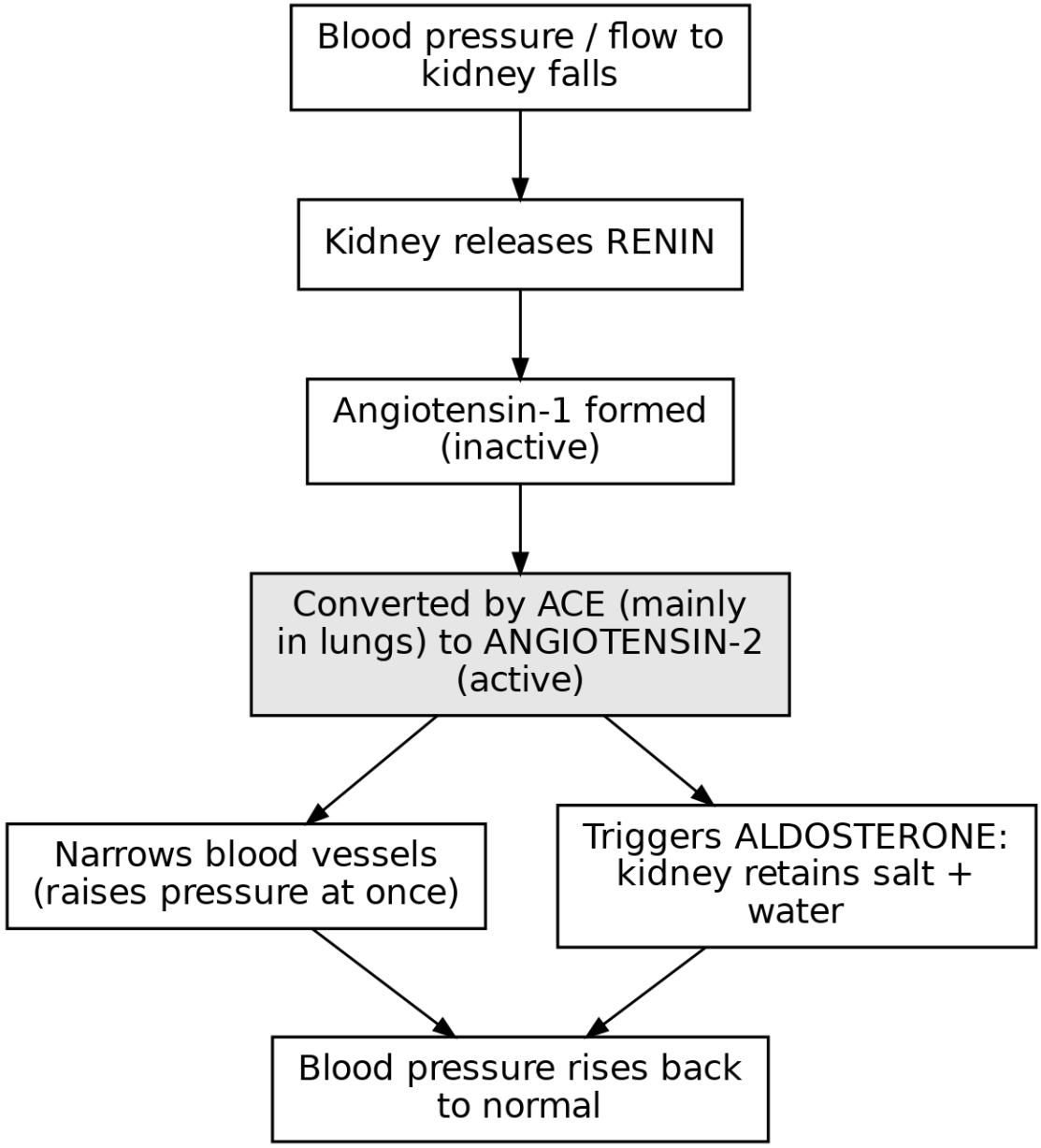


Figure 7.4 *The renin-angiotensin-aldosterone system.*

The system is switched on when the kidney senses that blood pressure or blood flow through it has fallen. The steps run in order:

1. The kidney releases an enzyme called **renin** into the blood.
2. Renin acts on a protein made by the liver and produces an inactive substance, the first angiotensin (written **angiotensin-1**, the inactive precursor).
3. This inactive precursor is converted, mainly in the lungs, into the active hormone **angiotensin-2** by an enzyme known as the angiotensin-converting enzyme (ACE).
4. Active angiotensin-2 does two things that raise blood pressure. It **narrows the blood vessels** directly, which raises pressure at once. And it triggers the adrenal gland to

release the hormone **aldosterone**, which makes the kidney reabsorb more salt and, with it, more water, increasing the blood volume and so the pressure.

(The two forms are written in many books with Roman numerals as angiotensin one and angiotensin two; the active form, angiotensin-2, is the one that raises blood pressure, and the enzyme that makes it, ACE, is blocked by a major class of blood-pressure drugs, the ACE inhibitors.)

The result is a rise in blood pressure back toward normal, which is exactly what the system is for: a feedback loop that defends blood pressure when it falls. The reason it matters so much to a pharmacist is that blocking it lowers blood pressure. Drugs that block the enzyme converting angiotensin-1 to angiotensin-2, and drugs that block the action of angiotensin-2, are mainstays of treating high blood pressure and heart failure, and they are understood entirely through this chain. Learn the steps here, and a large slice of cardiovascular pharmacology is already half done.

7.8 Pathophysiology of the urinary system

The syllabus names two kinds of disorder: failure of the kidney itself, in acute and chronic forms, and infection of the urinary tract. Table 7.1 contrasts acute and chronic renal failure.

Table 7.1: Acute versus chronic renal failure

Feature	Acute renal failure	Chronic renal failure
Onset	Sudden (hours to days)	Slow (months to years)
Reversible?	Often, if cause treated	No, progressive
Common causes	Bleeding, dehydration, toxins, blockage	Diabetes, high blood pressure
Nephrons	Temporarily not working	Permanently destroyed
Typical outcome	Recovery, sometimes after dialysis	End-stage disease: dialysis or transplant

Acute renal failure

Acute renal failure (acute kidney injury) is a sudden, rapid loss of kidney function over hours or days. The kidneys abruptly stop filtering properly, so waste products such as urea build up in the blood, fluid and salts are no longer balanced, and urine output often falls sharply. Because it comes on fast, it is frequently reversible if the cause is found and treated in time.

Its causes are grouped by where the problem lies, which is a clean and examinable scheme that echoes the three-part classification of jaundice in Chapter 5, before, in, and after the organ. **Pre-renal** causes lie before the kidney, a fall in blood flow to it, as from severe bleeding, dehydration or shock, so the kidney is starved of the blood it needs to filter; this is the commonest group and is quickly reversible if the blood flow is restored. **Renal** causes lie within the kidney itself, direct damage to the kidney tissue, as from certain drugs, toxins or its own diseases, and a pharmacist should note that several medicines can themselves injure the kidney. **Post-renal** causes lie after the kidney, a blockage to the outflow of urine, as from a stone or an enlarged prostate, so urine backs up and pressure damages the kidney. The grouping matters because the treatment differs: restore the blood flow, remove the toxin, or relieve the blockage. Acute renal failure is a medical emergency, sometimes needing temporary dialysis (an artificial filtering of the blood) until the kidneys recover.

Chronic renal failure

Chronic renal failure (chronic kidney disease) is the slow, progressive and irreversible loss of kidney function over months or years. Nephrons are gradually destroyed and do not regrow, so the working kidney tissue shrinks steadily. Its commonest causes are the long-term diseases that damage the kidney's small blood vessels: **diabetes** and **high blood pressure** are the two leading causes worldwide, which ties this disease directly to the endocrine and cardiovascular topics of the course.

Because the loss is gradual, the disease is often silent until much of the kidney is gone, and then the failures appear together: wastes build up in the blood, fluid overload causes swelling and breathlessness, the blood turns acidic as acid–base control fails, blood pressure rises, the blood count falls as the kidney stops making its red-cell hormone (causing anaemia), and the bones weaken as vitamin D activation fails. In its final stage, called end-stage renal disease, the kidneys can no longer sustain life, and the patient needs either lifelong **dialysis** or a kidney **transplant**. The whole picture is a reminder of how many jobs the kidney does, because chronic failure is the simultaneous loss of all of them.

Dialysis is worth understanding, because it is the artificial stand-in for a failed kidney and it makes the kidney's filtering job concrete. In **haemodialysis**, the patient's blood is passed through a machine where it flows along one side of a thin membrane while a special fluid flows along the other; wastes and excess salts and water pass across the membrane out of the blood, doing by a machine what the glomerulus and tubule once did, and the cleaned blood is returned. It is usually done a few times a week at a centre. In **peritoneal dialysis**, the membrane used is the patient's own lining of the abdomen, across which the same exchange happens with fluid run into the abdominal cavity. Dialysis keeps a person alive but does not

restore the kidney's hormonal jobs, so patients still need treatment for anaemia and bone disease, which is why a transplant, when possible, gives a fuller recovery.

Urinary tract infection

A **urinary tract infection (UTI)** is an infection of any part of the urinary tract, most often by bacteria that travel up the urethra from outside. When the infection is in the bladder it is called cystitis and causes a burning pain on passing urine, a frequent and urgent need to go, and cloudy or strong-smelling urine. If the infection climbs up the ureters to reach the kidney itself (pyelonephritis), it is more serious, adding fever, back pain and feeling unwell, and it can damage the kidney.

One anatomical fact explains a clear pattern: UTIs are much more common in women than in men, because the female urethra is shorter, so bacteria have a shorter journey to reach the bladder. Other things that raise the risk include anything that blocks or slows the flow of urine, such as a stone or an enlarged prostate, since stagnant urine lets bacteria multiply. Most UTIs are treated with a course of antibiotics, and drinking plenty of fluids to flush the tract helps. For a pharmacist, UTIs are among the most common infections met at the counter, and recognising the warning signs that an infection has reached the kidney, where it needs prompter, stronger treatment, is a useful skill.

One more common urinary problem deserves a mention, because it links to the post-renal failure above. **Kidney stones** are hard lumps that form when certain salts in the urine become too concentrated and crystallise, often when a person does not drink enough. A small stone may pass on its own, but a larger one can lodge in a ureter and block the flow of urine, causing severe waves of pain (renal colic) and, if it dams the urine back, threatening the kidney behind it. This is exactly the post-renal cause of kidney injury described earlier, seen from the patient's side. Prevention is largely a matter of drinking enough fluid to keep the urine dilute, a simple piece of advice a pharmacist can give that genuinely prevents disease.

7.9 Chapter summary

The urinary system filters the blood on a huge scale and reclaims almost all of it, passing only the waste and the right amount of water as urine. It is made of two kidneys, two ureters, a bladder and a urethra, and the working unit is the nephron, a filter (the glomerulus in Bowman's capsule) joined to a long tubule (proximal tubule, loop of Henle, distal tubule and collecting duct). Urine is formed in three steps: filtration, where pressure forces water and small molecules out of the glomerulus into the capsule while cells and proteins stay behind, giving a filtration rate of about 125 mL per minute; reabsorption, where more than ninety-nine percent of the filtrate, including all the glucose and amino acids, is taken back into the

blood; and secretion, where some wastes, ions and drugs are added to the urine. Antidiuretic hormone makes the final adjustment to water saving. The finished urine drains to the bladder and is passed by micturition, a spinal reflex the brain can postpone.

The kidney also holds the blood's acidity steady, excreting hydrogen and reabsorbing bicarbonate to work with the lungs in keeping blood pH near 7.4, and it defends blood pressure through the renin–angiotensin–aldosterone system, in which renin leads to angiotensin-2, which narrows vessels and, through aldosterone, makes the kidney retain salt and water, a chain that is a major target for blood-pressure drugs. When the kidney fails acutely, over hours to days from pre-renal, renal or post-renal causes, it is often reversible; when it fails chronically, over months to years from diabetes and high blood pressure, it is irreversible and ends in dialysis or transplant, with the loss of all the kidney's jobs at once. Urinary tract infections, more common in women because of the shorter urethra, range from bladder cystitis to the more serious kidney infection. With the blood-cleaning systems of this unit now complete, the book turns in Unit IV to the slower of the body's two great signalling networks, the chemical messengers that run the body over minutes to hours rather than milliseconds, the endocrine system.

7.10 Self-assessment

A. Multiple-choice questions

1. The functional unit of the kidney is the:
   (a) glomerulus (b) nephron (c) ureter (d) renal pelvis. Answer: (b).
2. Glomerular filtration is driven by:
   (a) active transport (b) blood pressure in the glomerulus (c) ADH (d) aldosterone. Answer: (b).
3. The approximate glomerular filtration rate in a healthy adult is:
   (a) 25 mL/min (b) 125 mL/min (c) 500 mL/min (d) 1250 mL/min. Answer: (b).
4. Glucose in the filtrate is normally:
   (a) excreted unchanged (b) completely reabsorbed (c) secreted into urine (d) filtered out as protein. Answer: (b).
5. Antidiuretic hormone makes the collecting ducts:
   (a) reabsorb more water (b) secrete more glucose (c) filter faster (d) make renin. Answer: (a).
6. In the renin–angiotensin–aldosterone system, angiotensin-2:
   (a) widens blood vessels (b) narrows blood vessels and triggers aldosterone (c) lowers blood pressure (d) increases urine output. Answer: (b).

7. Urinary tract infections are more common in women because:
   (a) women drink less (b) the female urethra is shorter (c) women have one kidney (d) of higher blood pressure. Answer: (b).
8. The two leading causes of chronic renal failure worldwide are:
   (a) infection and stones (b) diabetes and high blood pressure (c) dehydration and bleeding
   (b) drugs and toxins. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Describe the structure of a nephron. A nephron has two linked parts: a filter and a tubule. The filter is the glomerulus, a knot of capillaries inside the cup-shaped Bowman's capsule. The tubule leads away from the capsule as the proximal convoluted tubule, then the loop of Henle dipping into the medulla, then the distal convoluted tubule, which empties into a collecting duct. There are about a million nephrons in each kidney. *(High-yield.)*

2. Explain the three steps of urine formation. Filtration: blood pressure in the glomerulus forces water and small molecules into Bowman's capsule, while cells and proteins stay in the blood. Reabsorption: as the filtrate flows along the tubule, more than ninety-nine percent is reclaimed into the blood, including all glucose and amino acids by active transport. Secretion: some wastes, excess ions and drugs are added from the blood into the tubule to be excreted. *(High-yield.)*

3. How does the kidney help control the acid–base balance of the blood? The kidney adjusts blood acidity over hours to days, working with the lungs. When the blood is too acidic it secretes more hydrogen ions into the urine and reabsorbs more bicarbonate into the blood; when too alkaline it does the reverse. This keeps blood pH near 7.35 to 7.45.

4. Outline the renin–angiotensin–aldosterone system. When blood pressure or flow to the kidney falls, the kidney releases renin; renin makes the inactive angiotensin-1 from a liver protein; angiotensin-1 is converted (mainly in the lungs) to angiotensin-2; angiotensin-2 narrows blood vessels and triggers aldosterone, which makes the kidney retain salt and water. Both actions raise blood pressure.

5. Differentiate between acute and chronic renal failure. Acute renal failure is a sudden loss of kidney function over hours to days, often reversible if the cause (pre-renal, renal or post-renal) is treated. Chronic renal failure is a slow, progressive and irreversible loss over months to years, usually from diabetes or high blood pressure, ending in dialysis or transplant.

6. Why are urinary tract infections more common in women, and how do bladder and kidney infections differ? They are more common in women because the female urethra is shorter, so bacteria reach the bladder more easily. A bladder infection (cystitis) causes burning, frequency and cloudy urine, while a kidney infection (pyelonephritis) is more serious, adding fever, back pain and feeling unwell.

C. Long-answer questions (10 marks)

1. Describe the structure of the nephron and explain the physiology of urine formation. A full answer describes the nephron (glomerulus in Bowman's capsule, proximal tubule, loop of Henle, distal tubule, collecting duct) and then the three steps: filtration at the glomerulus (driven by blood pressure, small molecules pass, cells and proteins stay, GFR about 125 mL/min), reabsorption along the tubule (more than ninety-nine percent reclaimed, glucose and amino acids fully), and secretion of wastes, ions and drugs, with ADH adjusting final water reabsorption. A labelled nephron diagram (Figure 7.1) should be included. *(High-yield.)*

2. Explain the renin–angiotensin–aldosterone system and its importance. A full answer gives the trigger (fall in blood pressure or renal blood flow), the chain (renin, angiotensin-1, angiotensin-2 formed mainly in the lungs), and the two actions of angiotensin-2 (vasoconstriction and release of aldosterone causing salt and water retention), explaining how both raise blood pressure and why the system is a major target for blood-pressure drugs.

3. Discuss the causes, features and management of chronic renal failure. A full answer defines chronic renal failure as the slow, irreversible loss of kidney function; gives the leading causes (diabetes and high blood pressure); describes the consequences as the kidney's many jobs fail (waste build-up, fluid overload, acidosis, high blood pressure, anaemia, weak bones); and explains that end-stage disease requires dialysis or transplant.

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Chapter 8: The Endocrine System: Hormones and Glands

Learning outcomes

After working through this chapter the student will be able to:

1. Classify hormones and explain the two main mechanisms of hormone action.
2. Explain how the hypothalamus and pituitary gland control much of the endocrine system.
3. Describe the structure and functions of the thyroid and parathyroid glands.
4. Describe the structure and functions of the adrenal gland and the endocrine pancreas.
5. State the roles of the pineal gland and the thymus.
6. Explain how negative feedback keeps hormone levels steady.

8.1 The body's slow messengers

Chapter 1 introduced two signalling systems and then spent five chapters on the fast one. This chapter takes up the slow one. Where the nervous system sends brief electrical signals down private wires to exact targets in milliseconds, the **endocrine system** releases chemical messengers into the blood, which carries them everywhere, to act on whichever cells can receive them, over minutes, hours or days. The two systems are not rivals but partners; they share the work between them. The nervous system handles the quick, precise jobs, the endocrine system the slow, widespread, sustained ones: growth over years, the monthly cycle, the steady control of blood sugar and body water. The hypothalamus, met in Chapter 2, is the bridge where the two meet.

It is worth fixing the contrast between the two systems clearly, because it explains why the body needs both. A nerve signal is fast, brief and private: it reaches one target down a dedicated wire in a few milliseconds and stops the moment the firing stops. A hormone is slow, lasting and public: it spreads through the whole bloodstream over minutes to days and keeps acting as long as it circulates. A nerve signal is right for snatching a hand off a hot plate; a hormone is right for running a nine-month pregnancy or holding blood sugar steady through the day and night. Some jobs even use both: the adrenal medulla, met below, is a piece of nervous system that releases a hormone, blurring the line on purpose so the body can mount both a fast and a sustained response to danger.

The messengers are **hormones**, and a hormone is simply a chemical made by a gland, released into the blood, and carried to distant cells where it produces an effect. The glands that make them, the **endocrine glands**, are ductless: unlike the salivary glands or pancreas of Chapter 4, which pour their products down tubes, endocrine glands release their hormones

straight into the bloodstream. This chapter first sets out what hormones are and how they act, then takes the glands one by one, and closes with the feedback control that holds the whole system steady. For a pharmacy student the endocrine system is central, because many hormones are themselves medicines (insulin, thyroid hormone, steroids), many drugs work by acting on hormone receptors, and many of the diseases met in later chapters, from diabetes to thyroid disorders, are hormone disorders treated by adjusting the very signals this chapter describes.

8.2 Classification of hormones

Hormones are grouped by their chemical nature, and the grouping matters because it decides how a hormone travels in the blood and how it acts on its target, the subject of the next section. It is the endocrine version of the rule that has run through the book, that structure decides function, applied now to the structure of the hormone molecule itself. Figure 8.1 shows the classification as a tree. There are three main chemical classes.

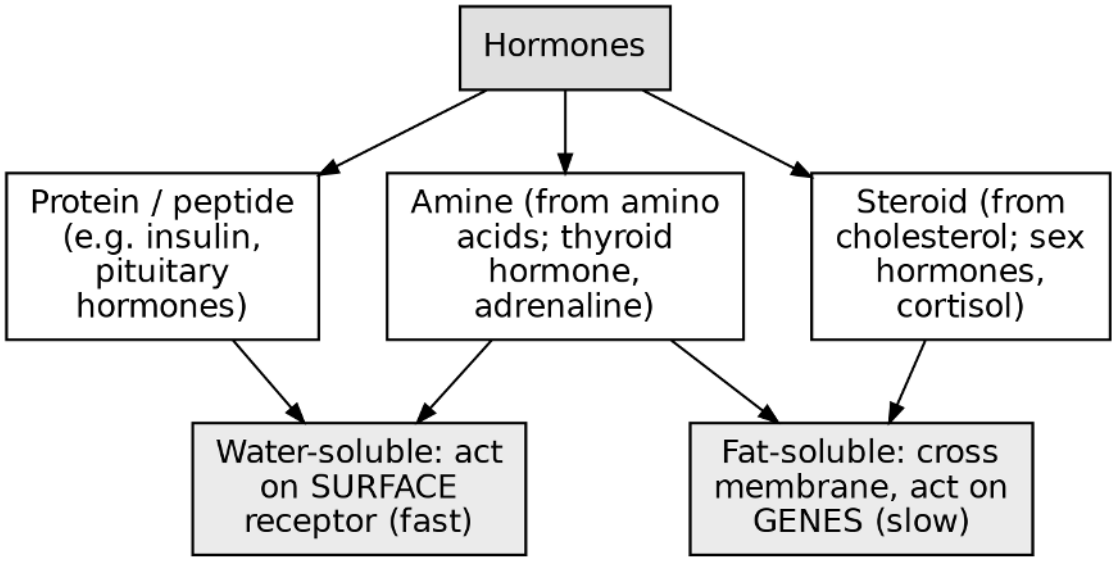


Figure 8.1 *Classification of hormones.*

- **Protein and peptide hormones** are made of amino acid chains, short or long. Most hormones fall here, including insulin and the hormones of the pituitary gland. They dissolve in water (the blood is watery) but cannot cross the fatty cell membrane, a fact that decides how they act.
- **Steroid hormones** are made from cholesterol and are fatty (lipid-soluble). They include the sex hormones and the hormones of the adrenal cortex. Being fatty, they cross cell membranes easily but do not dissolve well in blood, so they are carried bound to proteins.

- **Amine hormones** are made from single amino acids. They include the thyroid hormones and adrenaline. They are a small group with mixed properties, some behaving like the water-soluble group and some like the fatty group. Adrenaline behaves like the water-soluble hormones, acting fast from the cell surface, while thyroid hormone behaves like the fat-soluble ones, crossing into the cell, a reminder that the chemical class is only a guide and the real test is whether the hormone can cross the membrane.

This classification is more than a filing system. It predicts three practical things about a hormone: how it travels in the blood, how it acts on its target, and even how it can be given as a medicine. A protein hormone such as insulin is destroyed by the digestive enzymes of Chapter 4 if swallowed, so it must be injected, while a steroid or thyroid hormone survives digestion and can be taken as a tablet. So a fact of chemistry learned here decides the form a hormone medicine takes, which is the kind of link a pharmacy student should notice.

The single most useful split inside this scheme is between the **water-soluble** hormones (proteins, peptides and most amines), which cannot cross the cell membrane, and the **fat-soluble** hormones (steroids and thyroid hormone), which can. That one difference, can it cross the membrane or not, decides the whole mechanism of action below, so hold it in mind as the bridge to the next section.

8.3 Mechanism of hormone action

A hormone travels in the blood and reaches every cell, yet it acts only on some. The reason is the **receptor**, the same idea met for neurotransmitters in Chapter 1: a cell responds to a hormone only if it carries the matching receptor, so the hormone is broadcast widely but heard only by cells tuned to receive it. How the hormone acts then depends on whether it can cross the cell membrane, which is exactly the water-soluble versus fat-soluble split from the last section. The two mechanisms are shown in Figure 8.2.

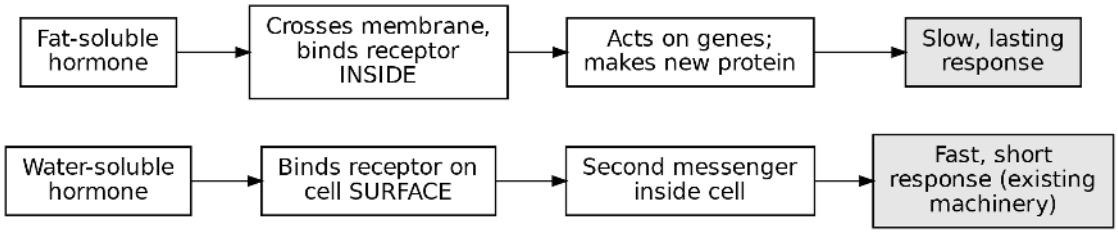


Figure 8.2 *The two mechanisms of hormone action.*

Water-soluble hormones act from outside the cell. Because a protein or peptide hormone cannot cross the fatty membrane, it binds to a receptor on the cell surface. The binding does not send the hormone in; instead it triggers a chain of events inside the cell, working through internal messenger molecules often called second messengers, that switches on the cell's

existing machinery. The effect is fast, because it uses machinery already present, and relatively short-lived. This is the same kind of surface-receptor signalling met for the fast neurotransmitters, one idea serving both systems.

Fat-soluble hormones act from inside the cell. Because a steroid or thyroid hormone can cross the membrane, it passes right into the cell and binds a receptor inside, in the cytoplasm or the nucleus. The hormone-receptor pair then acts on the cell's genes, switching particular genes on or off and so changing which proteins the cell makes. Because making new protein takes time, this effect is slower to start but longer-lasting and more profound. This is why steroid drugs act over hours and their effects persist, a point that matters in pharmacology.

So the same broadcast signal produces two quite different kinds of response depending on the hormone's chemistry: a quick nudge to existing machinery from the surface, or a slower, deeper change to gene activity from within. Learning which hormone uses which mechanism is mostly a matter of asking the one question from section 8.2: can it cross the membrane.

A worked comparison makes the difference real. Insulin is a protein, so it is water-soluble and cannot cross the membrane; it must act from the cell surface, and indeed it works within minutes, prompting cells to take up glucose using machinery they already have. A steroid such as cortisol is fat-soluble, so it slips into the cell and acts on the genes; its full effects take hours and last much longer, which is why a steroid injection for inflammation is not an instant painkiller but builds its effect over a day. Ask the membrane question of any hormone and you can predict both where it acts and how fast: surface and fast for the water-soluble ones, inside and slow for the fat-soluble ones. This single rule saves memorising each hormone's mechanism separately.

8.4 The hypothalamus and the pituitary gland

The endocrine system is not a set of independent glands; much of it is run from one place, where the nervous and endocrine systems join. The **hypothalamus**, part of the brain from Chapter 2, sits just above the **pituitary gland**, a pea-sized gland hanging below it, and together they form the control centre that directs many other glands. The pituitary is often called the master gland, because its hormones command the thyroid, the adrenal cortex and the reproductive glands; but the pituitary is itself directed by the hypothalamus, so the hypothalamus is the true top of the chain.

The pituitary has two parts that work in different ways. The **anterior (front) pituitary** makes and releases several hormones of its own, under the control of releasing hormones sent down from the hypothalamus in a short local blood supply. Its key hormones are signals to other glands: one drives the thyroid (thyroid-stimulating hormone), one drives the adrenal cortex,

two drive the reproductive glands, plus growth hormone (which controls body growth) and prolactin (which drives milk production). The **posterior (back) pituitary** does not make hormones itself; it stores and releases two hormones made in the hypothalamus, antidiuretic hormone (ADH, from Chapter 7, which makes the kidney save water) and oxytocin (which acts in childbirth and milk release, met in Chapter 10).

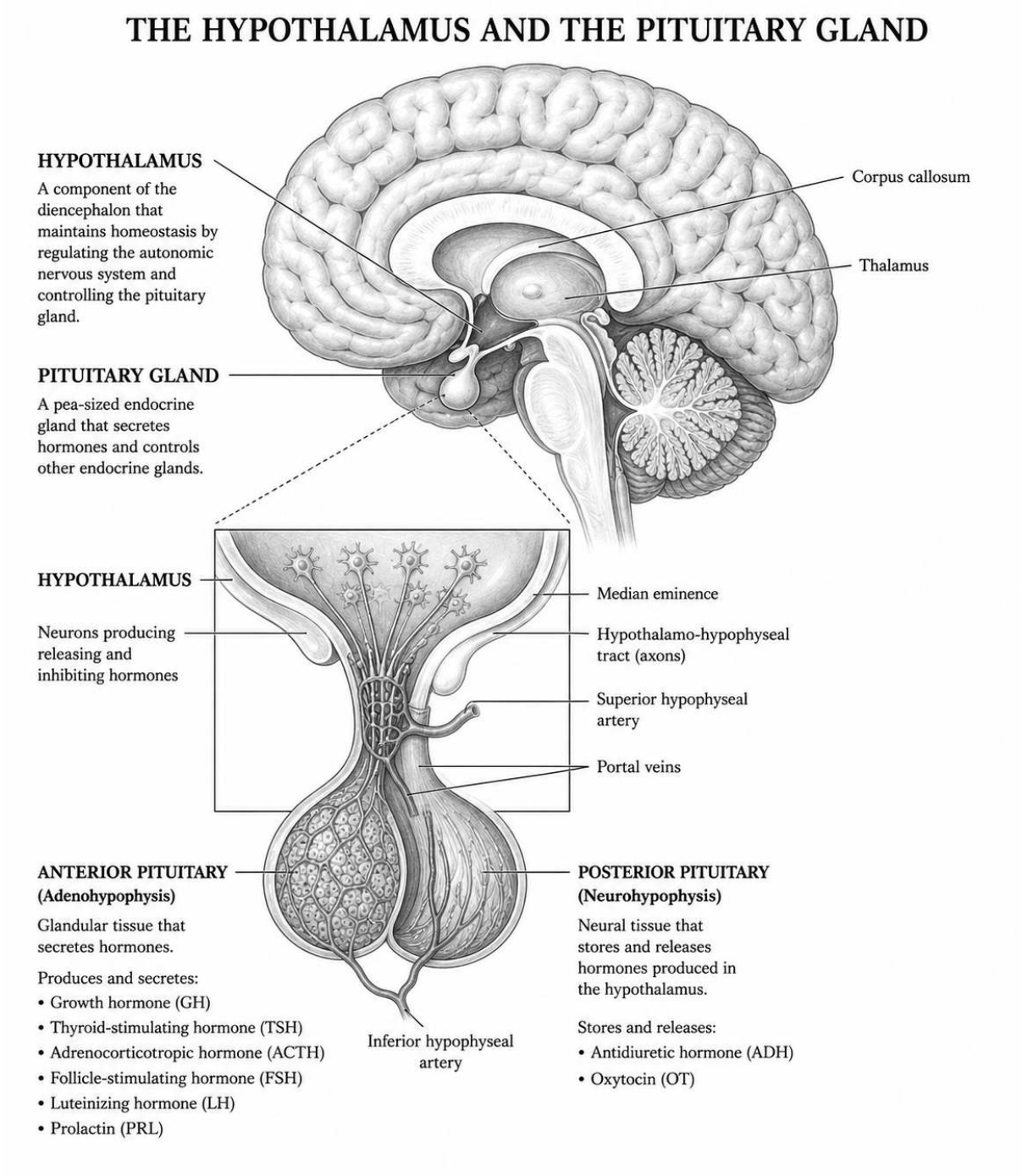


Figure 8.3 The hypothalamus and the pituitary gland

Two of the anterior pituitary's own hormones are worth a closer word because their disorders are visible. **Growth hormone** controls the growth of the body in childhood, driving the lengthening of bones and the building of tissues. Too little in a child gives short stature; too much gives overgrowth, with abnormally tall stature if it happens before the bones finish growing, and a coarsening and enlargement of the hands, feet and face if it happens in an adult. **Prolactin** drives the breast to make milk after childbirth. These are the clearest reminders that the pituitary, though tiny, reaches into growth, reproduction and metabolism across the whole body, which is why a tumour of the pituitary can cause such varied effects.

The two halves of the pituitary connect to the hypothalamus in two different ways, which is worth a moment because it explains how one small gland does two jobs. The anterior pituitary is linked to the hypothalamus by a short, private blood supply: the hypothalamus drips its releasing hormones into that blood, and they travel the short distance to switch the anterior pituitary on or off. The posterior pituitary is linked by nerves instead: the hormones it releases are actually made in the hypothalamus and travel down nerve fibres to be stored in the posterior pituitary until a nerve signal releases them. So one half is controlled by blood-borne hormones and the other by nerves, a small structural fact that explains why the two halves behave so differently.

The pattern to carry forward is a chain of command, shown in Figure 8.4: the hypothalamus signals the anterior pituitary, the anterior pituitary signals a target gland, and the target gland releases its hormone to act on the body. This three-step axis, hypothalamus to pituitary to gland, organises the thyroid, adrenal and reproductive systems alike, and it is the structure on which the feedback control of section 8.9 is built. Learn the axis once and it explains the control of three glands.

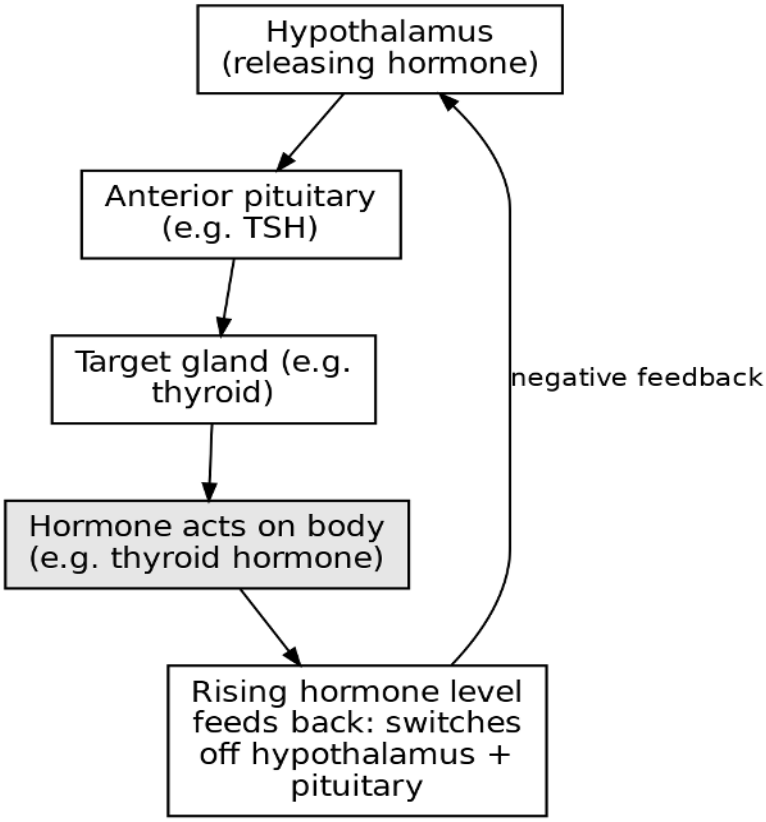


Figure 8.4 *The hypothalamus-pituitary axis and negative feedback.*

8.5 The thyroid and parathyroid glands

The thyroid gland

The **thyroid gland** is a butterfly-shaped gland in the front of the neck, wrapped around the windpipe. It makes the **thyroid hormones**, known as T3 and T4, which contain iodine taken from the diet, and these hormones set the body's **metabolic rate**, the speed at which its cells use energy. Thyroid hormone is the body's accelerator: the right amount keeps metabolism, heart rate, body temperature, growth and mental activity at their proper pace. Too much speeds everything up and too little slows everything down, which is the basis of the thyroid diseases in Chapter 9. Thyroid hormone is also essential for normal growth and brain development in children, so a lack of it early in life has serious effects.

The thyroid is controlled by the axis from section 8.4: the hypothalamus signals the pituitary, which releases thyroid-stimulating hormone (TSH), which tells the thyroid to make its hormones. Because the thyroid needs iodine to build T3 and T4, a lack of iodine in the diet limits hormone production, a cause of disease taken up in the next chapter. This dependence on dietary iodine is the reason many countries, India among them, add iodine to table salt: a public-health measure that prevents the thyroid disease of iodine lack across whole populations, and a clear example of how a small fact of physiology becomes national policy.

The effects of thyroid hormone reach almost every tissue, which is why a thyroid disorder shows up in so many ways: it sets the resting energy use, the heart rate, the warmth of the body, the speed of the gut, and even the sharpness of thought, so when it is wrong the whole body runs too fast or too slow. The thyroid also contains separate cells that make **calcitonin**, a hormone that lowers blood calcium, a minor partner to the parathyroid glands below.

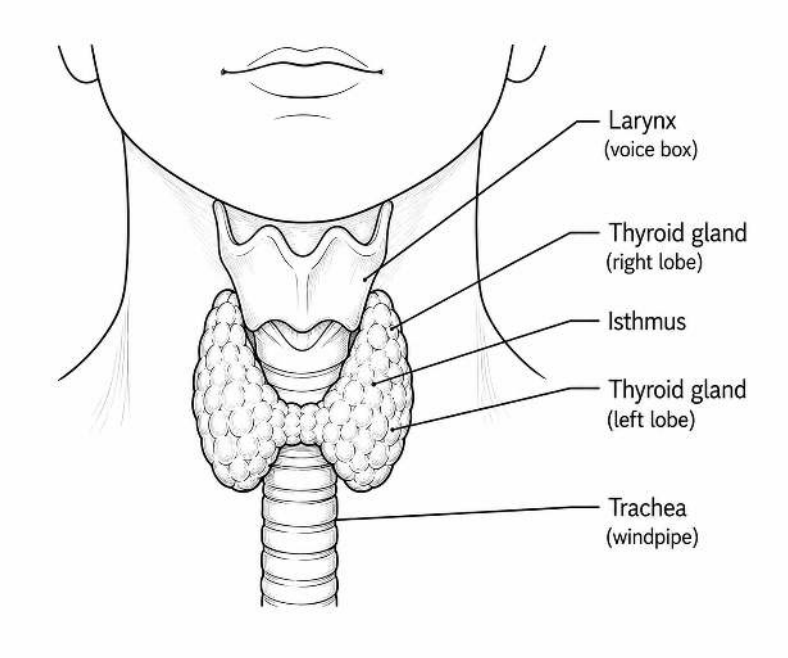


Figure 8.5 The thyroid gland

The parathyroid glands

Behind the thyroid sit four tiny **parathyroid glands**, and despite their small size they have one vital job: controlling the level of **calcium** in the blood. Calcium must be held within narrow limits because nerves and muscles, including the heart, depend on it to work, and bones depend on it for strength. The parathyroid glands make **parathyroid hormone (PTH)**, which raises blood calcium when it falls, by drawing calcium from the bones, making the kidney save calcium, and helping activate vitamin D so the gut absorbs more. PTH and the thyroid's calcitonin work in opposite directions, PTH raising blood calcium and calcitonin lowering it, and between them they hold the calcium steady. This opposing pair is the calcium version of the balance idea that runs through the book.

The control of calcium is itself a small feedback loop worth seeing, because it shows the principle without the pituitary axis. When blood calcium falls, the parathyroid glands sense it directly and release more PTH, which raises calcium back up; when calcium rises too high, PTH release falls and calcitonin helps bring it down. No brain or pituitary is needed: the gland reads the very substance it controls and adjusts its output to hold it steady. This direct

kind of feedback, a gland sensing its own target, is the simplest form of the negative feedback that section 8.9 explains in full, and it is the reason calcium stays so constant that nerves and the heart can rely on it from one beat to the next.

8.6 The adrenal glands

The two **adrenal glands** sit one on top of each kidney, like caps, and each has two distinct parts that make quite different hormones, so they are really two glands in one. Their position above the kidney is fitting for one hormone in particular: aldosterone acts on the kidney just below it, so the gland that controls salt and water sits right beside the organ it commands.

The outer part, the **adrenal cortex**, makes **steroid hormones** from cholesterol. Three groups matter. The first controls salt and water: **aldosterone**, met in the renin-angiotensin-aldosterone system of Chapter 7, makes the kidney retain salt and water and so helps control blood pressure. The second controls metabolism and the stress response: the **glucocorticoids**, chiefly cortisol, raise blood glucose, help the body cope with long-term stress, and damp down inflammation, which is why synthetic versions, the steroid drugs, are widely used to treat inflammation and allergy. This anti-inflammatory power makes the steroid drugs among the most useful medicines a pharmacist handles, but it comes at a price: long-term steroid use mimics an excess of cortisol and causes weight gain, thinning of the skin, raised blood sugar, weakened bones and a suppressed immune response, so these drugs must be used at the lowest effective dose and never stopped suddenly. Understanding cortisol here is the basis for understanding both why steroid drugs work and why they are handled with such care. The third group is a small amount of sex hormones. The cortex is under the control of the pituitary through the axis of section 8.4.

The inner part, the **adrenal medulla**, is really an extension of the sympathetic nervous system from Chapter 1. When the body faces sudden danger or stress, the medulla pours out **adrenaline** (and noradrenaline) into the blood, producing the fight-or-flight response: a faster, stronger heartbeat, widened airways, more blood to the muscles and a release of glucose for energy. This is the hormonal arm of the sympathetic response, and it explains why a fright makes the heart pound. So the cortex handles the slow, sustained adjustments through steroids, while the medulla handles the sudden emergency through adrenaline, two responses to stress on two timescales from the one gland.

The division of labour between the two parts is a neat lesson in how the body covers a problem on more than one timescale. Face a sudden threat and the medulla acts in seconds, flooding the blood with adrenaline to ready the body for action; if the stress continues for hours or days, the cortex takes over with cortisol, mobilising energy and damping inflammation for the long haul. The same gland thus answers both the sprint and the

marathon of stress, and it does so because a piece of fast nervous tissue (the medulla) sits packed inside a slow hormonal one (the cortex). It is one of the clearest places in the body where the fast nervous system and the slow endocrine system are built into a single organ, the very partnership this chapter opened with.

8.7 The endocrine pancreas

The **pancreas** appeared in Chapter 4 as a digestive gland, but it also has an endocrine part, small clusters of cells scattered through it called the **islets of Langerhans**, which make the hormones that control **blood glucose**. Two hormones do the work, and they pull in opposite directions, the balance that the next chapter's diabetes is the failure of.

Insulin, made by the beta cells of the islets, is the hormone that lowers blood glucose. After a meal, when blood sugar rises, insulin is released and tells the body's cells to take glucose in from the blood and use or store it, and it tells the liver to store glucose as glycogen. The blood sugar falls back to normal. **Glucagon**, made by the alpha cells, does the reverse: when blood sugar falls too low, as between meals or overnight, glucagon tells the liver to release its stored glucose back into the blood, raising it again. The two hormones thus act as a pair of opposing controls, one lowering and one raising, so that whatever a person eats or however long they fast, the blood glucose is nudged back toward a steady set point from either direction. Together insulin and glucagon hold blood glucose in a steady range whatever the person is eating or doing, which is one of the clearest feedback systems in the body.

It is worth seeing a little of how insulin actually lowers blood glucose, because it explains what goes wrong in diabetes. Most body cells cannot let glucose in by themselves; they need insulin to act as the key that opens the door, prompting the cell to bring glucose-carrying gateways to its surface so the sugar can enter. When insulin is present, glucose pours from the blood into muscle and fat cells and the blood level falls. When insulin is absent or the cells stop responding to it, glucose cannot get into the cells however much is in the blood, so it piles up in the bloodstream while the cells starve. That single picture, plenty of glucose outside the cell and none inside, is the heart of diabetes in Chapter 9. Insulin is the more important of the two hormones to remember, because its lack or failure is diabetes, the major disease of the next chapter, and because injected insulin is a life-saving medicine for those who cannot make their own.

8.8 The pineal gland and the thymus

Two smaller endocrine organs complete the syllabus. The **pineal gland** is a tiny gland deep in the brain that makes the hormone **melatonin**, which is released in darkness and helps control the daily sleep-wake cycle, the body clock. It is why melatonin rises at night and

helps signal that it is time to sleep, and why disturbances of light, such as jet lag or night-shift work, upset sleep by confusing the signal. Because light falling on the eye suppresses melatonin, the bright screens of phones and computers late at night can delay sleep, a modern example of a very old piece of physiology. Melatonin is also sold as a medicine to help with jet lag and some sleep problems, which is why a pharmacist meets it as more than a textbook hormone. The **thymus** is a gland in the upper chest that is large in childhood and shrinks with age; it is part of the immune system, and it is where a class of white blood cells, the T-lymphocytes, mature and learn to fight infection. The thymus matters most in early life, when the immune system is being built. The T in the name of the T-lymphocyte comes from the thymus, a small fact worth holding because those same T-cells return in Chapter 11 as the cells destroyed by HIV. As a person ages the thymus shrinks and is largely replaced by fat, having done most of its work by adulthood, which is one reason the immune system is most adaptable in the young. Both glands are minor compared with the glands above, but the syllabus names them and they each have one clear job worth knowing: melatonin for the body clock, the thymus for training immune cells. Table 8.1 brings all the glands together so the whole system can be revised at a glance.

Table 8.1: The main endocrine glands and their hormones

Gland	Main hormone(s)	Chief action
Hypothalamus	Releasing hormones; ADH, oxytocin	Controls the pituitary; water balance, childbirth
Anterior pituitary	TSH, ACTH, FSH/LH, growth hormone, prolactin	Commands other glands; growth; milk
Thyroid	T3, T4 (and calcitonin)	Sets metabolic rate; lowers blood calcium
Parathyroid	Parathyroid hormone (PTH)	Raises blood calcium
Adrenal cortex	Aldosterone, cortisol, sex steroids	Salt/water, stress and metabolism
Adrenal medulla	Adrenaline	Fast fight-or-flight response
Pancreas (islets)	Insulin, glucagon	Lowers / raises blood glucose
Pineal	Melatonin	Sleep-wake (body clock)
Thymus	Thymic hormones	Matures immune T-cells

8.9 Negative feedback: keeping hormones steady

The endocrine system would be useless if hormone levels simply drifted, so the body holds them steady by **negative feedback**, the single most important control idea in this chapter and one that runs through the whole book. Negative feedback means that the result of a process feeds back to switch off the process that produced it, like a thermostat that turns off the heating once the room is warm enough.

The clearest example is the thyroid axis from section 8.4, and it is worth following all the way round, as in Figure 8.3. The hypothalamus and pituitary drive the thyroid to make thyroid hormone. As the level of thyroid hormone in the blood rises, that rising level feeds back to the hypothalamus and pituitary and tells them to ease off, so they reduce their signals and the thyroid slows down. If the thyroid hormone level falls, the feedback eases, the pituitary signals harder, and the thyroid speeds up again. The result is a level held steady around a set point, adjusting itself automatically, exactly like the thermostat. The same loop controls the adrenal cortex and the reproductive glands.

Not every endocrine control works this way. A few processes use **positive feedback**, where the result feeds back to increase the process rather than switch it off, driving it harder until a definite end. The clearest example is the hormone oxytocin in childbirth, met in Chapter 10: the stretching of the womb releases oxytocin, which strengthens the contractions, which stretch the womb more, which releases more oxytocin, building to the powerful contractions that deliver the baby and then stopping once the birth is over. Positive feedback is rare because it is, by nature, unstable; the body uses it only where a process needs to be pushed quickly to a finish. Naming it here as the exception throws the rule into relief: almost all hormone control is negative feedback holding things steady, and positive feedback is the unusual case kept for events that must build to completion.

This idea is more than tidy theory; it explains disease and its diagnosis. When a gland fails, the feedback signal from the pituitary often rises as the pituitary tries harder to drive a gland that cannot respond, so measuring that signal tells a doctor where the fault lies. The high pituitary signal in an underactive thyroid, met in Chapter 9, is exactly this feedback at work, which is why understanding negative feedback here makes the thyroid diseases there straightforward rather than mysterious.

> **Quick-recall box 8.1: The endocrine system in brief** Hormones are blood-borne chemical messengers from ductless glands. Water-soluble hormones (peptides, most amines) act on surface receptors, fast; fat-soluble hormones (steroids, thyroid) cross into the cell and act on genes, slow. The hypothalamus controls the pituitary,

which controls the thyroid, adrenal cortex and reproductive glands. Negative feedback holds each hormone steady around a set point.

8.10 Chapter summary

The endocrine system is the body's slow signalling network, releasing hormones, chemical messengers, from ductless glands into the blood to act on distant cells over minutes to days, the partner of the fast nervous system. Hormones are classed by chemistry into protein and peptide, steroid, and amine hormones, and the key split is between water-soluble hormones, which cannot cross the cell membrane and so act on surface receptors through second messengers (fast, short), and fat-soluble hormones, which cross into the cell and act on genes (slow, lasting). A cell responds only if it has the matching receptor.

Much of the system is run by the hypothalamus and pituitary gland: the hypothalamus directs the anterior pituitary, which sends hormones to command the thyroid, adrenal cortex and reproductive glands, while the posterior pituitary stores and releases the hypothalamic hormones ADH and oxytocin. The thyroid gland sets the metabolic rate through its iodine-containing hormones T3 and T4; the parathyroid glands raise blood calcium through PTH, opposed by the thyroid's calcitonin. The adrenal glands are two glands in one: the cortex makes steroid hormones (aldosterone for salt and water, cortisol for stress and metabolism, and some sex hormones), while the medulla pours out adrenaline for the fast fight-or-flight response. The endocrine pancreas controls blood glucose through insulin (which lowers it) and glucagon (which raises it). The pineal gland makes melatonin for the body clock, and the thymus matures immune T-cells in early life. Holding the whole system steady is negative feedback, in which a rising hormone level feeds back to switch off the signals that produced it, like a thermostat, with positive feedback kept only for events such as childbirth that must build to a finish. With the healthy endocrine system now mapped, gland by gland and held steady by feedback, Chapter 9 turns to what happens when these controls fail, in the common hormone disorders of diabetes, thyroid disease and polycystic ovary syndrome.

8.11 Self-assessment

A. Multiple-choice questions

1. Endocrine glands release their hormones:
   (a) through ducts into the gut (b) directly into the blood (c) into the urine (d) into the air. Answer: (b).
2. Fat-soluble (steroid) hormones act by:
   (a) binding surface receptors only (b) crossing into the cell and acting on genes (c) being destroyed at the membrane (d) dissolving in plasma freely. Answer: (b).

3. The gland often called the master gland is the:
   (a) thyroid (b) adrenal (c) pituitary (d) pineal. Answer: (c).
4. The hormone that sets the body's metabolic rate is:
   (a) insulin (b) thyroid hormone (c) parathyroid hormone (d) melatonin. Answer: (b).
5. Parathyroid hormone acts to:
   (a) lower blood calcium (b) raise blood calcium (c) lower blood glucose (d) raise blood glucose. Answer: (b).
6. Adrenaline is released by the:
   (a) adrenal cortex (b) adrenal medulla (c) thyroid (d) pancreas. Answer: (b).
7. Insulin is made by the ____ cells of the islets of Langerhans:
   (a) alpha (b) beta (c) chief (d) parietal. Answer: (b).
8. Negative feedback in the endocrine system works to:
   (a) amplify hormone levels endlessly (b) hold hormone levels steady around a set point (c) stop all hormone release (d) speed up nerve signals. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Differentiate between the mechanism of action of water-soluble and fat-soluble hormones. Water-soluble hormones (proteins, peptides, most amines) cannot cross the cell membrane, so they bind receptors on the cell surface and act through internal second messengers, giving a fast, short response. Fat-soluble hormones (steroids and thyroid hormone) cross the membrane, bind receptors inside the cell, and act on the genes, giving a slower but longer-lasting response. *(High-yield.)*

2. Describe the relationship between the hypothalamus and the pituitary gland. The hypothalamus, part of the brain, controls the pituitary gland below it. It sends releasing hormones to the anterior pituitary, which then releases hormones that command other glands, and it makes the hormones (ADH and oxytocin) that the posterior pituitary stores and releases. So the hypothalamus is the true controller and the pituitary the relay.

3. State the functions of the thyroid and parathyroid glands. The thyroid gland makes thyroid hormones (T3 and T4), which contain iodine and set the body's metabolic rate, and it also makes calcitonin, which lowers blood calcium. The parathyroid glands make parathyroid hormone, which raises blood calcium by acting on bone, kidney and gut. Together they control metabolism and calcium balance.

4. Describe the two parts of the adrenal gland and their hormones. The adrenal cortex (outer part) makes steroid hormones: aldosterone (salt and water balance), cortisol (stress and metabolism, damps inflammation) and some sex hormones. The adrenal medulla (inner part)

makes adrenaline, producing the fast fight-or-flight response. The cortex gives slow, sustained effects; the medulla gives a fast emergency response.

5. Explain how insulin and glucagon control blood glucose. Insulin, from the beta cells, lowers blood glucose after a meal by making cells take up glucose and the liver store it as glycogen. Glucagon, from the alpha cells, raises blood glucose between meals by making the liver release stored glucose. Together they hold blood glucose steady. *(High-yield.)*

6. What is negative feedback, and how does it control thyroid hormone? Negative feedback means the result of a process feeds back to switch off the process that made it. For the thyroid, a rising level of thyroid hormone feeds back to the hypothalamus and pituitary and reduces their stimulating signals, so the thyroid slows; a falling level eases the feedback and the thyroid speeds up. This holds the hormone steady around a set point.

C. Long-answer questions (10 marks)

1. Classify hormones and explain the two mechanisms of hormone action with examples. A full answer classifies hormones into protein/peptide, steroid and amine groups, and into the water-soluble and fat-soluble split; then explains that water-soluble hormones (e.g. insulin) act on surface receptors through second messengers for a fast response, while fat-soluble hormones (e.g. steroids, thyroid hormone) cross the membrane and act on genes for a slow, lasting response, with the receptor deciding which cells respond. A diagram of the two mechanisms (Figure 8.2) should be included. *(High-yield.)*

2. Describe the structure and functions of the pituitary gland and its relationship with the hypothalamus. A full answer describes the anterior pituitary (makes hormones under hypothalamic releasing hormones: TSH, ACTH, the reproductive hormones, growth hormone, prolactin) and the posterior pituitary (stores and releases the hypothalamic hormones ADH and oxytocin); explains the hypothalamus as the true controller; and lays out the hypothalamus-pituitary-target gland axis.

3. Describe the endocrine functions of the pancreas and the role of the adrenal glands. A full answer covers the islets of Langerhans with insulin (beta cells, lowers blood glucose) and glucagon (alpha cells, raises it) and their opposing control of blood sugar; and the adrenal cortex (steroid hormones: aldosterone, cortisol, sex hormones) and medulla (adrenaline, fight-or-flight), distinguishing the slow cortical and fast medullary responses.

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Chapter 9: Endocrine Pathophysiology

Learning outcomes

After working through this chapter the student will be able to:

1. Explain the types, pathophysiology, features and complications of diabetes mellitus.
2. Distinguish type 1 from type 2 diabetes.
3. Describe the causes and features of hypothyroidism and hyperthyroidism.
4. Explain what a goitre is and why iodine deficiency causes it.
5. Describe the features and basis of polycystic ovary syndrome.
6. Relate each endocrine disorder to the gland and hormone involved.

9.1 Too much or too little

Chapter 8 showed an endocrine system held steady by feedback, each hormone kept near a set point like a room held at a set temperature by a thermostat. The diseases in this chapter are what happens when that control breaks, and they come in a pattern worth seeing at the start. Most endocrine disease is either too little of a hormone or too much of it. The thyroid runs slow or fast; the pancreas makes too little insulin or the body ignores what it makes. Name the hormone and the direction, too little or too much, and the disease almost describes itself, because the signs are simply the hormone's normal job turned down or turned up. A slow thyroid gives a slow body; a fast thyroid gives a fast one. This matched pairing of "hypo" and "hyper" is the simplest way to organise the whole chapter.

The diseases here are also among the most common a pharmacist will ever meet. Diabetes alone affects a large and growing share of the population, especially in India, which has one of the highest numbers of people with diabetes of any country, and thyroid disorders are common too, particularly in women. They are mostly long-term conditions managed by medicines that replace, block or supplement a hormone, so understanding the disordered physiology is the direct foundation for the pharmacology that treats it. Table 9.1 collects the disorders; the sections build them one at a time, starting with the most important.

Table 9.1: Endocrine disorders at a glance

Disorder	Hormone problem	Direction	Key feature
Type 1 diabetes	Insulin (beta cells destroyed)	Too little (absolute)	High blood glucose, young onset
Type 2 diabetes	Insulin (resistance)	Too little (relative)	High blood glucose,

			obesity-linked
Hypothyroidism	Thyroid hormone	Too little	Slow body (tired, cold, weight gain)
Hyperthyroidism	Thyroid hormone	Too much	Fast body (weight loss, fast heart)
Goitre	Thyroid (often iodine lack)	Variable	Swollen thyroid in the neck
PCOS	Reproductive hormones, androgens	Disturbed/excess androgen	Irregular periods, excess hair

9.2 Diabetes mellitus

Diabetes mellitus is a chronic disease in which the level of glucose in the blood is too high, because the body either cannot make enough **insulin** or cannot respond to it properly. Insulin, from Chapter 8, is the hormone that lets glucose move from the blood into the cells; without its action, glucose cannot get into the cells and instead builds up in the blood while the cells go hungry. The result is the central paradox of diabetes: the blood is awash with sugar, yet the cells are starved of it.

There are two main types, and telling them apart is essential because they arise differently and are treated differently. Table 9.2 sets them side by side.

Table 9.2: Type 1 versus type 2 diabetes

Feature	Type 1	Type 2
Cause	Autoimmune destruction of beta cells	Insulin resistance, then relative lack
Insulin	Absent (absolute deficiency)	Present at first, then falls
Usual onset	Childhood / young adult	Older adult (now younger too)
Body weight	Often normal or thin	Often overweight
Frequency	Less common	Far more common
Treatment	Insulin for life	Lifestyle, then tablets, then insulin

Type 1 diabetes is caused by the destruction of the insulin-making beta cells of the pancreas, usually by the body's own immune system attacking them. The result is an almost total lack of insulin, an absolute deficiency. It often begins in childhood or young adulthood, comes on quickly, and because there is no insulin at all, it must be treated with insulin injections for life. Without insulin the person cannot survive, which is why the discovery of insulin as a medicine was one of the great advances of medicine. Because the insulin is given by injection

rather than swallowed, the reason traces straight back to Chapter 8: insulin is a protein, so the digestive enzymes of Chapter 4 would destroy it if it were taken as a tablet, and a chemistry fact learnt earlier becomes the reason a patient must inject. Managing type 1 diabetes is a careful daily balance of insulin against food and activity, and a pharmacist has a real part in helping patients get that balance right and avoid the blood sugar swinging too high or too low.

Type 2 diabetes is different. Here the pancreas still makes insulin, at least at first, but the body's cells stop responding to it properly, a state called **insulin resistance**, and over time the pancreas cannot keep up with the extra demand, so a relative shortage develops too. It is strongly linked to being overweight, inactive and older, though it is now appearing in younger people as these risks spread. It comes on slowly and is often silent for years. Type 2 is far more common than type 1, making up the great majority of cases, and it is managed first by diet, weight loss and exercise, then by tablets that help the body use insulin or make more of it, and only later, if needed, by insulin itself.

Symptoms and how they arise

The classic symptoms of diabetes follow directly from the high blood glucose, and they are worth tracing because each one explains itself. When blood glucose rises high enough, it spills into the urine, the point met at the kidney in Chapter 7, and it drags water with it by osmosis, so the person passes large amounts of urine (**polyuria**). Losing all that water makes them thirsty, so they drink a great deal (**polydipsia**). Because the cells cannot get glucose for energy, the person feels hungry (**polyphagia**) and tired, and the body starts breaking down fat and muscle for fuel, so they lose weight despite eating. These four, passing much urine, great thirst, hunger and weight loss, are the classic picture, and a pharmacist who recognises them can prompt a person toward diagnosis. In type 2 diabetes these symptoms are often mild or absent for years, so the disease is frequently found only on a blood test or after a complication has already begun, which is why screening those at risk matters.

Diagnosis rests on measuring the blood glucose, either after fasting or after a glucose drink, and on a test called HbA1c, which reflects the average blood glucose over the previous two to three months by measuring how much glucose has stuck to the haemoglobin in the red cells. HbA1c is especially useful because it shows long-term control rather than a single moment, and it is the number a pharmacist will often see used to judge how well a patient's diabetes is being managed. One further type deserves a mention: **gestational diabetes** is diabetes that appears during pregnancy, when the hormones of pregnancy work against insulin; it usually settles after the birth but marks the mother as being at higher risk of type 2 diabetes later, and it needs careful control to protect the baby.

Complications

The danger of diabetes is less the high sugar itself than the long-term damage it does, and the complications fall into two groups, shown in Figure 9.1. The **acute** complications are emergencies of blood sugar going badly wrong: in type 1, a lack of insulin can let the body turn dangerously acidic as it breaks down fat (a state needing urgent hospital care), and in anyone on treatment, too much glucose-lowering medicine can send the blood sugar too low (hypoglycaemia), causing confusion, collapse and, if untreated, danger to life. The **chronic** complications develop silently over years of high blood sugar, which damages blood vessels throughout the body. The small vessels are harmed in the eyes (threatening sight), the kidneys (a leading cause of the chronic renal failure of Chapter 7) and the nerves (causing numbness and pain, especially in the feet). The large vessels are harmed too, greatly raising the risk of heart attack and stroke. This is why good control of blood sugar over the long term, rather than mere relief of symptoms, is the whole aim of diabetes care, and why a pharmacist's help in keeping patients on their treatment genuinely prevents blindness, kidney failure and amputation.

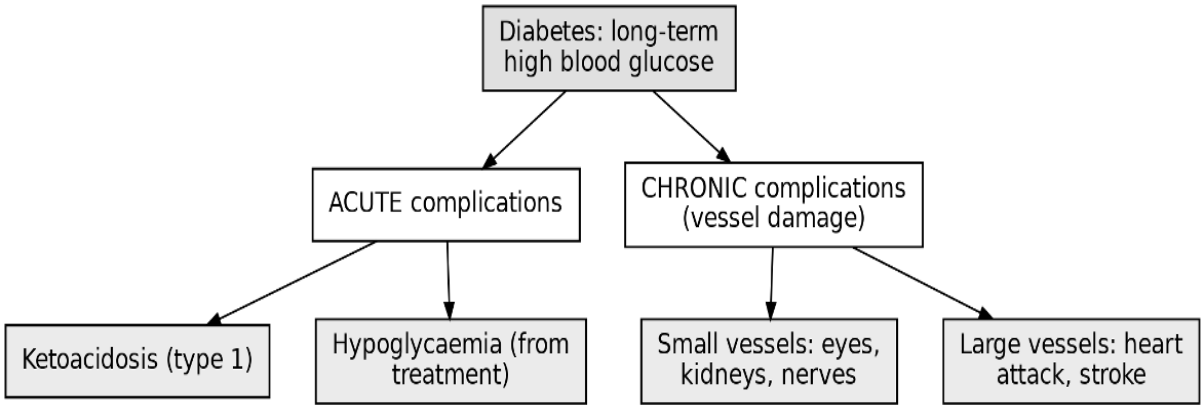


Figure 9.1 *Acute and chronic complications of diabetes.*

Quick-recall box 9.1: Diabetes at a glance Too little insulin action, so blood glucose is high but cells starve. Type 1: beta cells destroyed (autoimmune), absolute insulin lack, young, needs insulin. Type 2: insulin resistance, relative lack, older and overweight, far more common, managed by lifestyle and tablets first. Symptoms: polyuria, polydipsia, polyphagia, weight loss. Complications: acute (ketoacidosis, hypoglycaemia) and chronic (eyes, kidneys, nerves, heart and vessels).

9.3 Hypothyroidism

Hypothyroidism is the disease of too little thyroid hormone, an underactive thyroid. Since thyroid hormone sets the body's metabolic rate, the accelerator of Chapter 8, too little of it

slows everything down. The picture is, point for point, a slow body: tiredness and sluggishness, weight gain despite a poor appetite, feeling cold when others are comfortable, a slow heart rate, constipation, dry skin and hair, and a slowing of thought and mood that can look like depression. Each symptom is simply metabolism turned down.

Its causes include a lack of iodine in the diet, since the thyroid needs iodine to make its hormone, and an autoimmune disease in which the body's immune system gradually destroys the thyroid. A special and serious case is hypothyroidism in a newborn or young child: because thyroid hormone is needed for normal growth and brain development, an untreated deficiency early in life causes stunted growth and intellectual disability, a condition that screening at birth now aims to catch and prevent. The treatment of hypothyroidism is simple and effective: the missing hormone is replaced by a daily tablet of thyroxine, taken for life, which restores metabolism to normal. It is one of the neatest examples in medicine of replacing exactly what is missing.

The diagnosis again shows the feedback of Chapter 8 at work, and it is worth following because it catches students out. In hypothyroidism the thyroid hormone level in the blood is low, but the pituitary signal that drives the thyroid, thyroid-stimulating hormone (TSH), is high, because the pituitary senses the low hormone and pushes harder to correct it. So a high TSH with a low thyroid hormone is the fingerprint of an underactive thyroid, and the dose of replacement thyroxine is adjusted until the TSH comes back to normal, the feedback signal telling the doctor the dose is right. The disease is common, especially in women and with increasing age, and because its slow, vague symptoms are easily mistaken for ordinary tiredness or low mood, it is often found only when the blood is tested.

9.4 Hyperthyroidism

Hyperthyroidism is the mirror image, the disease of too much thyroid hormone, an overactive thyroid. With the accelerator pressed down, everything speeds up: weight loss despite a good appetite, feeling hot and sweating when others are comfortable, a fast and sometimes irregular heartbeat, restlessness, anxiety and a fine trembling of the hands, and frequent bowel movements. Again each sign is metabolism turned up, the exact opposite of the slow body of hypothyroidism, which is why the two diseases are best learnt as a pair.

The commonest cause is an autoimmune condition in which the immune system, instead of destroying the thyroid, wrongly stimulates it to overwork; in this form the eyes may also bulge forward, a characteristic sign. Because the symptoms come from too much hormone, treatment aims to bring the level down, by drugs that block the thyroid's hormone production, by radioactive iodine that is taken up by the overactive gland and destroys part of it, or by

surgery to remove part of the gland. The contrast with hypothyroidism runs through the treatment too: there the aim is to add hormone, here to take it away.

The feedback fingerprint is the mirror image as well. In hyperthyroidism the thyroid hormone level is high, and the pituitary, sensing the excess, switches off its stimulating signal, so the TSH is low. A low TSH with a high thyroid hormone is therefore the mark of an overactive thyroid, the exact opposite of the underactive pattern, and the two can be told apart by this one pair of measurements. One feature of severe hyperthyroidism deserves a word of caution for a pharmacist: the fast, sometimes irregular heartbeat it causes can strain the heart, and in older people it can bring on heart rhythm problems, so the racing heart of an overactive thyroid is more than an uncomfortable symptom. The good news is that hyperthyroidism is very treatable, and bringing the hormone level down usually settles the whole cluster of fast-body symptoms together.

9.5 Goitre

A **goitre** is simply a visible enlargement of the thyroid gland, seen as a swelling in the front of the neck. It is a sign, not a disease in itself, and it can occur whether the thyroid is making too little, too much or a normal amount of hormone, so a goitre must always be understood alongside the gland's function.

The most important cause to understand is **iodine deficiency**, because it shows the feedback of Chapter 8 at work in reverse. When the diet lacks iodine, the thyroid cannot make enough hormone, so the hormone level falls; the low level eases the negative feedback, and the pituitary responds by sending more and more thyroid-stimulating hormone to drive the struggling gland harder. Under this constant strong stimulation the thyroid grows larger and larger, trying to make hormone it has no iodine to build, and the result is a goitre. So the swelling is the gland straining against a shortage it cannot overcome. This is exactly why adding iodine to salt, the public-health measure from Chapter 8, has greatly reduced goitre in many countries: remove the shortage and the gland need not strain. A goitre can also come from the autoimmune diseases above, so finding one prompts a check of thyroid function to see which way, if any, the hormone level has gone. The lesson to carry from the goitre is that a swelling tells you the gland is under strain but not which way its hormone has moved, so the size of the thyroid and the level of its hormone are two separate questions that must each be answered.

9.6 Polycystic ovary syndrome

Polycystic ovary syndrome (PCOS) is one of the commonest hormone disorders in women of childbearing age, and it is included here as an endocrine disorder of the reproductive

system, which Chapter 10 describes in full. In PCOS the balance of reproductive hormones is disturbed, the ovaries often carry many small undeveloped follicles (the “cysts” of the name), and the body makes too much of the male-type hormones (androgens), which all women make in small amounts.

The disturbed hormones produce a recognisable cluster of features. The release of an egg each month becomes irregular or stops, so periods are irregular or absent and fertility is reduced, a common reason women with PCOS seek help. The excess androgens cause signs such as extra body and facial hair, acne and sometimes scalp hair thinning. Many women with PCOS also have insulin resistance, the same problem that underlies type 2 diabetes above, which links PCOS to weight gain and a raised risk of later diabetes, and which is why the two conditions are often discussed together. Figure 9.2 sets out how the disturbance produces the features.

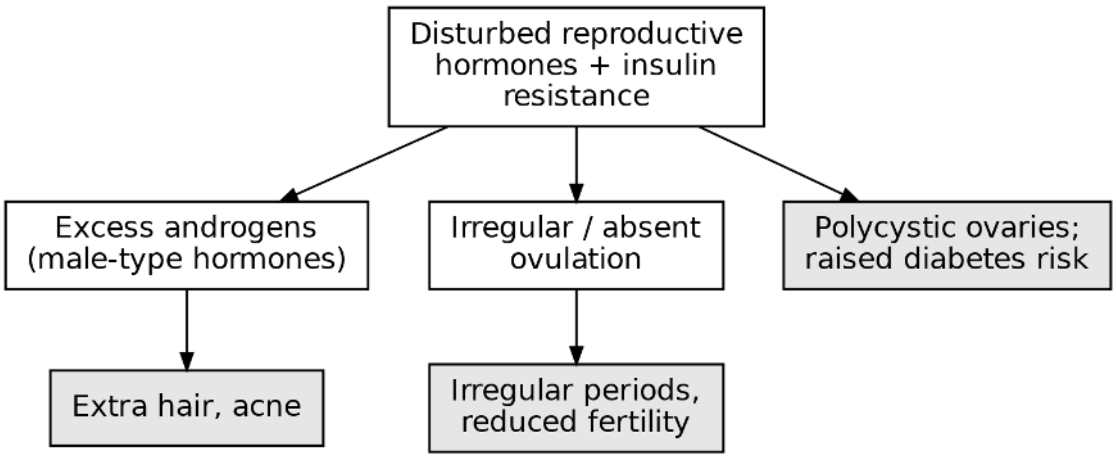


Figure 9.2 *Pathophysiology of polycystic ovary syndrome.*

Because PCOS has several strands, its management is aimed at whichever troubles the woman most: lifestyle measures and weight loss, which improve the insulin resistance and often the cycles; medicines to regulate periods or reduce the effects of excess androgens; and, when pregnancy is wanted, treatment to help ovulation. It is a clear example of an endocrine disorder where the disturbed physiology, once understood, points directly to each part of the treatment.

PCOS also shows how the body’s systems are linked rather than separate, which is a fitting note to close the endocrine unit on. The insulin resistance that connects PCOS to diabetes is the same problem seen in type 2 diabetes earlier in this chapter; the disturbed reproductive hormones belong to the system of Chapter 10; and the raised long-term risks of diabetes and heart disease tie back to the metabolic and cardiovascular themes of the course. A disorder that might look like a narrow gynaecological problem turns out to sit at the crossroads of the

endocrine, reproductive and metabolic systems, which is exactly why it is managed by attending to the whole person rather than a single symptom. For a pharmacy student it is a reminder that the body's control systems do not work in isolation, and that a medicine aimed at one may help or harm another.

9.7 Chapter summary

The diseases of the endocrine system are mostly failures of the feedback control of Chapter 8, and most come as too little or too much of a hormone. Diabetes mellitus is high blood glucose from too little insulin action: type 1, an absolute lack from autoimmune destruction of the beta cells, beginning young and needing insulin for life; and type 2, far more common, a resistance to insulin linked to obesity and age, managed first by lifestyle and tablets. Its classic symptoms, much urine, great thirst, hunger and weight loss, follow from the high blood glucose, and its danger lies in the long-term complications, acute (ketoacidosis and hypoglycaemia) and chronic (damage to the eyes, kidneys, nerves and blood vessels). Hypothyroidism, too little thyroid hormone, slows the whole body and is treated by replacing the hormone with a daily tablet; hyperthyroidism, too much, speeds the body up and is treated by reducing the hormone, the two being mirror images that are best learnt as a pair. A goitre is a swelling of the thyroid, most importantly from iodine deficiency, in which the gland strains under strong pituitary drive to make hormone it cannot build, the feedback of Chapter 8 running in reverse. Finally, polycystic ovary syndrome is a common disorder in which disturbed reproductive hormones and excess androgens, often with insulin resistance, cause irregular periods, reduced fertility and signs of androgen excess. Across the chapter the rule holds: name the hormone and the direction of its failure, and the disease, its signs and its treatment follow. With the disorders of hormone control now understood as the failures of the feedback system built in the last chapter, Unit V turns to the reproductive system itself, whose hormones PCOS has already touched, and to the disease of uncontrolled cell growth, cancer.

9.8 Self-assessment

A. Multiple-choice questions

1. In diabetes mellitus, the blood glucose is high because of a lack of action of:
   (a) glucagon (b) insulin (c) thyroid hormone (d) cortisol. Answer: (b).
2. Type 1 diabetes is caused by:
   (a) insulin resistance (b) destruction of the insulin-making beta cells (c) too much insulin
   (b) iodine deficiency. Answer: (b).

3. The more common type of diabetes, linked to obesity and insulin resistance, is:
   (a) type 1 (b) type 2 (c) gestational only (d) none. Answer: (b).
4. Which is a classic symptom of diabetes?
   (a) weight gain and thirst (b) passing much urine and great thirst (c) slow heart rate (d) cold intolerance. Answer: (b).
5. Hypothyroidism typically causes:
   (a) weight loss and fast heart rate (b) weight gain, cold intolerance and a slow heart rate (c) bulging eyes (d) high blood glucose. Answer: (b).
6. A goitre is:
   (a) a tumour of the pancreas (b) an enlargement of the thyroid gland (c) a kidney stone (d) an ovarian cyst. Answer: (b).
7. Iodine deficiency causes a goitre because the gland is:
   (a) destroyed at once (b) driven harder by the pituitary and enlarges (c) filled with cancer (d) blocked by a stone. Answer: (b).
8. A common feature of polycystic ovary syndrome is:
   (a) regular heavy periods (b) irregular periods with signs of excess androgens (c) low blood glucose (d) an overactive thyroid. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Differentiate between type 1 and type 2 diabetes mellitus. Type 1 diabetes is caused by autoimmune destruction of the insulin-making beta cells, giving an absolute lack of insulin; it usually begins in the young, comes on quickly, and needs insulin injections for life. Type 2 diabetes is caused by insulin resistance with a relative shortage of insulin, is linked to obesity and older age, is far more common, comes on slowly, and is managed first by lifestyle and tablets. *(High-yield.)*

2. Explain why diabetes causes excessive urination and thirst. When blood glucose rises very high, the excess glucose spills into the urine and drags water with it by osmosis, so the person passes large amounts of urine (polyuria). Losing that water makes the person thirsty, so they drink a great deal (polydipsia). Both follow directly from the high blood glucose.

3. List the chronic complications of diabetes. Long-term high blood glucose damages blood vessels, causing harm to the small vessels of the eyes (threatening sight), the kidneys (causing chronic renal failure) and the nerves (causing numbness and pain), and to the large vessels, greatly raising the risk of heart attack and stroke.

4. Compare hypothyroidism and hyperthyroidism. Hypothyroidism is too little thyroid hormone, slowing the body: tiredness, weight gain, cold intolerance, slow heart rate and

constipation, treated by replacing the hormone. Hyperthyroidism is too much thyroid hormone, speeding the body: weight loss, heat intolerance, fast heart rate, anxiety and tremor, treated by reducing the hormone. They are mirror images. *(High-yield.)*

5. Why does iodine deficiency cause a goitre? The thyroid needs iodine to make its hormone, so a lack of iodine lowers hormone production. The low hormone level eases the negative feedback, so the pituitary sends more thyroid-stimulating hormone to drive the gland harder. Under this constant strong stimulation the thyroid enlarges, producing a goitre.

6. Describe the main features of polycystic ovary syndrome. PCOS is a common hormone disorder of women of childbearing age, with disturbed reproductive hormones, excess male-type hormones (androgens) and ovaries carrying many small follicles. It causes irregular or absent periods and reduced fertility, signs of androgen excess such as extra hair and acne, and is often associated with insulin resistance and weight gain.

C. Long-answer questions (10 marks)

1. Discuss the types, pathophysiology, clinical features and complications of diabetes mellitus. A full answer defines diabetes as chronic high blood glucose from too little insulin action; distinguishes type 1 (autoimmune beta-cell destruction, absolute insulin lack, young, insulin-dependent) from type 2 (insulin resistance with relative lack, obesity-linked, common, lifestyle and tablets); explains the classic symptoms (polyuria, polydipsia, polyphagia, weight loss) from the high glucose; and describes the acute complications (ketoacidosis, hypoglycaemia) and chronic complications (eyes, kidneys, nerves, heart and large vessels). *(High-yield.)*

2. Write notes on hypothyroidism and hyperthyroidism. For hypothyroidism: too little thyroid hormone, the slow-body features (tiredness, weight gain, cold intolerance, slow heart, constipation), causes (iodine lack, autoimmune), the danger in children, and treatment by thyroxine replacement. For hyperthyroidism: too much thyroid hormone, the fast-body features (weight loss, heat intolerance, fast heart, anxiety, tremor, sometimes bulging eyes), the autoimmune cause, and treatment by anti-thyroid drugs, radioiodine or surgery.

3. Explain goitre and polycystic ovary syndrome. For goitre: an enlargement of the thyroid, the iodine-deficiency mechanism (low hormone, raised pituitary drive, gland enlarges), that it can occur with high, low or normal function, and prevention by iodised salt. For PCOS: disturbed reproductive hormones with excess androgens and insulin resistance, causing irregular periods, reduced fertility and androgen-excess signs, managed by lifestyle, hormone-regulating medicines and fertility treatment as needed.

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Chapter 10: The Reproductive System

Learning outcomes

After working through this chapter the student will be able to:

1. Describe the anatomy of the male and female reproductive systems.
2. State the functions of the male and female reproductive systems and name the sex hormones.
3. Explain spermatogenesis and oogenesis and compare them.
4. Describe the menstrual cycle and the hormones that control it.
5. Explain fertilization and the main events of pregnancy.
6. Describe parturition and the role of oxytocin.

10.1 A system for the next generation

Every other system in this book works to keep one body alive: the lungs feed it oxygen, the kidneys clean its blood, the nerves and hormones run its affairs. The reproductive system is the exception. It does nothing to keep its owner alive, and a person is perfectly healthy without using it. Its job lies beyond the individual altogether, in making the next generation. That is why it stays switched off through childhood and only matures at puberty, when the body is ready, and why it is run by hormones that prepare the body for producing and, in the female, carrying a new life.

Puberty itself is worth a word, because it is where this system switches on. At a certain age the hypothalamus begins, for the first time, to drive the pituitary to release the reproductive hormones in earnest. In response the testes or ovaries mature and start to make the sex hormones, and those hormones bring about the changes of puberty: the growth spurt, the development of the sex organs, and the secondary sexual characteristics, the deeper voice and body hair in boys, the breast development and the start of menstruation in girls. So puberty is not a sudden event but the switching-on of the hypothalamus-pituitary axis from Chapter 8, applied to the gonads. From that point the system is active until, in the female, it winds down at menopause when the store of ova runs out, while in the male sperm production continues, though declining, into old age.

This chapter sets out how that is done. First the anatomy of the male and female systems, then the sex hormones that drive them, then the making of the sex cells, sperm and ova, in spermatogenesis and oogenesis. After that comes the monthly rhythm of the female cycle, the meeting of sperm and ovum in fertilization, and the events of pregnancy and birth. Throughout, two ideas from earlier chapters return: the hypothalamus-pituitary axis of

Chapter 8 controls the sex glands just as it controls the thyroid and adrenal, and the positive feedback named in Chapter 8 reappears at childbirth. For a pharmacy student the system matters because its hormones are the basis of contraception, fertility treatment and hormone therapy, some of the most widely used medicines of all.

10.2 The male reproductive system

The male system has one main task: to make sperm and deliver them. Its parts, shown in Figure 10.1, are built around that task.

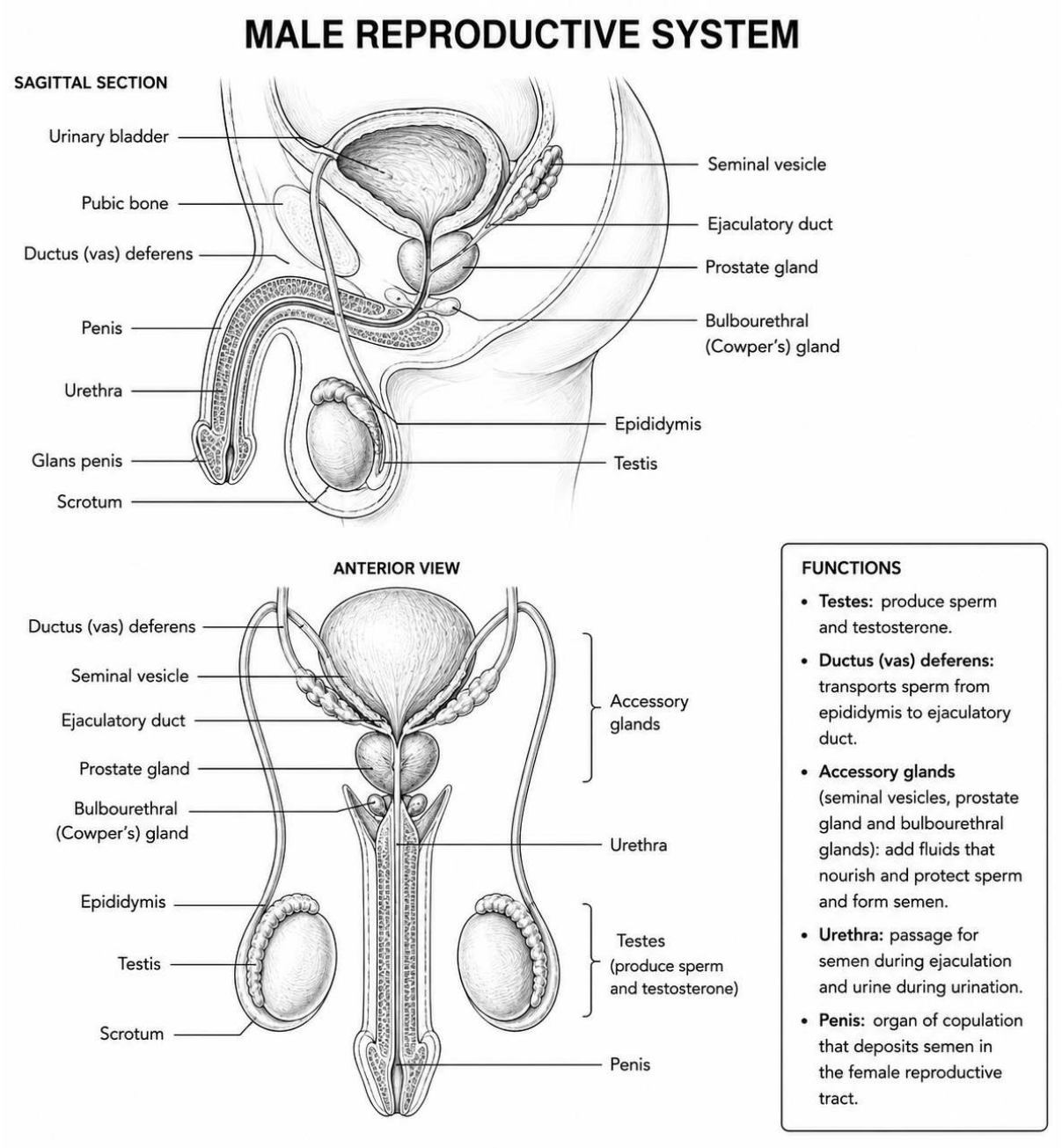


Figure 10.1 *The male reproductive system.*

The **testes** are the two oval glands held outside the body in the scrotum, and they have two jobs. They make the **sperm**, the male sex cells, in a mass of tiny coiled tubes called the seminiferous tubules, and they make the male sex hormone **testosterone**, in separate cells between the tubules. The testes sit outside the body because sperm production needs a temperature a little below body heat, a neat example of structure serving function: the scrotum keeps the testes cool enough to work. This small fact has a real consequence, since anything that keeps the testes too warm can lower sperm production, one recognised contributor to reduced male fertility. The two roles of the testis, making sperm and making testosterone, are carried out by two different sets of cells lying side by side: the sperm form in the walls of the coiled seminiferous tubules, while the testosterone is made by separate cells packed in the spaces between the tubules. So one small organ runs both a factory for cells and a gland for hormones, kept neatly apart inside it.

From each testis the sperm pass into the **epididymis**, a long coiled tube on the back of the testis where they mature and are stored, and then into the **vas deferens**, the tube that carries them up and forward toward the urethra. Along the way, glands add fluid to the sperm to make **semen**: the **seminal vesicles** and the **prostate gland** secrete a nourishing, protective fluid that gives the sperm energy and the right conditions to survive. The combined semen passes through the **urethra**, which runs through the **penis** and carries the semen out of the body. The urethra in the male thus serves both the urinary and reproductive systems, the one tube met already in Chapter 7.

The added fluids are more than packaging. The seminal vesicle fluid is rich in fructose sugar, which gives the sperm the energy to swim, and the prostate fluid is slightly alkaline, which helps protect the sperm from the acidity they meet in the female tract. So the semen is a carefully made medium that nourishes and protects the sperm on their journey, an example of several glands contributing to one product. The prostate gland is worth remembering for another reason a pharmacist will meet often: because it surrounds the urethra, an enlargement of the prostate, common in older men, squeezes the urethra and makes passing urine difficult, linking the reproductive anatomy here to the urinary problems of Chapter 7. A single gland thus sits at the crossroads of the two systems that share the male urethra.

10.3 The female reproductive system

The female system has a larger task: to make ova, to receive sperm, and then to carry and nourish a developing baby until birth. Its parts, shown in Figure 10.2, reflect that fuller role.

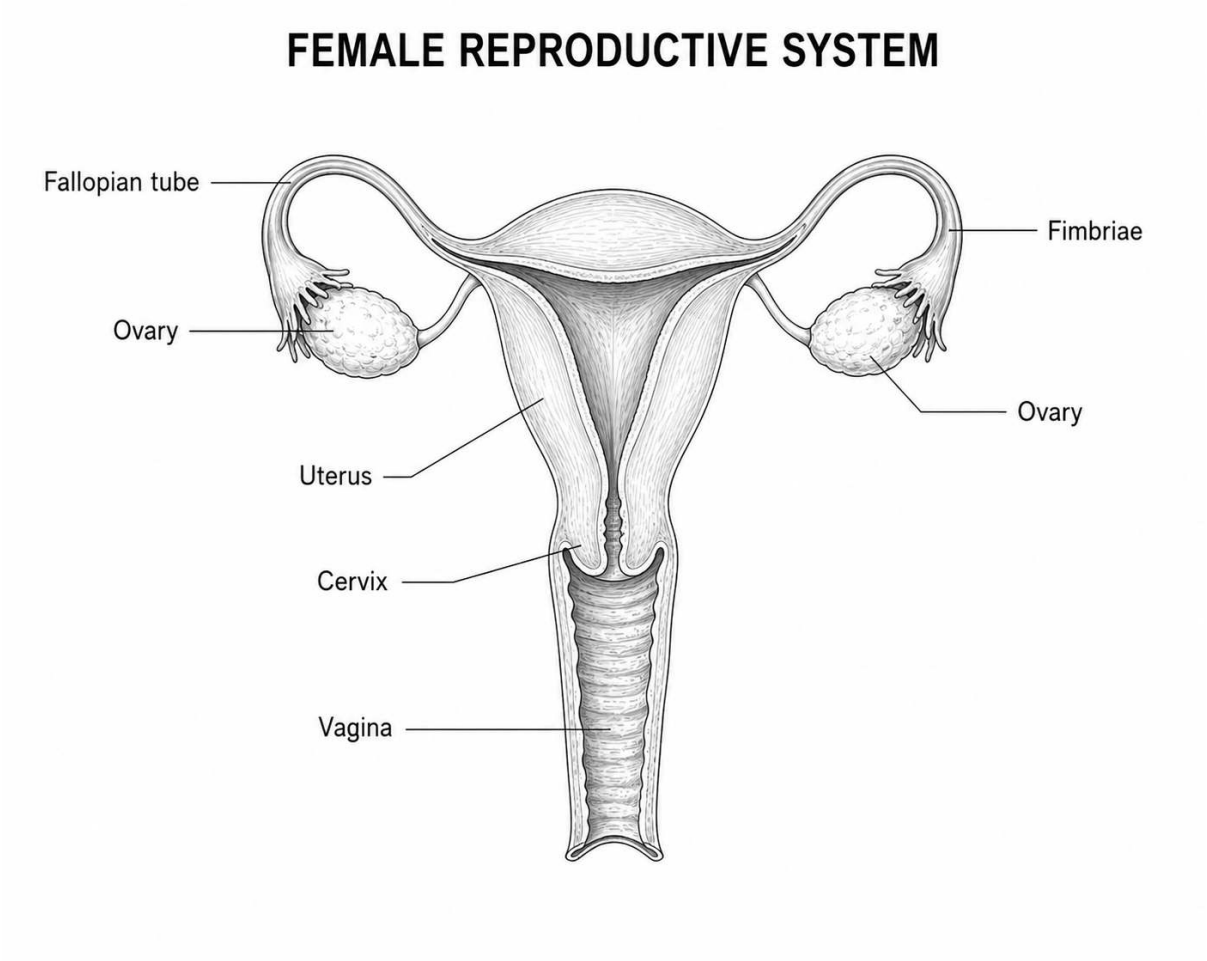


Figure 10.2 *The female reproductive pathway.*

The **ovaries** are the two almond-shaped glands in the lower abdomen, the female counterpart of the testes, and like them they have two jobs. They make the **ova** (egg cells), the female sex cells, and they make the female sex hormones, **oestrogen** and **progesterone**. Unlike the testes, which make sperm continuously, the ovaries release usually one mature ovum about once a month. Inside each ovary the immature ova sit in tiny sacs called follicles, and in each cycle one follicle grows, ripens its ovum, and bursts to release it, the event of ovulation. The ovaries also alternate roughly month by month, so the two share the work over time. A girl is born with all her follicles already present, a fixed store that slowly declines through life, which is the deep reason a woman's fertile years have a natural end at menopause while a man can father children much later. This single fact, a fixed store of ova set before birth, shapes much of female reproductive life.

When an ovum is released it is caught by a **fallopian tube** (uterine tube), one of two tubes that lead from near each ovary to the uterus. The fallopian tube carries the ovum toward the uterus, and it is here, in the tube, that fertilization usually happens if sperm are present. The **uterus** (womb) is a muscular, pear-shaped organ where a fertilized ovum implants and grows

into a baby; its thick muscular wall can stretch enormously during pregnancy and then contract powerfully to push the baby out at birth. Its lining, the **endometrium**, is built up and shed each month in the menstrual cycle, the building and shedding that the hormones of section 10.6 control. The lower neck of the uterus is the **cervix**, a narrow muscular gateway that stays tightly closed through pregnancy to hold the baby in and then widens dramatically in labour to let it out; it also produces mucus whose thickness changes across the cycle, helping or hindering the passage of sperm. The cervix opens into the **vagina**, the passage that receives the penis during intercourse and through which the baby is born. So the female tract is a connected path from ovary to outside, designed to bring sperm and ovum together and then to house the result.

10.4 The sex hormones and their control

The reproductive systems are run by hormones, and the control follows the familiar hypothalamus-pituitary axis of Chapter 8. The hypothalamus signals the pituitary, which releases two hormones, **follicle-stimulating hormone (FSH)** and **luteinising hormone (LH)**, that act on the testes or ovaries; these in turn make the sex hormones, which act on the body and feed back to control the axis. The same three-step chain that controls the thyroid controls reproduction, learned once and used again. The economy of this is worth noticing: the body does not build a separate control system for each gland but reuses one design, the hypothalamus-pituitary axis, plugging a different target gland onto the end of it each time. The thyroid, the adrenal cortex and now the gonads all hang from the same kind of chain, differing only in the releasing hormone, the pituitary hormone and the gland at the end. A student who has understood the thyroid axis of Chapter 8 already understands the framework here and need only learn the new names that fill it.

In the **male**, FSH and LH drive the testes to make sperm and to secrete **testosterone**. Testosterone is the main male sex hormone: it brings about the male characteristics that appear at puberty (deeper voice, facial and body hair, muscle growth), drives sperm production, and maintains the male reproductive tissues. Its level is fairly steady from day to day, held there by the same negative feedback that steadies the thyroid: a rising testosterone level feeds back to the hypothalamus and pituitary and eases their drive, so the level is kept around a set point. This steadiness is the key contrast with the female, where the hormones are deliberately made to swing in a monthly rhythm. The muscle-building action of testosterone, met here, is also why related steroids are sometimes misused by athletes to build muscle, a misuse a pharmacist should recognise, since it carries real harm.

In the **female**, FSH and LH drive the ovaries through a monthly cycle to mature and release an ovum and to secrete **oestrogen** and **progesterone**. Oestrogen brings about the female

characteristics at puberty and builds up the uterine lining; progesterone prepares and maintains that lining for a possible pregnancy. Unlike the steady male hormones, the female hormones rise and fall in a regular monthly pattern, and that pattern is the menstrual cycle of the next section. Both oestrogen and testosterone are steroid hormones, the fat-soluble kind from Chapter 8 that cross into the cell and act on its genes, which is why their effects are slow to appear and long-lasting, shaping the whole body over the years of puberty.

10.5 Spermatogenesis and oogenesis

The making of the sex cells is called **gametogenesis**: **spermatogenesis** in the male and **oogenesis** in the female. Both produce sex cells with half the usual number of chromosomes, so that when sperm and ovum join, the normal number is restored. But the two processes differ in striking ways, set out in Table 10.1, and comparing them is a favourite exam task.

Table 10.1: Spermatogenesis versus oogenesis

Feature	Spermatogenesis	Oogenesis
Site	Seminiferous tubules (testes)	Ovaries
Begins	At puberty	Before birth
Continues	Throughout life, continuously	Until menopause, one a month
Cells per parent cell	Four functional sperm	One ovum (+ polar bodies)
Number produced	Millions per day	A few hundred in a lifetime
Cell size	Small, motile (tail)	Large, non-motile, food-rich

Spermatogenesis, the formation of sperm, takes place in the seminiferous tubules of the testes, shown as a sequence in Figure 10.3. It begins at puberty and continues throughout life. A parent cell divides and matures through several stages, and crucially each parent cell gives rise to four sperm. The process is continuous and prolific: a healthy man makes many millions of sperm every day, and the whole sequence for one sperm takes a little over two months. The finished sperm is a tiny, streamlined cell built for one task, reaching and fertilising an ovum, and its three parts each serve that task. The **head** carries the genetic material and is tipped with a cap (the acrosome) full of enzymes that help it break into the ovum. The **midpiece** is packed with the energy-making machinery (mitochondria) that powers the journey. And the **tail** lashes from side to side to drive the sperm forward through the female tract. So the sperm is the most stripped-down cell in the body, carrying only what it needs to deliver its genes and nothing more, the opposite of the large, well-stocked ovum. The two sex cells are specialised in opposite directions for the same shared goal.

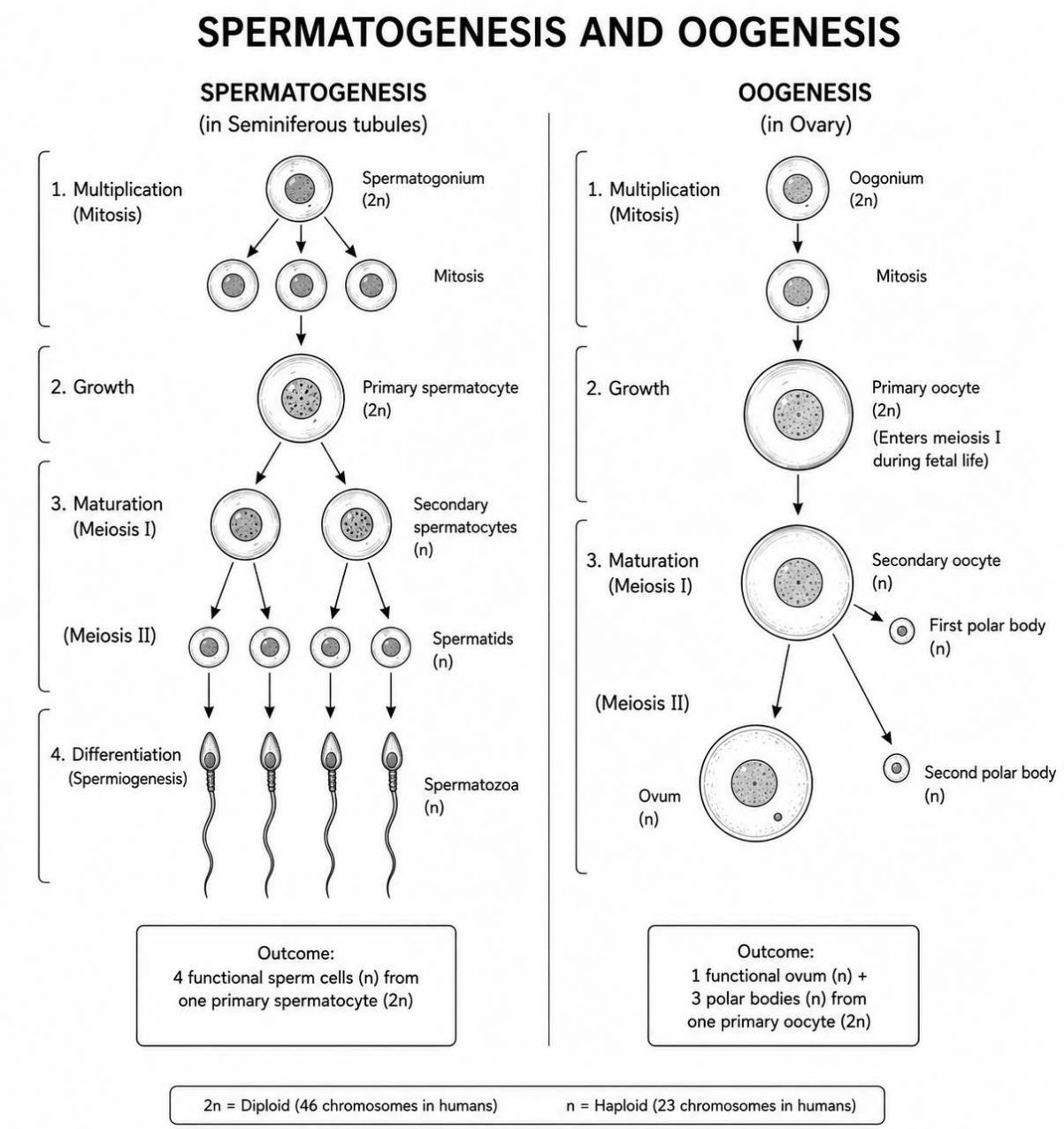


Figure 10.3 *Spermatogenesis and oogenesis compared.*

Oogenesis, the formation of ova, is different in almost every respect. It begins before birth: a baby girl is born with all the immature egg cells she will ever have, far fewer than the sperm a man makes, and they wait, paused, for years. From puberty, usually one matures and is released each month through the reproductive years, so a woman releases only a few hundred ova in a lifetime. And where a parent cell in the male makes four equal sperm, in the female it makes effectively one ovum, the unequal divisions concentrating the cell's material and food into a single large egg cell while the spare portions (the polar bodies) are discarded. So the male strategy is many small cheap cells made continuously, and the female strategy is few

large well-provisioned cells made one at a time, each difference fitting the different roles the two cells play.

10.6 The menstrual cycle

The **menstrual cycle** is the regular monthly sequence, lasting about 28 days on average, by which the female body prepares an ovum and readies the uterus for a possible pregnancy. If no pregnancy occurs, the prepared lining is shed and the cycle begins again. It is driven by the four hormones from section 10.4, FSH and LH from the pituitary and oestrogen and progesterone from the ovary, rising and falling in a set pattern, plotted in Figure 10.4. The cycle is usually described in phases, counting from the first day of bleeding.

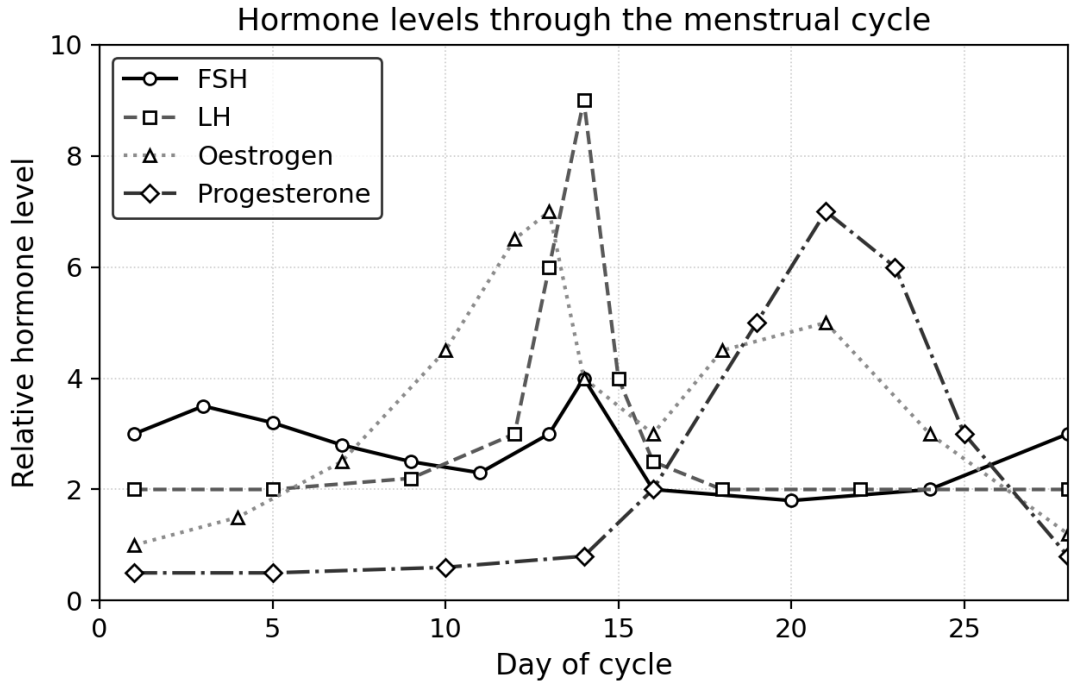


Figure 10.4 *Hormone levels through the menstrual cycle.*

In the first few days comes **menstruation** itself (about days 1 to 5), when the thickened uterine lining of the previous cycle, no longer needed, is shed as the monthly period. At the same time, FSH from the pituitary begins to stimulate a follicle in the ovary to mature, carrying an ovum. As that follicle grows it secretes **oestrogen**, which rises through the next week or so and rebuilds the uterine lining, thickening it again. This building-up phase runs to about the middle of the cycle.

Around the middle, about day 14, a surge of **LH** from the pituitary triggers **ovulation**, the release of the mature ovum from the ovary into the fallopian tube. This is the fertile point of the cycle, the only time an ovum is available to be fertilised, which is why it matters so much

in both achieving and avoiding pregnancy. After ovulation, the emptied follicle turns into a structure called the corpus luteum, which secretes **progesterone** (along with oestrogen). Progesterone maintains and further prepares the uterine lining, making it ready to receive a fertilised ovum, through the second half of the cycle.

What happens next depends on whether the ovum is fertilised. If it is not, the corpus luteum breaks down after about two weeks, so progesterone and oestrogen fall sharply; without these hormones to maintain it, the uterine lining is shed, menstruation begins, and the cycle starts over. If the ovum is fertilised and a pregnancy begins, the corpus luteum is kept going by a signal from the early embryo, so the hormones do not fall, the lining is not shed, and the periods stop, often the first sign of pregnancy. The whole cycle is a beautiful piece of timed hormonal control, and understanding it is the basis for understanding the contraceptive pill, which works by supplying steady hormones that prevent the FSH and LH surge and so stop ovulation.

It helps to see that the cycle is really two cycles running together in step, one in the ovary and one in the uterus, kept in time by the hormones. In the ovary the events are the maturing of the follicle, ovulation, and the corpus luteum; in the uterine lining the matching events are the shedding (the period), the rebuilding under oestrogen (often called the proliferative phase), and the maintenance under progesterone (the secretory phase, when the lining is made ready to receive an embryo). The oestrogen made by the growing follicle drives the uterine rebuilding, and the progesterone made by the corpus luteum drives the uterine maintenance, so the ovary's hormones keep the uterus in step with it. Seeing the two cycles side by side is the clearest way to hold the whole sequence together, because each ovarian event has its matching uterine event. This coordination is also why a disturbance of the hormones, as in the polycystic ovary syndrome of Chapter 9, throws the periods out of their regular rhythm.

> **Quick-recall box 10.1: The menstrual cycle** About 28 days. Menstruation (days 1 to 5): lining shed. Follicular phase: FSH matures a follicle, oestrogen rises and rebuilds the lining. Ovulation (about day 14): LH surge releases the ovum. Luteal phase: corpus luteum makes progesterone, maintaining the lining. No pregnancy: hormones fall, lining shed, cycle repeats.

10.7 Fertilization and pregnancy

Fertilization is the joining of a sperm and an ovum to form a single new cell, the **zygote**, which carries genetic material from both parents and is the beginning of a new individual. It usually takes place in the fallopian tube: after intercourse, sperm swim up through the uterus and into the tube, and although millions set out, only one penetrates and fuses with the ovum.

Once one sperm has entered, the ovum blocks the rest, so the chromosome number stays correct.

The journey and its timing are worth a moment, because they explain why fertilisation is possible only around a narrow window. The released ovum survives for only about a day, and sperm survive for a few days in the female tract, so fertilisation can happen only if intercourse falls within a few days around ovulation. This narrow fertile window is the basis both of natural family planning and of understanding why timing matters in trying to conceive. The few sperm that reach the ovum must then get through its outer coat, and this is where the enzyme-filled cap on the sperm head earns its place, helping to digest a path in; the moment one sperm fuses, the ovum changes its coat to shut the others out. It is also worth noting that it is the sperm that carries the chromosome deciding the baby's sex, so it is the father's sperm, not the mother's ovum, that determines whether the child is a boy or a girl, a point of real importance given the social weight often wrongly placed on it.

The zygote then begins to divide as it travels down the tube to the uterus, and after a few days it **implants** into the prepared uterine lining, where it will grow. The implanted embryo develops the **placenta**, a remarkable organ that grows into the uterine wall and acts as the meeting point between the mother's blood and the baby's: across it the baby receives oxygen and nutrients from the mother and passes back its waste, without the two bloodstreams actually mixing. The baby is joined to the placenta by the umbilical cord, which carries its blood to and from this exchange surface. The arrangement is elegant, because it lets the mother do the baby's breathing, feeding and waste-clearing for it, standing in for the lungs, gut and kidneys the baby cannot yet use, until birth lets those organs take over. In effect the placenta is a temporary organ that performs several of the jobs this whole book has described, on the baby's behalf, for nine months. The placenta is also an endocrine organ, taking over the making of oestrogen and progesterone to maintain the pregnancy. The early embryo, and then the placenta, releases a hormone (human chorionic gonadotropin, hCG) that keeps the corpus luteum alive in the first weeks; it is this hormone that pregnancy tests detect. Pregnancy lasts about 40 weeks, around nine months, during which the single zygote grows into a fully formed baby and the mother's body adapts in many ways to support it.

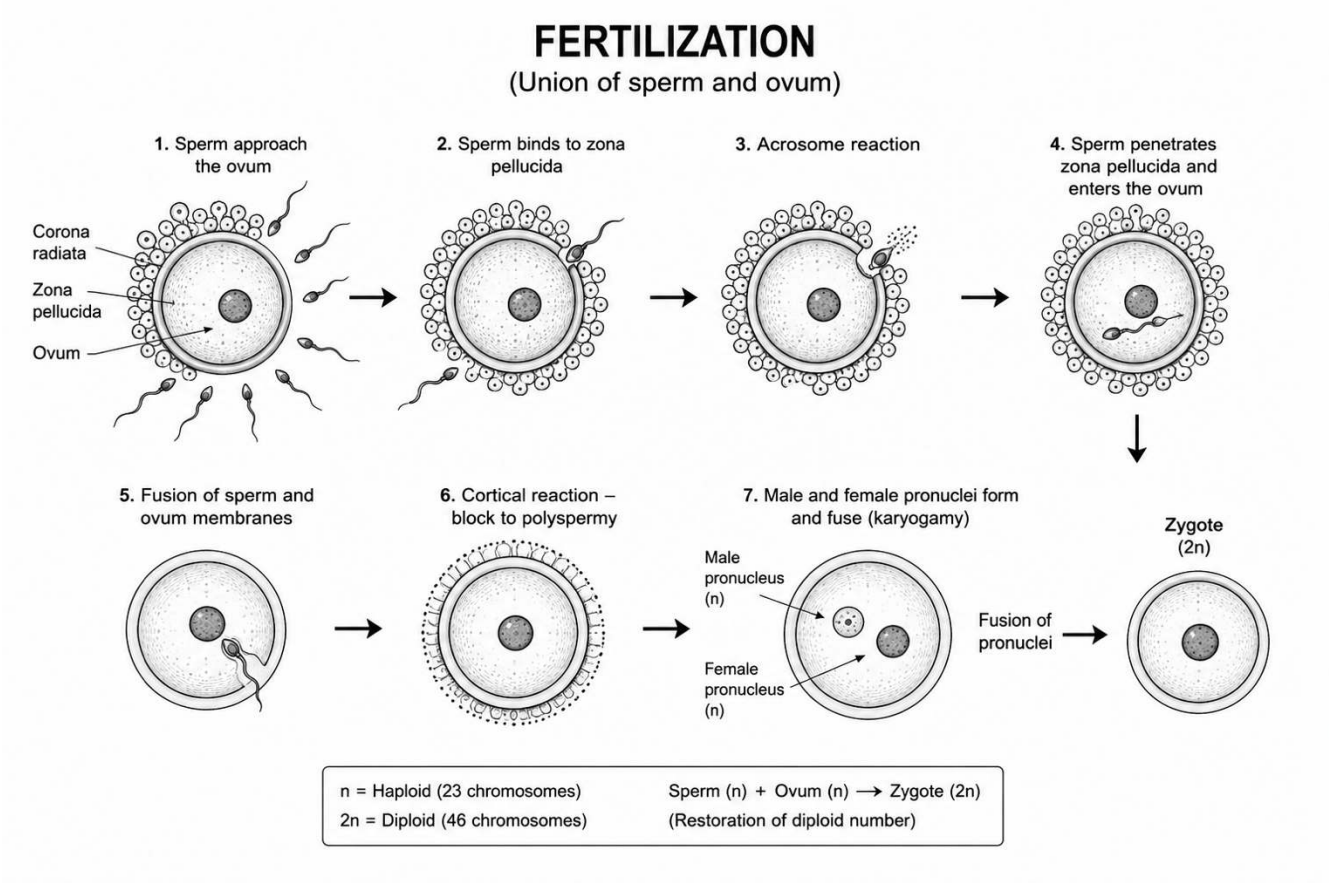


Figure 10.5 Fertilization

Pregnancy is usually divided into three roughly equal stages called trimesters, and knowing the broad shape of each is useful. In the first trimester the basic body plan is laid down and all the major organs begin to form, which is why this is the most vulnerable period: harmful substances, infections or some drugs taken now can disturb the forming organs and cause birth defects. In the second trimester the baby grows and its organs mature, and the mother usually feels well. In the third trimester the baby puts on most of its weight and prepares for life outside, and the mother's body readies for birth. Throughout, the mother's heart, lungs and kidneys all work harder to support two, and her blood volume rises, which is one reason her physiology, and her response to medicines, changes during pregnancy.

The vulnerability of the first trimester is the single most important point for a pharmacy student to carry away, because it is when the warning to avoid unnecessary medicines is most urgent. A drug that would be harmless to the mother can still harm the forming baby, so the safe default in early pregnancy is to use a medicine only when it is genuinely needed and known to be safe, a judgement a pharmacist helps make every day.

A pharmacy note belongs here. Because the placenta lets substances pass from mother to baby, many drugs taken by a pregnant woman can cross it and reach the developing baby,

where they may cause harm, especially in the early weeks when the organs are forming. This is why great care is taken with medicines in pregnancy, and why a pharmacist always checks before supplying a medicine to a pregnant woman. The physiology of the placenta becomes, directly, a rule of safe prescribing.

10.8 Parturition

Parturition is childbirth, the process by which the baby is delivered from the uterus at the end of pregnancy. It is brought about by powerful contractions of the muscular wall of the uterus, which push the baby down through the cervix, which widens to let it pass, and out through the vagina. The contractions build in strength and frequency through labour until the baby is born, followed shortly by the placenta, whose delivery is sometimes called the afterbirth. Labour is usually described in three stages: the first, in which the cervix gradually widens enough to let the baby through; the second, in which the strong contractions push the baby out; and the third, in which the placenta is expelled. The whole process can take many hours, especially for a first baby, and it is one of the most demanding events the body undergoes.

The hormone that drives the contractions is **oxytocin**, from the posterior pituitary of Chapter 8, and parturition is the textbook example of the **positive feedback** named in that chapter. As labour begins, the baby's head presses on and stretches the cervix; this stretch triggers the release of oxytocin, which strengthens the contractions, which push the baby harder against the cervix, which stretches it more, which releases still more oxytocin. The loop builds on itself, the contractions growing stronger and stronger, until the baby is delivered and the stretching stops, breaking the loop. This is exactly why positive feedback is the rare exception that Chapter 8 reserved for a process that must build quickly to a definite end: childbirth is that process. After birth, oxytocin also drives the release of milk from the breasts when the baby feeds, and a synthetic form of oxytocin is used in medicine to start or strengthen labour, a direct application of the physiology described here.

It is worth closing the chapter by drawing the medicines together, because the reproductive system is one of the most pharmacologically managed of all. The contraceptive pill uses steady doses of oestrogen and progesterone (or progesterone alone) to switch off the FSH and LH surge and so prevent ovulation, a direct use of the feedback that controls the cycle. Fertility treatments do the opposite, giving hormones to stimulate the ovary to release eggs. Hormone therapy is used to ease the effects of the fall in oestrogen at menopause. And the hormones of pregnancy and birth, hCG in pregnancy tests and oxytocin in labour, are used in diagnosis and obstetrics. Every one of these rests on the physiology of this chapter, which is

why a pharmacy student who understands the sex hormones and their control already understands the logic of a large and widely used group of medicines.

10.9 Chapter summary

The reproductive system exists not to keep the individual alive but to make the next generation, and it matures at puberty under hormonal control. The male system centres on the testes, which make sperm in the seminiferous tubules and testosterone in between, with the sperm maturing in the epididymis, travelling through the vas deferens, mixed with fluid from the seminal vesicles and prostate into semen, and delivered through the urethra. The female system centres on the ovaries, which make ova and the hormones oestrogen and progesterone, with the released ovum caught by a fallopian tube where fertilization occurs, the uterus housing and nourishing a developing baby, and the cervix and vagina forming the lower tract. Both gonads are controlled by the hypothalamus-pituitary axis through FSH and LH.

The sex cells are made by gametogenesis: spermatogenesis makes four small sperm from each parent cell, continuously and in huge numbers from puberty, while oogenesis makes effectively one large ovum from each parent cell, from a fixed store laid down before birth and released about one a month. The menstrual cycle, about 28 days, runs on the four hormones: menstruation sheds the old lining, FSH matures a follicle whose oestrogen rebuilds the lining, an LH surge causes ovulation around day 14, and the corpus luteum's progesterone maintains the lining; if no pregnancy follows, the hormones fall and the lining is shed to begin again. Fertilization of an ovum by a sperm in the fallopian tube forms a zygote, which implants in the uterus and develops a placenta that exchanges oxygen, nutrients and waste between mother and baby and maintains the pregnancy of about 40 weeks. Parturition, childbirth, is driven by oxytocin through positive feedback, the contractions building on themselves until the baby is born. With the system that makes new life now described, the final chapter turns to two kinds of disease that touch it: the sexually transmitted infections that spread through this system, and cancer, the disease of uncontrolled growth that can arise in any tissue of the body.

10.10 Self-assessment

A. Multiple-choice questions

1. Sperm are produced in the:

   (a) epididymis (b) prostate gland (c) seminiferous tubules of the testes (d) vas deferens. Answer: (c).

2. The main male sex hormone is:

(a) oestrogen (b) testosterone (c) progesterone (d) oxytocin. Answer: (b).

3. Fertilization usually takes place in the:

   (a) uterus (b) ovary (c) fallopian tube (d) vagina. Answer: (c).

4. Ovulation in a typical 28-day cycle occurs around day:

   (a) 1 (b) 7 (c) 14 (d) 28. Answer: (c).

5. The hormone whose surge triggers ovulation is:

   (a) FSH (b) LH (c) progesterone (d) oxytocin. Answer: (b).

6. In spermatogenesis, each parent cell gives rise to ____ sperm:

   (a) one (b) two (c) four (d) eight. Answer: (c).

7. The organ that exchanges oxygen and nutrients between mother and baby is the:

   (a) uterus (b) placenta (c) cervix (d) corpus luteum. Answer: (b).

8. The hormone that drives the contractions of childbirth by positive feedback is:

   (a) progesterone (b) oxytocin (c) FSH (d) testosterone. Answer: (b).

B. Short-answer questions (2–5 marks)

1. Describe the functions of the testes. The testes have two functions: they produce sperm, the male sex cells, in the seminiferous tubules, and they secrete the male sex hormone testosterone in the cells between the tubules. The testes lie outside the body in the scrotum because sperm production needs a temperature slightly below body heat.

2. Compare spermatogenesis and oogenesis. Spermatogenesis makes sperm in the testes, begins at puberty, is continuous, produces huge numbers, and gives four sperm from each parent cell. Oogenesis makes ova in the ovaries, begins before birth from a fixed store, releases about one ovum a month, and gives effectively one ovum (plus discarded polar bodies) from each parent cell. *(High-yield.)*

3. Outline the hormonal control of the menstrual cycle. FSH from the pituitary matures an ovarian follicle, which secretes oestrogen that rebuilds the uterine lining. A surge of LH around day 14 triggers ovulation. The emptied follicle becomes the corpus luteum, which secretes progesterone to maintain the lining. If there is no pregnancy, the corpus luteum breaks down, the hormones fall, and the lining is shed as menstruation. *(High-yield.)*

4. What is fertilization, and where does it occur? Fertilization is the joining of a sperm and an ovum to form a single new cell, the zygote, which carries genetic material from both parents. It usually occurs in the fallopian tube, where sperm that have swum up from the uterus meet the released ovum, and only one sperm fuses with it.

5. Describe the structure and role of the placenta. The placenta is an organ that grows into the uterine wall during pregnancy and forms the meeting point between the mother's blood and the baby's. Across it the baby receives oxygen and nutrients and returns waste, without the bloodstreams mixing, and it also makes the hormones that maintain the pregnancy.

6. Explain how oxytocin acts in childbirth as positive feedback. As labour begins, the baby's head stretches the cervix, which triggers the release of oxytocin from the pituitary. Oxytocin strengthens the uterine contractions, which press the baby harder on the cervix and stretch it more, releasing yet more oxytocin. This self-building loop is positive feedback, and it continues until the baby is born.

C. Long-answer questions (10 marks)

1. Describe the anatomy of the female reproductive system and the events of the menstrual cycle. A full answer describes the ovaries (making ova and the hormones oestrogen and progesterone), the fallopian tubes (site of fertilization), the uterus and its endometrium, the cervix and the vagina; then the menstrual cycle phase by phase: menstruation, the oestrogen-driven rebuilding of the lining, the LH surge and ovulation around day 14, and the progesterone-driven maintenance by the corpus luteum, with the fall in hormones leading to the next period. A labelled diagram (Figure 10.2) and the hormone graph (Figure 10.4) should be included. *(High-yield.)*

2. Compare spermatogenesis and oogenesis, and explain fertilization. A full answer sets the two processes side by side (site, timing, number produced, cells per parent cell, continuous versus one-at-a-time) and explains that both halve the chromosome number; then describes fertilization in the fallopian tube, the fusion of one sperm with the ovum to form the zygote, and the restoration of the full chromosome number.

3. Describe the main events of pregnancy and parturition. A full answer covers fertilization forming the zygote, its division and implantation in the uterus, the development and role of the placenta (exchange and hormone production), the maintenance of pregnancy for about 40 weeks; then parturition by uterine contractions driven by oxytocin through positive feedback, with the cervix widening and the baby delivered, followed by the placenta.

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Chapter 11: Sexually Transmitted Diseases and Cancer

Learning outcomes

After working through this chapter the student will be able to:

1. Explain how sexually transmitted diseases spread and why they matter.
2. Describe the cause, effect on the immune system and course of AIDS.
3. Describe the cause, stages and treatment of syphilis.
4. Describe the cause, features and treatment of gonorrhea.
5. Define cancer and explain its causes (etiology).
6. Explain the pathogenesis of cancer, including the difference between benign and malignant tumours and the meaning of metastasis.

These outcomes serve CO3 (etiology and development of disease, including cancer), CO4 and CO5.

11.1 Two diseases of the cell

This last chapter takes up two topics the syllabus places together, and although they look unrelated at first, they share a thread. Both are diseases that begin at the level of the cell. A sexually transmitted infection is a foreign organism, a virus or a bacterium, invading the body's cells; cancer is the body's own cell breaking the rules that govern its growth. In both, the trouble starts small, inside or between cells, and then spreads. Keeping that shared idea in view helps the chapter hang together: the first half is about cells invaded from outside, the second about cells gone wrong from within.

The chapter first covers the three sexually transmitted diseases the syllabus names, AIDS, syphilis and gonorrhea, which spread chiefly through sexual contact and which a pharmacist meets both as diseases to treat and as conditions to help prevent. It then turns to cancer, one of the most important diseases in all of medicine, explaining what it is, what causes it, and how it develops. Throughout, two threads from earlier chapters return: the immune system and its T-cells from Chapter 8, which AIDS destroys, and the controlled cell division that cancer escapes.

A word on why these diseases matter to a pharmacy student in particular. The sexually transmitted diseases are treated almost entirely with medicines, antibiotics for the bacterial ones and antiviral drugs for HIV, and their control depends heavily on people taking those medicines correctly and completing courses, which is the daily work of a pharmacist. Cancer, meanwhile, is treated with some of the most powerful and hazardous drugs in the whole

pharmacy, drugs that must be handled, dosed and monitored with great care. And both areas turn on prevention, where the pharmacist, as an accessible source of advice, has a real role. So this final chapter is not a distant pathology lesson but a direct preparation for the pharmacology and the patient care that the rest of the course will build.

11.2 Sexually transmitted diseases

A **sexually transmitted disease (STD)**, also called a sexually transmitted infection, is an infection passed mainly from person to person through sexual contact. Because they spread through intimate contact, they are best prevented by safe practices, and several can also pass from an infected mother to her baby during pregnancy or birth, which makes them a concern beyond the two partners. They are caused by different organisms, viruses and bacteria, and the cause decides the treatment: bacterial STDs can be cured with antibiotics, while viral ones can often be controlled but not cured. Table 11.1 sets the three named diseases side by side. A common feature worth stating at the outset is that many STDs can be present with mild symptoms or none at all, especially early, so a person may pass on an infection without knowing they carry it, which is exactly why testing and prevention matter so much.

Table 11.1: The three sexually transmitted diseases

Disease	Cause	Type	Curable?	Key point
AIDS	HIV (virus)	Viral	No (controlled by ART)	Destroys CD4 T-cells; immune collapse
Syphilis	Treponema pallidum	Bacterial	Yes (penicillin)	Progresses in stages if untreated
Gonorrhea	Neisseria gonorrhoeae	Bacterial	Yes (antibiotics)	Often silent; rising resistance

The shared theme of the table is the split by cause: the bacterial diseases (syphilis and gonorrhea) are curable with antibiotics, while the viral one (HIV) can be controlled but not cured, the same divide met with the hepatitis viruses in Chapter 5. Prevention, by contrast, is the same for all three: safe sexual practice, testing, and the prompt treatment of partners so the infection is not passed back and forth.

11.3 AIDS

AIDS (acquired immunodeficiency syndrome) is the advanced stage of infection with a virus called **HIV** (human immunodeficiency virus). It is the most serious of the three STDs here,

because of what the virus does: it attacks and destroys the very cells that defend the body against infection.

HIV targets a particular kind of white blood cell, the **CD4 helper T-lymphocyte**, one of the T-cells that mature in the thymus from Chapter 8 and that act as the commanders of the immune response. These helper cells do not kill germs directly; instead they direct and coordinate the rest of the immune system, switching on the cells that do the fighting. That is exactly why losing them is so catastrophic: HIV does not attack the foot soldiers of the immune system but its commanders, so the whole defence falls apart even though many of its other cells are intact. Striking at the coordinator rather than the soldiers is what makes this one virus able to disable the entire immune system. The virus enters these cells, uses them to make copies of itself, and destroys them in the process. Over years, the number of CD4 cells falls steadily, and as it does the immune system is gradually disarmed. This is the pathway from infection to disease: a person may carry HIV for years feeling well, but as the CD4 cells are depleted the body loses its defences, and when they fall low enough the person reaches **AIDS**, the stage at which the weakened immune system can no longer fight off infections.

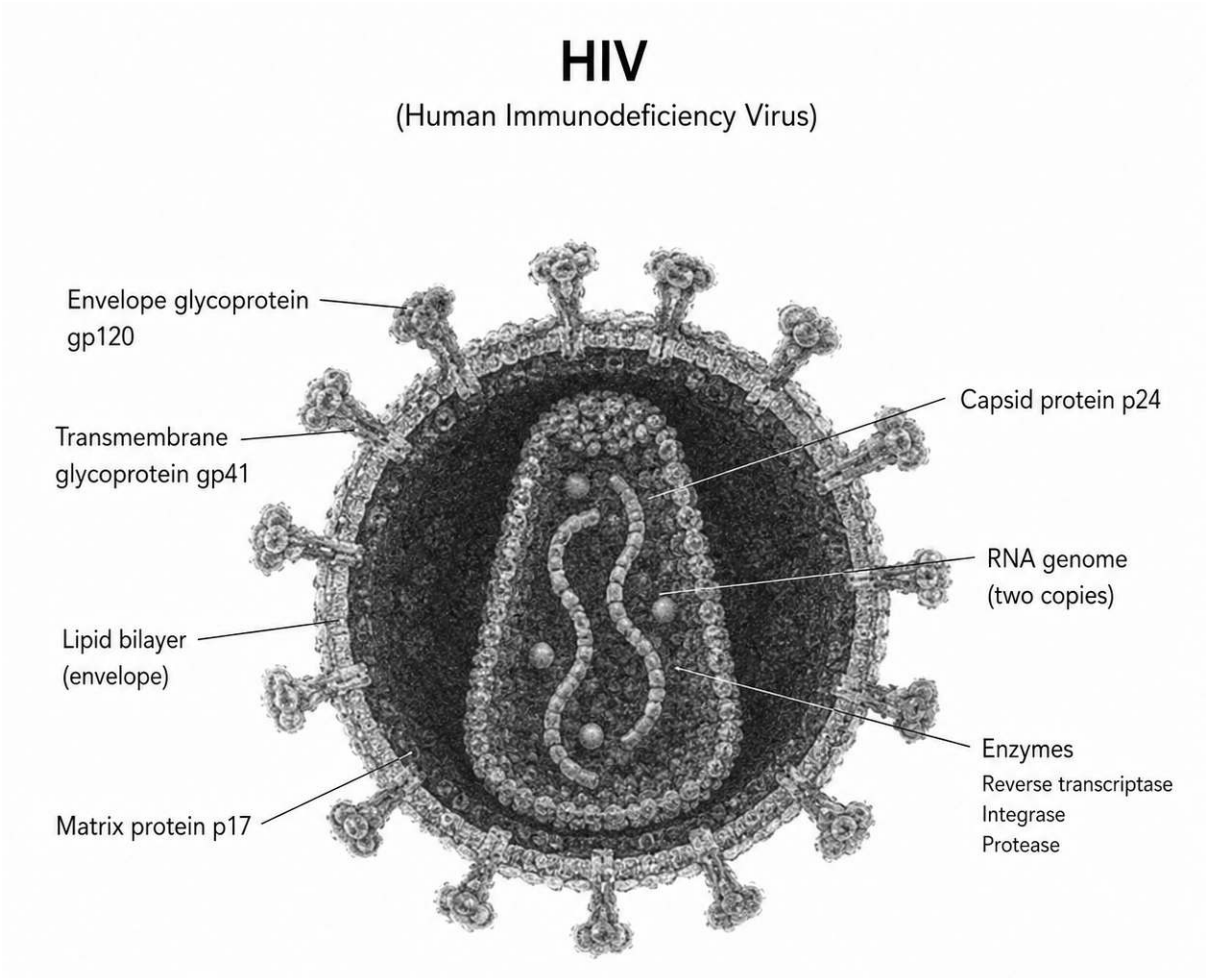


Figure 11.1 The HIV Virus

The result is that the patient falls prey to **opportunistic infections** and certain cancers, illnesses that a healthy immune system would easily hold off but that take hold once it is crippled. One of the most important of these is tuberculosis from Chapter 6, which is a leading cause of death in people with HIV precisely because their weakened immunity lets the latent infection break out, the link flagged in that chapter. So AIDS does not kill directly; it removes the defences and lets other diseases do the damage.

HIV spreads through infected blood and body fluids: through unprotected sex, through infected blood (for example from shared needles or unsafe injections), and from an infected mother to her baby during pregnancy, birth or breastfeeding. There is at present no cure and no fully effective vaccine, but the disease has been transformed by **antiretroviral therapy (ART)**, a combination of drugs that suppresses the virus, keeps the CD4 count up and lets a person live a long and healthy life while greatly reducing the risk of passing the virus on. Prevention rests on safe sex, safe blood and injection practice, and treating infected mothers to protect their babies, and great progress has been made in all of these. For a pharmacist, HIV is a condition where helping patients take a demanding combination of medicines correctly, every day, directly determines whether the treatment works.

It is worth understanding why HIV is so hard to defeat, because it explains both the lack of a cure and the design of the treatment. HIV is a kind of virus that inserts a copy of its own genes into the genetic material of the cells it infects, so the virus becomes hidden inside the body's own cells and cannot simply be flushed out; this is why stopping treatment lets it return. It also changes (mutates) rapidly, so it can become resistant to a single drug quickly, which is the reason it is treated with a combination of several drugs at once, attacking it in different ways so that resistance to all of them together is far less likely. The same logic of combination therapy was met with tuberculosis in Chapter 6, and for the same reason. Understanding that HIV hides in the body's genes and mutates fast is the key to understanding why the treatment is lifelong and combined rather than a short, single-drug cure.

11.4 Syphilis

Syphilis is a sexually transmitted disease caused by a spiral-shaped bacterium called *Treponema pallidum*. Unlike HIV it is a bacterial infection, and so, importantly, it can be cured with antibiotics. What makes syphilis distinctive is that, left untreated, it progresses through recognisable **stages** over months and years, each different from the last, shown in Figure 11.2.

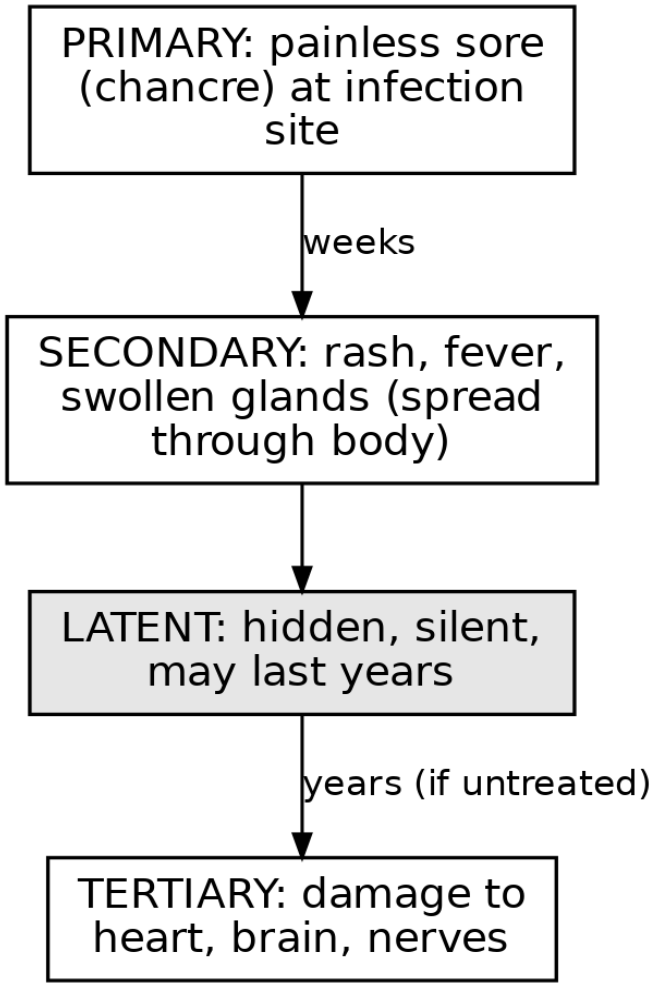


Figure 11.2 *The stages of untreated syphilis.*

In the **primary stage**, a painless sore (called a chancre) appears at the site where the bacteria entered, usually within a few weeks of infection. Because it is painless and heals on its own, it is easily missed, yet the person is infectious. In the **secondary stage**, weeks later, the bacteria have spread through the body and cause a more general illness, classically a skin rash (often on the palms and soles), along with fever and swollen glands; this too settles by itself. The infection then enters a **latent stage**, hidden and silent, sometimes for many years. In some untreated people it finally reaches the **tertiary stage**, in which the long-standing infection damages major organs, including the heart, and the brain and nerves, causing serious and sometimes fatal disease. Syphilis can also pass from an infected mother to her unborn baby, causing congenital syphilis with serious harm, which is why pregnant women are screened for it.

The crucial practical point is that syphilis is curable, especially in its early stages, with antibiotics, penicillin being the classic and still effective treatment. So the whole grim progression through the stages can be stopped at any point by treatment, which is why early

detection is so valuable. The staged course also makes syphilis a clear teaching example of how an untreated infection can hide and then return, a pattern echoed in tuberculosis and in HIV.

The tertiary stage deserves a closer word because of how it links to earlier chapters. When syphilis reaches the brain and nerves, late in untreated disease, it can cause a form of damage once known as neurosyphilis, with effects on movement, sensation and even the mind, including a kind of dementia. So an infection that began as a small painless sore can, decades later and untreated, become a disease of the nervous system covered in the first unit of this book. This long reach through the body is what made syphilis so feared before antibiotics, and it is the strongest argument for treating it early, when a simple course of penicillin cures it completely. The lesson a pharmacist takes is that an STD which seems to have gone away, because its visible signs have healed, may not have left the body at all.

11.5 Gonorrhea

Gonorrhea is a sexually transmitted disease caused by the bacterium *Neisseria gonorrhoeae*. Like syphilis it is bacterial and treatable with antibiotics, but it acts more quickly and locally. It infects the lining of the reproductive and urinary tracts, and its common symptoms are a discharge from the genitals and pain or burning on passing urine, appearing within days to a couple of weeks of infection. The burning on passing urine overlaps with the symptoms of the urinary tract infection from Chapter 7, which is one reason a proper diagnosis matters rather than guessing: the same symptom can come from a simple urinary infection or from a sexually transmitted one, and the two need different management. This is a good example of why a pharmacist refers a patient for testing rather than assuming the cause of a common symptom.

A key difficulty is that gonorrhea, particularly in women, often causes few or no symptoms, so it can go unnoticed and untreated. That matters because, left untreated, the infection can spread upward and cause serious complications: in women it can reach the reproductive organs and cause pelvic inflammatory disease, which can damage the fallopian tubes from Chapter 10 and lead to infertility; in men it can cause inflammation of the reproductive tract; and in both it can occasionally spread through the body. It can also pass from mother to baby during birth, classically causing a serious eye infection in the newborn, which is why newborns' eyes are protected at birth in many places.

Gonorrhea is treated with antibiotics, but it carries a serious modern warning that a pharmacist should know: the bacterium has become increasingly **resistant** to one antibiotic after another, so the choice of effective treatment has narrowed and must follow current guidance. This makes gonorrhea one of the clearest everyday examples of antibiotic

resistance, and a reminder of why antibiotics must be used carefully. As with the other STDs, prevention through safe sex and prompt treatment of partners is central to control.

It is worth drawing the three STDs together before turning to cancer, because they make a useful contrast. All three spread the same way and can be prevented the same way, yet they differ sharply in what they do and how they are handled. Gonorrhea acts fast and locally, causing trouble within days but curable quickly; syphilis acts slowly and in stages, hiding for years before doing its worst, yet also curable; and HIV acts slowest of all, silently destroying the immune system over years, and cannot be cured but can be controlled. The bacterial two yield to antibiotics; the viral one needs lifelong combination therapy. Holding the three side by side, as in Table 11.1, shows how the cause of an infection shapes its whole behaviour and its treatment, the same principle that has organised every disease in this book.

11.6 Cancer: what it is and what causes it

Cancer is not one disease but a large group of diseases that share one defining feature: **uncontrolled cell growth**. Normally, the cells of the body divide only when and where they are needed, under tight control, and they stop when they should; this controlled division is what builds and repairs tissues. In cancer, a cell escapes that control and divides without restraint, and its descendants do the same, so a growing mass of abnormal cells builds up. That, at its simplest, is cancer: cells that will not stop dividing.

It helps to see what a cancer cell does differently from a normal one, because these changes explain the whole behaviour of the disease. A normal cell divides only when signalled to, stops when it should, stays where it belongs, and destroys itself if it becomes badly damaged, by the programmed cell death you met as apoptosis. A cancer cell breaks all of these rules: it divides without waiting for a signal, ignores the signals that should stop it, refuses to destroy itself when damaged, persuades the body to grow new blood vessels to feed the tumour, and finally loses its anchorage and wanders to other tissues. Each of these is a normal control switched off or a normal restraint removed. So a cancer is not a cell doing something new and exotic; it is a cell with its ordinary safeguards disabled one by one, which is why understanding the normal controls is the way to understand the disease.

Cancers are also named according to the tissue they arise from, a piece of vocabulary worth knowing. A cancer of the covering and lining tissues (the commonest kind, including most cancers of the skin, lung, breast and gut) is called a **carcinoma**; a cancer of the connective and supporting tissues such as bone or muscle is a **sarcoma**; and cancers of the blood-forming and immune tissues are the leukaemias and lymphomas. The names recur throughout pathology and pharmacology, so meeting them here, attached to their tissues, makes them easier to hold later.

Etiology: the causes of cancer

Cancer arises from **mutations**, changes in the genes that normally control how a cell divides. The genes involved are of two kinds: genes that drive cell division, which when faulty can become stuck in the on position, and genes that restrain division or trigger a damaged cell to destroy itself, which when faulty can no longer apply the brakes. When enough of these control genes are damaged, the cell loses the governance of its own division and becomes cancerous. So at root, cancer is a disease of damaged genes inside the cell.

What damages those genes are agents called **carcinogens**, and they fall into three groups worth knowing, shown in Figure 11.3:

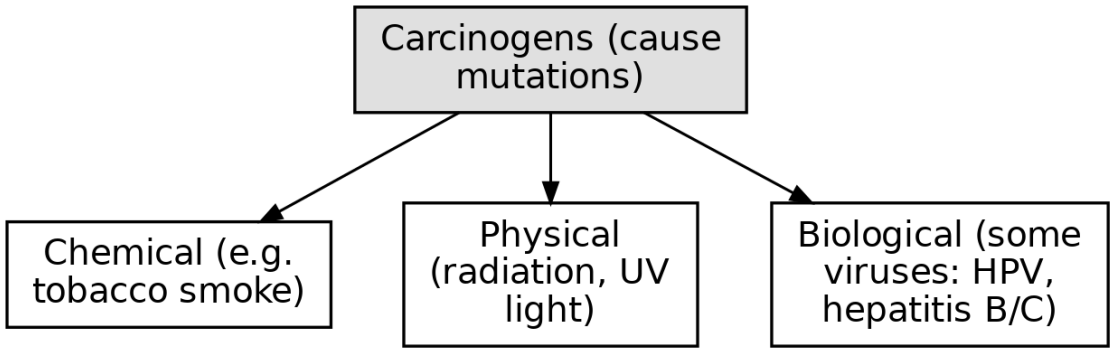


Figure 11.3 *The three types of carcinogen.*

- **Chemical carcinogens:** substances such as those in tobacco smoke, which is the leading preventable cause of cancer, and various industrial and dietary chemicals.
- **Physical carcinogens:** chiefly radiation, including the ultraviolet rays of the sun (a cause of skin cancer) and ionising radiation.
- **Biological carcinogens:** certain viruses and other infections, for example the human papillomavirus that causes cervical cancer, and the hepatitis B and C viruses from Chapter 5 that can lead to liver cancer.

Alongside these, some people inherit a raised risk through faulty genes passed down in the family, and the risk of most cancers rises with age, as mutations accumulate over a lifetime. This is why cancer is largely, though not only, a disease of later life: the longer a person lives, the more chances their cells have had to gather the several mutations a cancer needs, the point that the staged pathogenesis below explains. It also explains why a single exposure rarely causes cancer at once, and why the cancers from smoking or sun usually appear only after years of exposure. The practical message is hopeful: because so many carcinogens are things that can be avoided, such as tobacco, excessive sun and some infections that vaccines now prevent, a large share of cancers can be prevented, which is one of the most important facts in public health.

11.7 The pathogenesis of cancer

Understanding how a cancer develops, its **pathogenesis**, ties the chapter together and explains why cancer is so dangerous. Two ideas matter most: how a normal cell becomes a cancer over time, and how a cancer differs from a harmless growth.

From normal cell to cancer

Cancer does not appear in a single step; it develops gradually, as damage accumulates in a cell's control genes over years. The process is usually described in three stages, shown in Figure 11.3. **Initiation** is the first mutation, the initial genetic damage caused by a carcinogen, which changes a cell but does not by itself make a cancer; the cell looks normal but carries a hidden fault. **Promotion** is the stage in which the changed cell is repeatedly encouraged to divide, often by continued exposure to the same or other agents, expanding into a population of altered cells. **Progression** is the final stage, in which further mutations accumulate and the cells become fully malignant, able to invade and spread. The importance of this three-stage picture is that it shows cancer as a process, not an event: there are years, often, between the first damage and a true cancer, and that gap is the opportunity for prevention (removing the carcinogen, such as stopping smoking, before promotion does its work) and for early detection (finding the changed cells before they progress). The stepwise model is therefore more than biology; it is the basis of how cancer is fought, through prevention at the start and screening in the middle. This stepwise picture explains why cancer usually takes years to develop and why it becomes commoner with age: it takes time and repeated damage for a cell to gather all the changes it needs to become a true cancer.

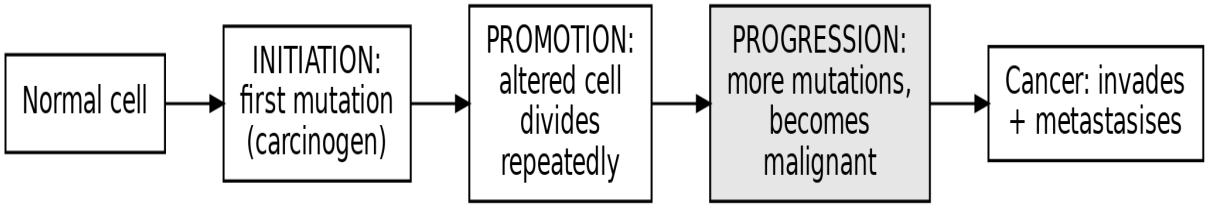


Figure 11.4 *The stages of carcinogenesis.*

Benign and malignant tumours

A **tumour (neoplasm)** is simply a new growth, an abnormal mass of cells, and not every tumour is a cancer. The crucial distinction, set out in Table 11.2, is between benign and malignant tumours. A **benign tumour** grows slowly, stays in one place within a capsule, does not invade surrounding tissues, and does not spread to other parts of the body; it is usually harmless unless its size presses on something important, and removing it usually cures it. A **malignant tumour** is what is meant by cancer: it grows faster, invades and

destroys the surrounding tissues, and, most dangerously, can spread to distant parts of the body.

Table 11.2: Benign versus malignant tumours

Feature	Benign tumour	Malignant tumour (cancer)
Growth	Slow	Faster
Border	Stays local, often capsuled	Invades surrounding tissue
Spread (metastasis)	Does not spread	Spreads via blood and lymph
Effect on the body	Usually harmless (unless pressing)	Destroys tissue; often life-threatening
Treatment	Removal usually curative	Harder, especially once spread

That spread is called **metastasis**, and it is the feature that makes cancer so deadly. Cells break away from the original (primary) tumour, travel through the blood or lymph to other organs, and settle and grow there as new (secondary) tumours. Once a cancer has spread in this way, it is far harder to treat, because it is no longer in one place that can simply be removed. So the danger of cancer lies less in the original growth than in its ability to invade and to seed itself elsewhere. This is why catching cancer early, before it has spread, makes such a difference to whether it can be cured, and why screening programmes that find cancers early are so valuable.

How cancer is treated

A brief look at treatment closes the topic and brings it back to pharmacy. Cancer is treated in three main ways, often in combination. **Surgery** removes a tumour that is still in one place, and is most effective before the cancer has spread. **Radiotherapy** uses focused radiation to kill cancer cells in a particular area. **Chemotherapy** uses drugs that kill rapidly dividing cells, carried in the blood to reach cancer throughout the body, which is why it is used when the cancer has spread or might have. Because chemotherapy drugs attack dividing cells in general, they also harm the body's own fast-dividing tissues, the lining of the gut from Chapter 4, the hair and the blood-forming marrow, which is the source of their well-known side effects. Newer treatments aim more precisely at the specific faults in cancer cells, sparing normal tissue. For a pharmacy student, the anticancer drugs are among the most powerful and most carefully handled medicines of all, and the physiology of this chapter, controlled cell division and its failure, is exactly what they are designed to act on.

Warning signs and the value of early detection

Because early cancer is so much more treatable than late cancer, recognising the warning signs matters. A persistent lump, an unexplained change such as a sore that will not heal, unusual bleeding, a lasting change in the bowel or bladder, a persistent cough or hoarseness, or unexplained weight loss are among the signs that should prompt a person to seek medical advice. None of these means cancer by itself, since most have harmless causes, but they are reasons to be checked. Screening tests, which look for cancer in people before any symptoms appear, are valuable for exactly this reason: they can catch a cancer, or even a pre-cancerous change, while it is still curable. A pharmacist, often the most accessible health professional, has a real part in encouraging people not to ignore warning signs and to take up screening when it is offered.

> **Quick-recall box 11.1: Cancer in brief** Cancer is uncontrolled cell growth from mutations in the genes controlling cell division. Causes (carcinogens): chemical (tobacco), physical (radiation, UV), biological (some viruses). Develops in stages: initiation, promotion, progression. Benign tumour: slow, local, does not spread. Malignant tumour (cancer): invades and metastasises (spreads) through blood and lymph. Early detection saves lives.

11.8 Chapter summary

This chapter covered two kinds of disease that begin at the level of the cell. The sexually transmitted diseases spread mainly through sexual contact, may be silent in their early stages, and divide by cause into the curable bacterial infections and the controllable viral ones. AIDS is the advanced stage of infection with HIV, a virus that destroys the CD4 helper T-cells of the immune system, so that over years the body's defences collapse and it falls prey to opportunistic infections such as tuberculosis; it spreads through blood and body fluids, has no cure, but is controlled by antiretroviral therapy. Syphilis, caused by the bacterium Treponema pallidum, progresses if untreated through primary (a painless sore), secondary (a rash and general illness), latent and tertiary (organ and nerve damage) stages, yet is curable with antibiotics, especially penicillin, at any stage. Gonorrhea, caused by Neisseria gonorrhoeae, infects the reproductive and urinary tracts, often with few symptoms, and can cause infertility if it spreads; it is treatable with antibiotics but is an important example of growing antibiotic resistance.

Cancer is a group of diseases defined by uncontrolled cell growth, arising from mutations in the genes that control cell division, caused by carcinogens that are chemical (tobacco), physical (radiation, UV) or biological (some viruses), with inherited risk and age adding to the picture. It develops in stages, initiation, promotion and progression, over years. A tumour

is a new growth, and the key distinction is between benign tumours, which are slow and local and do not spread, and malignant tumours, true cancers, which invade surrounding tissue and spread to distant sites by metastasis through the blood and lymph, the feature that makes cancer so dangerous and makes early detection so valuable. Across both halves of the chapter the lesson is the same one that has run through the whole book: understand the normal process, here the immune defence and the controlled division of cells, and the disease becomes the clear and explicable failure of it. With this, the study of human anatomy, physiology and pathophysiology that began with the single neuron reaches the body's smallest battles, those fought between and within its cells, and the foundation for the pharmacology that treats them is now complete.

11.9 Self-assessment

A. Multiple-choice questions

1. AIDS is caused by a virus that destroys:
   (a) red blood cells (b) CD4 helper T-cells (c) liver cells (d) nerve cells. Answer: (b).
2. Which infection commonly takes hold in people with AIDS because of their weakened immunity?
   (a) tuberculosis (b) diabetes (c) asthma (d) goitre. Answer: (a).
3. Syphilis is caused by:
   (a) a virus (b) the bacterium Treponema pallidum (c) a fungus (d) the bacterium Neisseria. Answer: (b).
4. The painless sore of early syphilis is called a:
   (a) chancre (b) rash (c) tumour (d) ulcer of the stomach. Answer: (a).
5. Gonorrhea is an important example of growing:
   (a) viral mutation (b) antibiotic resistance (c) hormone deficiency (d) iodine deficiency. Answer: (b).
6. Cancer is best defined as:
   (a) an infection of the blood (b) uncontrolled cell growth (c) a hormone disorder (d) inflammation only. Answer: (b).
7. The spread of cancer to distant parts of the body is called:
   (a) initiation (b) promotion (c) metastasis (d) remission. Answer: (c).
8. Which is a benign tumour's feature?
   (a) invades surrounding tissue (b) spreads to other organs (c) stays local and does not spread
   (b) is always fatal. Answer: (c).

B. Short-answer questions (2–5 marks)

1. Explain how HIV leads to AIDS. HIV infects and destroys the CD4 helper T-cells of the immune system, using them to make copies of itself. Over years the number of CD4 cells falls, so the immune system is gradually disarmed. When the cells fall low enough the person reaches AIDS, the stage at which the weakened immune system can no longer fight off infections and cancers. *(High-yield.)*

2. Describe the stages of syphilis. Primary: a painless sore (chancre) at the site of infection. Secondary: weeks later, a general illness with a skin rash, fever and swollen glands. Latent: a hidden, silent stage that may last years. Tertiary: in some untreated people, serious damage to the heart, brain and nerves. Syphilis is curable with antibiotics at any stage.

3. Why is gonorrhea a concern even when it causes few symptoms? Because it often causes few or no symptoms, especially in women, gonorrhea can go untreated and spread upward, causing pelvic inflammatory disease and damage to the fallopian tubes that can lead to infertility. It can also pass to a baby during birth. Untreated, silent infection is therefore still harmful.

4. Define cancer and name the three types of carcinogen. Cancer is a group of diseases characterised by uncontrolled cell growth, arising from mutations in the genes that control cell division. The three types of carcinogen are chemical (such as tobacco smoke), physical (such as radiation and ultraviolet light) and biological (such as certain viruses). *(High-yield.)*

5. Differentiate between a benign and a malignant tumour. A benign tumour grows slowly, stays in one place, does not invade surrounding tissue and does not spread; it is usually harmless and removable. A malignant tumour (cancer) grows faster, invades and destroys surrounding tissue, and spreads to distant parts of the body by metastasis. *(High-yield.)*

6. What is metastasis, and why does it make cancer dangerous? Metastasis is the spread of cancer cells from the original tumour, through the blood or lymph, to distant organs where they form new secondary tumours. It makes cancer dangerous because once the disease has spread it is no longer in one place that can be removed, so it is much harder to treat, which is why early detection matters.

C. Long-answer questions (10 marks)

1. Describe the cause, effect on the immune system, course and management of AIDS. A full answer identifies HIV as the cause; explains that it destroys the CD4 helper T-cells, so the immune system is gradually weakened; describes the course from symptom-free infection to AIDS as the CD4 count falls, with opportunistic infections such as tuberculosis taking hold;

gives the routes of spread (blood and body fluids, mother to baby); and explains management by antiretroviral therapy and prevention by safe practices, noting there is no cure. *(High-yield.)*

2. Explain the etiology and pathogenesis of cancer. A full answer defines cancer as uncontrolled cell growth from mutations in cell-division control genes; gives the carcinogens (chemical, physical, biological) and the roles of inheritance and age; explains the stepwise development through initiation, promotion and progression; distinguishes benign from malignant tumours; and explains metastasis as the spread that makes cancer dangerous, with the value of early detection. A diagram of the stages or hallmarks (Figure 11.2 or 11.3) should be included. *(High-yield.)*

3. Write notes on syphilis and gonorrhea. For syphilis: cause (Treponema pallidum), the four stages (primary chancre, secondary rash and illness, latent, tertiary organ and nerve damage), spread including to the unborn baby, and cure with antibiotics, especially penicillin. For gonorrhea: cause (Neisseria gonorrhoeae), infection of the reproductive and urinary tracts with discharge and painful urination, the frequent lack of symptoms, complications such as infertility, spread to the newborn's eyes, treatment with antibiotics, and the problem of antibiotic resistance.

References

1. Mohan H. Textbook of Pathology. 8th ed. New Delhi: Jaypee Brothers; 2018.
2. Kumar V, Abbas AK, Aster JC, Deyrup AT. Robbins and Kumar Basic Pathology. 11th ed. Philadelphia: Elsevier; 2022.
3. Porth CM. Pathophysiology: Concepts of Altered Health States. 10th ed. Philadelphia: Wolters Kluwer;
4. Waugh A, Grant A. Ross and Wilson Anatomy and Physiology in Health and Illness. 14th ed. Edinburgh: Elsevier; 2023.
5. Hall JE, Hall ME. Guyton and Hall Textbook of Medical Physiology. 14th ed. Philadelphia: Elsevier;

Glossary

Action potential — A rapid, brief, all-or-none reversal of the membrane voltage that travels along a nerve fibre; the nerve impulse.

Afferent — Carrying signals toward the central nervous system (sensory).

Aldosterone — An adrenal cortex hormone that makes the kidney retain salt and water, raising blood pressure.

Alveolus — A tiny thin-walled air sac in the lung, the site of gas exchange.

Apoptosis — Programmed cell death, by which the body removes damaged or unwanted cells.

Bilirubin — A yellow pigment formed from the breakdown of red blood cells; its build-up causes jaundice.

Carcinogen — An agent (chemical, physical or biological) that causes the mutations leading to cancer.

Carcinoma — A malignant tumour of covering or lining (epithelial) tissue.

Chyme — The creamy, acidic mixture of food and gastric juice that leaves the stomach.

Cirrhosis — Permanent scarring of the liver in which working tissue is replaced by scar.

Corpus luteum — The structure formed from an emptied ovarian follicle after ovulation; it secretes progesterone.

Diabetes mellitus — A chronic disease of high blood glucose from too little insulin action.

Efferent — Carrying signals away from the central nervous system (motor).

Endometrium — The lining of the uterus, built up and shed each menstrual cycle.

Gametogenesis — The making of the sex cells: spermatogenesis in the male, oogenesis in the female.

Glomerular filtration rate (GFR) — The volume of fluid filtered by all the nephrons per minute, about 125 mL/min.

Glomerulus — The knot of capillaries in the nephron where blood is filtered.

Goitre — A visible enlargement of the thyroid gland.

Homeostasis — The maintenance of a steady internal state in the body.

Insulin — The hormone from the pancreatic beta cells that lowers blood glucose.

Metastasis — The spread of cancer cells from the original tumour to distant parts of the body.

Micturition — The act of passing urine.

Nephron — The functional filtering unit of the kidney.

Neuroglia — The supporting cells of nervous tissue.

Neuron — The signal-carrying cell of the nervous system.

Neurotransmitter — A chemical messenger released at a synapse.

Negative feedback — A control in which the result of a process switches off the process that produced it, holding a value steady.

Oogenesis — The formation of ova (egg cells) in the ovary.

Peristalsis — A wave of muscle contraction that propels contents along the gut.

Pepsin — The protein-digesting enzyme of the stomach, active only in acid.

Resting membrane potential — The steady voltage (about −70 mV) across the membrane of a resting neuron.

Spermatogenesis — The formation of sperm in the testes.

Synapse — The junction across which a signal passes from one neuron to the next.

Tumour (neoplasm) — A new abnormal growth of cells; benign if local, malignant (cancer) if it invades and spreads

Consolidated reference list

The following standard texts, in their latest available editions, are the prescribed and supporting references for this course. They are cited by number at the end of each chapter.

1. Waugh A, Grant A. *Ross and Wilson Anatomy and Physiology in Health and Illness.* 14th ed. Edinburgh: Elsevier; 2023.
2. Tortora GJ, Derrickson B. *Principles of Anatomy and Physiology.* 16th ed. Hoboken (NJ): Wiley;
3. Hall JE, Hall ME. *Guyton and Hall Textbook of Medical Physiology.* 14th ed. Philadelphia: Elsevier; 2021.
4. Chatterjee CC. *Human Physiology.* Vol. 1 & 2. Kolkata: Academic Publishers; 2020.
5. Mohan H. *Textbook of Pathology.* 8th ed. New Delhi: Jaypee Brothers; 2018.
6. Porth CM. *Pathophysiology: Concepts of Altered Health States.* 10th ed. Philadelphia: Wolters Kluwer; 2019.
7. Kumar V, Abbas AK, Aster JC, Deyrup AT. *Robbins and Kumar Basic Pathology.* 11th ed. Philadelphia: Elsevier; 2022.
8. Barrett KE, Barman SM, Brooks HL, Yuan JX. *Ganong's Review of Medical Physiology.* 26th ed. New York: McGraw-Hill; 2019.

Subject index

The numbers refer to the chapter in which the topic is principally treated.

A — Acetylcholine, 1, 3; Action potential, 1; Adrenal glands, 8; AIDS, 11; Aldosterone, 7, 8; Alveoli, 6; Alzheimer's disease, 3; Asthma, 6; Autonomic nervous system, 1.

B — Basal ganglia, 2, 3; Benign tumour, 11; Bile, 4; Bilirubin, 4, 5; Brain, 2; Brain stem, 2.

C — Cancer, 11; Cerebellum, 2; Cerebrospinal fluid, 2; Cerebrum, 2; Chyme, 4; Cirrhosis, 5; COPD, 6; Corpus luteum, 10.

D — Depression, 3; Diabetes mellitus, 9; Digestion, 4.

E — Endocrine system, 8; Epilepsy, 3.

F — Fertilization, 10; Fatty liver disease, 5.

G — Gastric acid, 4; Glomerulus, 7; Goitre, 9; Gonorrhea, 11.

H — Haemoglobin, 6; Hepatitis, 5; Hormones, 8; Hyperthyroidism, 9; Hypothalamus, 2, 8; Hypothyroidism, 9.

I — Inflammatory bowel disease, 5; Insulin, 8, 9.

J — Jaundice, 5.

K — Kidney, 7.

L — Liver, 4; Lung volumes, 6.

M — Meninges, 2; Meningitis, 3; Menstrual cycle, 10; Metastasis, 11; Migraine, 3; Micturition, 7.

N — Negative feedback, 8; Nephron, 7; Neuron, 1; Neurotransmitters, 1.

O — Oogenesis, 10; Ovaries, 10.

P — Pancreas, 4, 8; Parathyroid, 8; Parkinson's disease, 3; Peptic ulcer, 5; Pituitary gland, 8; Placenta, 10; Polycystic ovary syndrome, 9.

R — Reflex arc, 2; Renal failure, 7; Reproductive system, 10; Respiratory system, 6; Renin-angiotensin-aldosterone system, 7.

S — Schizophrenia, 3; Spermatogenesis, 10; Spinal cord, 2; Stomach, 4; Stroke, 3; Synapse, 1; Syphilis, 11.

T — Thymus, 8; Thyroid gland, 8; Tuberculosis, 6.

U — Urine formation, 7; Urinary tract infection, 7.