Biochemistry

Unit 4 · Nucleic Acids, Vitamins and Minerals

DNA and RNA are long chains of nucleotides; vitamins and minerals are the small helpers that let enzymes do chemistry. After this unit you can draw the bases and the double helix, use Chargaff’s rules, compare A, B and Z DNA, tell the three RNAs apart, and link each vitamin and key mineral to its coenzyme, its job and its deficiency disease.

Taught at 8 of 10 | Usually Sem 3 | 8 chapters

About this unit

This unit is about the molecules that carry information and the small nutrients that keep enzymes working. It starts with the purine and pyrimidine bases, joins them to sugars and phosphate to make nucleosides and nucleotides, and builds the DNA double helix, its A, B and Z forms, and the three main kinds of RNA. The second half turns to vitamins, most of which become coenzymes, and to the minerals the body needs in large and small amounts. Each chapter uses the one before it: you cannot read a helix without knowing its bases, and you cannot understand a B vitamin without the nucleotide coenzymes it becomes.

Chapters

1. Purine and pyrimidine bases
2. Nucleosides and nucleotides
3. DNA double helix: Watson-Crick model and Chargaff's rules
4. Forms of DNA: A, B and Z ADVANCED
5. Types of RNA: mRNA, tRNA and rRNA
6. Water-soluble vitamins: B complex and C
7. Fat-soluble vitamins: A, D, E and K
8. Macro and micro minerals

How to use this book

- Read the lead paragraph and the figure of each chapter first; they carry the one idea you must keep.
- Cover the solution of each worked example and do it yourself on paper, then compare step by step.
- Answer every “Check yourself” question in your head or in your notebook before you open it.

4.1 Purine and pyrimidine bases

The letters of DNA and RNA are five small, flat molecules called nitrogenous bases. They are rings of carbon and nitrogen atoms, and they come in two families: the purines (adenine and guanine), which have two fused rings, and the pyrimidines (cytosine, thymine and uracil), which have one. The pattern of hydrogen-bond donors and acceptors on each ring decides which base pairs with which, so this chapter is the alphabet for every chapter that follows.

Two parent rings

A **heterocycle** is a ring that contains at least one atom other than carbon. Both base families are heterocycles with nitrogen in the ring.

- **Pyrimidine**: one six-membered ring with nitrogen at positions 1 and 3 (four carbons, two nitrogens).
- **Purine**: a pyrimidine ring fused to a five-membered imidazole ring, nine ring atoms in all, with nitrogen at positions 1, 3, 7 and 9. The two rings share the C4–C5 bond.

The rings are numbered so that the atom which joins the sugar gets a fixed number: **N1 of a pyrimidine** and **N9 of a purine**. Sugar atoms get primes (1′, 2′, …) so they are never confused with ring atoms.

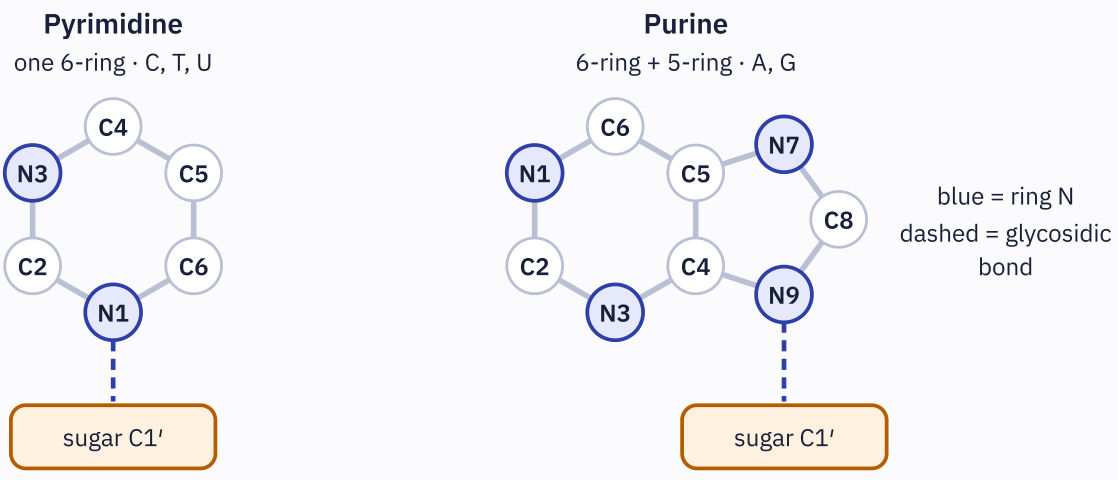


Figure 4.1.1 The two parent rings with their atom numbers (double bonds omitted for clarity). Notice that the sugar joins a pyrimidine at N1 and a purine at N9, and that the purine is a pyrimidine ring with a five-membered ring fused on at C4–C5.

The five common bases

Each base is a parent ring carrying amino ($-NH_2$), oxo (C=O) or methyl ($-CH_3$) groups at fixed positions. Learn the positions; examiners ask you to draw them.

BASE	FAMILY	GROUPS ON THE RING	FORMULA	FOUND IN
Adenine (A)	Purine	6-amino	$C_5H_5N_5$	DNA and RNA
Guanine (G)	Purine	2-amino, 6-oxo	$C_5H_5N_5O$	DNA and RNA
Cytosine (C)	Pyrimidine	4-amino, 2-oxo	$C_4H_5N_3O$	DNA and RNA
Thymine (T)	Pyrimidine	2,4-dioxo, 5-methyl	$C_5H_6N_2O_2$	DNA
Uracil (U)	Pyrimidine	2,4-dioxo	$C_4H_4N_2O_2$	RNA

Thymine is simply 5-methyluracil. The extra methyl group lets DNA repair enzymes tell a real T from a U made when cytosine loses its amino group (deamination of C gives U), which is one accepted reason why DNA uses T.

Properties that matter

1. **Flat and aromatic.** The rings have conjugated double bonds, so they are planar and stack on top of each other like coins. Stacking is a major force that holds the double helix together (Chapter 4.3).
2. **UV absorption near 260 nm.** The conjugated rings absorb ultraviolet light strongly around 260 nm. Proteins absorb mostly at 280 nm, so the ratio A260/A280 is used to judge DNA purity.
3. **Tautomers.** A tautomer is the same molecule with a hydrogen moved to another atom. Bases can exist in keto or enol forms (–C=O versus –C–OH) and amino or imino forms (–NH_2 versus =NH). At pH 7 the **keto and amino forms** dominate, and these forms set the hydrogen-bond pattern that makes A pair with T and G with C. A rare tautomer present at the moment of copying can pair wrongly and cause a point mutation.
4. **Weakly basic, poorly soluble.** Ring nitrogens can accept a proton at low pH. Guanine and the purine end product uric acid are poorly soluble in water; uric acid crystals in joints cause gout (Unit 6).

Unusual (minor) bases

These are the common bases changed after they are built into a chain, or close relatives of them.

- **In DNA:** 5-methylcytosine (switches genes off in plants and animals.

- **In tRNA:** pseudouridine (ψ, where uracil is joined to ribose through C5 instead of N1), dihydrouridine (D), inosine (its base is hypoxanthine; it sits at the wobble position of some anticodons), ribothymidine and methylated guanosines.
- **In mRNA:** 7-methylguanosine in the 5′ cap of eukaryotic mRNA (Chapter 4.5).
- **Free purine derivatives:** hypoxanthine, xanthine and uric acid (steps of purine breakdown) and the methylxanthines caffeine (1,3,7-trimethylxanthine), theophylline (1,3-dimethyl) and theobromine (3,7-dimethyl) in tea, coffee and cocoa.

WORKED EXAMPLE

Question (6 marks). (a) Calculate the molar mass and percentage of nitrogen by mass in adenine ($C_5H_5N_5$) and cytosine ($C_4H_5N_3O$). Use C = 12.011, H = 1.008, N = 14.007, O = 15.999 g/mol. (b) A base from a hydrolysed nucleic acid is a single-ring compound with oxo groups at C2 and C4 and a methyl group at C5. Name it and say which nucleic acid it came from.

1. Adenine: C = 5 × 12.011 = 60.055; H = 5 × 1.008 = 5.040; N = 5 × 14.007 = 70.035. Molar mass = 135.13 g/mol.
2. %N in adenine = 70.035 ÷ 135.13 × 100 = **51.8%**.
3. Cytosine: C = 4 × 12.011 = 48.044; H = 5.040; N = 3 × 14.007 = 42.021; O = 15.999. Molar mass = 111.10 g/mol.
4. %N in cytosine = 42.021 ÷ 111.10 × 100 = **37.8%**. The purine has more ring nitrogens (four ring N plus one amino N), so it is richer in nitrogen.
5. (b) One ring means a pyrimidine; 2,4-dioxo with 5-methyl is **thymine** (5-methyluracil), so the sample was **DNA**.

EXAM TRAPS

- Purines are A and G (two rings); pyrimidines are C, T and U (one ring). The bigger name, pyrimidine, is the smaller molecule.
- The sugar bond is at N9 of a purine and N1 of a pyrimidine; writing N1 for adenine loses marks.
- Thymine is in DNA, uracil in RNA. Thymine is not a purine because it has a methyl group.
- Caffeine and uric acid are purines but are not bases of nucleic acids.
- When asked “draw the structure”, show the ring numbering and the keto and amino forms.

CHECK YOURSELF

– REMEMBER **Name the two purines and the three pyrimidines found in nucleic acids.** 2 marks

Purines: adenine, guanine. Pyrimidines: cytosine, thymine (DNA), uracil (RNA).

– REMEMBER **Which ring atom of a purine forms the glycosidic bond?** 1 mark

N9 (for pyrimidines it is N1).

– UNDERSTAND **Why do the keto and amino tautomers matter for base pairing?** 3 marks

They fix which atoms are hydrogen-bond donors and acceptors. In these forms A presents a pattern that matches T, and G one that matches C. A rare enol or imino form changes the pattern and can pair with the wrong partner, causing a mutation during replication.

– UNDERSTAND **Why is pseudouridine called unusual even though its base is uracil?** 2 marks

Its uracil is linked to ribose through C5, a carbon–carbon glycosidic bond, instead of the usual N1–C1′ bond.

– APPLY **Calculate the molar mass of thymine, $C_5H_6N_2O_2$.** 2 marks

5(12.011) + 6(1.008) + 2(14.007) + 2(15.999) = 60.055 + 6.048 + 28.014 + 31.998 = **126.12 g/mol**.

– APPLY **Caffeine is 1,3,7-trimethylxanthine. Which family does it belong to, and where are its methyl groups?** 2 marks

Purine family (xanthine is 2,6-dioxopurine). Methyl groups on N1, N3 and N7.

– ANALYZE **Cytosine slowly deaminates to uracil. Explain how using thymine instead of uracil helps DNA stay correct.** 4 marks

If DNA normally contained U, a U made from damaged C could not be told apart from a genuine U, and repair could not decide which was wrong. Because DNA uses T (methylated U), any U found in DNA is recognised as damage and removed by uracil-DNA glycosylase, restoring C.

BEYOND THE SYLLABUS

Chemists have built extra, synthetic base pairs that are not found in nature and that polymerases can copy, which expands the genetic alphabet beyond four letters. Many drugs are base look-alikes: 5-fluorouracil (cancer) and acyclovir (herpes) work because enzymes mistake them for natural bases or nucleosides. Methylated cytosine is now read genome-wide by bisulfite and nanopore sequencing in epigenetics research. Search “unnatural base pair” and “nucleoside analogue drugs” to go further. This is not for the exam.

4.2 Nucleosides and nucleotides

A base on its own carries no information; it has to be fixed to a backbone. Join a base to a five-carbon sugar and you get a **nucleoside**; add one or more phosphate groups to that sugar and you get a **nucleotide**. Nucleotides are the monomers of DNA and RNA, and as free molecules they are also the cell’s energy currency (ATP), its signals (cAMP) and parts of its coenzymes (NAD^+, FAD, coenzyme A).

You need: the bases and their numbering from Chapter 4.1; pentoses and the glycosidic bond from Unit 1.

The sugar: ribose or deoxyribose

Both nucleic acids use a pentose in its five-membered (furanose) ring form. RNA uses **β-D-ribose**; DNA uses **2′-deoxy-β-D-ribose**, which has H instead of OH at carbon 2′. That single missing oxygen has large effects. The 2′-OH of RNA can attack the neighbouring phosphate, so RNA is broken down by dilute alkali into 2′,3′-cyclic nucleotides and then 2′- and 3′-monophosphates. DNA has no 2′-OH and survives alkali, which is one reason it is the better long-term store of genes.

From base to nucleoside to nucleotide

1. **Nucleoside = base + sugar.** The C1′ of the sugar is joined to N9 of a purine or N1 of a pyrimidine by a **β-N-glycosidic bond** (β means the base sits on the same face of the ring as C5′).
2. **Nucleotide = nucleoside + phosphate.** Phosphoric acid forms an ester with a sugar hydroxyl, nearly always the 5′-OH. One phosphate gives a nucleoside monophosphate (AMP), two give a diphosphate (ADP), three a triphosphate (ATP). The phosphates are called α, β and γ counting outward from the sugar.

3 **Polynucleotide.** A phosphate links the 3′-OH of one nucleotide to the 5′-OH of the next. This **3′,5′-phosphodiester bond** repeats to form the sugar–phosphate backbone. The chain has a free 5′-phosphate at one end and a free 3′-OH at the other, and sequences are always written 5′ → 3′.

BASE	RIBONUCLEOSIDE	DEOXYRIBONUCLEOSIDE	5′-MONOPHOSPHATE (RNA / DNA)
Adenine	Adenosine	Deoxyadenosine	AMP / dAMP (adenylate)
Guanine	Guanosine	Deoxyguanosine	GMP / dGMP (guanylate)
Cytosine	Cytidine	Deoxycytidine	CMP / dCMP (cytidylate)
Uracil	Uridine	(rare)	UMP
Thymine	(rare)	Deoxythymidine (thymidine)	dTMP

A handy pattern: purine nucleosides end in *-osine*, pyrimidine nucleosides in *-idine*.

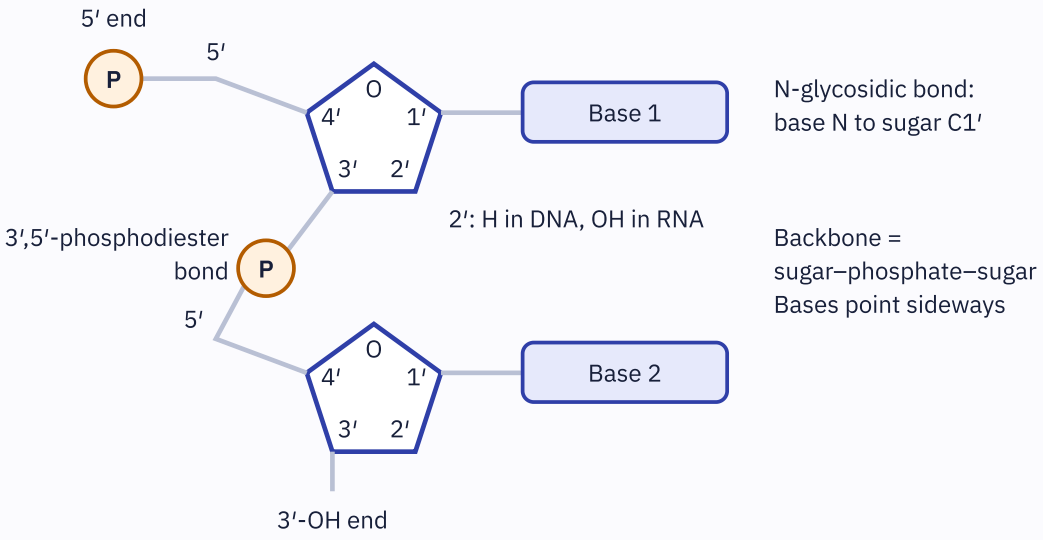


Figure 4.2.1 Two nucleotides of one strand. Each base hangs from C1′ of its sugar; a phosphate bridges C3′ of the upper sugar and C5′ of the lower one. Notice the direction: the chain starts at a 5′-phosphate and ends at a 3′-OH.

Bonds in nucleic acids and the jobs of free nucleotides

Inside one strand they are covalent: the N-glycosidic bond (base–sugar), the phosphoester bond (sugar–phosphate) and the 3′,5′-phosphodiester bond (between nucleotides). Between the phosphates of ATP are **phosphoanhydride** bonds, whose hydrolysis releases a lot of free energy (Unit 5, Bioenergetics). Holding two strands together are non-covalent forces: hydrogen bonds between bases and stacking between neighbouring base pairs (Chapter 4.3). Each backbone

phosphate carries a negative charge at pH 7, which makes nucleic acids acids and makes them move to the positive electrode in gel electrophoresis.

Free nucleotides do much more than build chains. ATP transfers energy; GTP powers protein synthesis and switches G proteins; cyclic AMP (cAMP, with one phosphate bridging 3′ and 5′ of the same ribose) carries hormone signals inside the cell. NAD^+, $NADP^+$, FAD and coenzyme A all contain an adenine nucleotide joined to a vitamin-derived part (Chapter 4.6). UDP-glucose and CDP-choline are activated building blocks for glycogen and phospholipid synthesis, and S-adenosylmethionine is the cell's main methyl donor.

Estimating DNA: the diphenylamine method

In hot acid (diphenylamine dissolved in glacial acetic acid with concentrated sulfuric acid) the glycosidic bonds between purines and deoxyribose break, and the freed 2-deoxyribose is converted to ω-hydroxylevulinyl aldehyde. This aldehyde reacts with diphenylamine to give a blue colour, read at about 595–600 nm. Ribose does not give this reaction, so RNA does not interfere (RNA is estimated with orcinol instead). The colour is proportional to DNA concentration, so a standard curve of known DNA amounts gives the unknown.

WORKED EXAMPLE

Question (6 marks). (a) For the DNA strand 5′-pATGCA-3′, name the nucleotides, count the phosphodiester bonds and estimate the net charge of the backbone phosphates at pH 7. (b) In a diphenylamine assay, a 100 µg/mL DNA standard gives absorbance 0.40 and the blank gives 0.00. The unknown, assayed the same way, gives 0.26. Assuming a straight-line standard curve through zero, find the DNA concentration of the unknown.

1. The nucleotides are dAMP, dTMP, dGMP, dCMP, dAMP (deoxyribonucleotides, because it is DNA and contains T).
2. Five nucleotides are joined by 5 − 1 = **4 phosphodiester bonds**. The "p" at the 5′ end is one extra terminal phosphate.
3. Each internal phosphodiester carries one negative charge (4); the 5′-terminal monophosphate carries between one and two, because its second acidic group has a pKa near 6.5. Net backbone charge is about **−5 to −6** (counting only the phosphates).
4. (b) Slope of the standard line = 0.40 ÷ 100 = 0.0040 per µg/mL.
5. Unknown = 0.26 ÷ 0.0040 = **65 µg/mL DNA**. In a real assay you would use five or six standards and read the value from the fitted line.

EXAM TRAPS

- Nucleoside has no phosphate; nucleotide has at least one. “Adenosine” is a nucleoside; “adenylate” or AMP is a nucleotide.
- A chain of n nucleotides has n – 1 phosphodiester bonds.
- Always write strand direction 5′ → 3′; the 5′ end carries the phosphate, the 3′ end the free OH.
- RNA, not DNA, is hydrolysed by alkali, because of its 2′-OH.
- The diphenylamine test detects deoxyribose, so it measures DNA, not RNA.

CHECK YOURSELF

– REMEMBER **Define a nucleoside and a nucleotide.** 2 marks

Nucleoside: a base joined to a pentose by a β-N-glycosidic bond. Nucleotide: a nucleoside with one or more phosphate groups esterified to the sugar, usually at 5′.

– REMEMBER **Name the bond that links nucleotides in a strand.** 1 mark

The 3′,5′-phosphodiester bond.

– UNDERSTAND **Why is RNA hydrolysed by 0.1 M NaOH while DNA is not?** 3 marks

RNA’s 2′-OH, made more reactive in alkali, attacks the adjacent phosphorus, forming a 2′,3′-cyclic phosphate and cutting the chain. DNA lacks the 2′-OH, so this route is not available.

– UNDERSTAND **Why does the diphenylamine reagent not respond to RNA?** 2 marks

The colour comes from 2-deoxyribose, which forms ω-hydroxylevulinyl aldehyde in hot acid; ribose does not form this product.

– APPLY **Write the full names of dGTP and UMP and say which nucleic acid each is built into.** 2 marks

dGTP: deoxyguanosine 5′-triphosphate, a DNA precursor. UMP: uridine 5′-monophosphate, an RNA unit.

– APPLY **A standard of 50 µg/mL DNA gives A = 0.21 in the diphenylamine assay. An unknown gives 0.63. Find its concentration.** 2 marks

Slope = 0.21/50 = 0.0042. Unknown = 0.63/0.0042 = **150 µg/mL**.

– ANALYZE **NAD⁺ and FAD are called nucleotide coenzymes. Analyse which part of each molecule is a nucleotide and which part does the chemistry.** 4 marks

Both contain an AMP unit (adenine–ribose–phosphate) that mainly helps enzymes bind them. The reacting part comes from a vitamin: the nicotinamide ring of niacin in NAD⁺, and the isoalloxazine ring of riboflavin in FAD, which carry electrons and hydrogen.

BEYOND THE SYLLABUS

Short DNA strands (oligonucleotides) for PCR primers are made by machines using phosphoramidite chemistry, which adds one protected nucleotide at a time from 3′ to 5′. Modified nucleotides with a phosphorothioate backbone or a 2′-O-methyl sugar make antisense and siRNA drugs last longer in the body, and the mRNA vaccines used N1-methylpseudouridine in place of uridine. Search “phosphoramidite synthesis” and “modified nucleosides in mRNA vaccines”. This is not for the exam.

4.3 DNA double helix: Watson-Crick model and Chargaff's rules

In 1953 James Watson and Francis Crick proposed that DNA is two strands wound around each other, with the bases paired inside, A with T and G with C. The model explained two sets of facts at once: Erwin Chargaff’s measurements that A equals T and G equals C, and the X-ray pictures of DNA fibres taken by Rosalind Franklin and Maurice Wilkins. Because each strand fixes the sequence of the other, the model also showed how genes can be copied, which is why it is the most examined structure in this unit.

You need: nucleotides and the 5′ → 3′ direction from Chapter 4.2.

Chargaff’s rules

Around 1950 Chargaff hydrolysed DNA from many species, separated the bases by paper chromatography and measured each one. For double-stranded DNA he found:

1. **A = T and G = C** (as moles or mole percent).
2. So total purines equal total pyrimidines: **A + G = T + C**, and also A + C = G + T.
3. Base composition **differs between species**, usually stated as the ratio (A + T)/(G + C) or as GC content.

4. Within one species, composition is the **same in every tissue** and does not change with age, diet or environment.

The rules hold for double-stranded DNA only. Single-stranded DNA (bacteriophage φX174) and RNA do not obey A = T or G = C, because their bases are not paired.

The Watson–Crick model, point by point

Franklin's fibre diffraction pattern (with Raymond Gosling) showed a helix with a repeat of 3.4 nm and a spacing of 0.34 nm. Watson and Crick built a model that fitted those numbers and Chargaff's ratios. Watson, Crick and Wilkins received the 1962 Nobel Prize; Franklin had died in 1958.

1. **Two strands, one axis.** Two polynucleotide chains coil around a common axis to form a right-handed double helix.
2. **Antiparallel.** One strand runs 5′ → 3′ upward and the other 5′ → 3′ downward.
3. **Backbone outside, bases inside.** The charged sugar–phosphate backbones face the water; the flat bases lie inside, nearly perpendicular to the axis.
4. **Complementary pairing.** A pairs with T through two hydrogen bonds; G pairs with C through three. Every pair is one purine plus one pyrimidine, so the helix has a constant diameter of about 2 nm.
5. **Dimensions.** Neighbouring pairs are 0.34 nm apart and the model had 10 pairs per turn, so one turn is 3.4 nm. Later measurements of DNA in solution give about 10.5 pairs per turn.
6. **Two grooves.** The sugars of a base pair are not exactly opposite each other, so the backbones leave a wide **major groove** and a narrow **minor groove**. Proteins that read DNA sequence, such as transcription factors, mostly do so in the major groove.

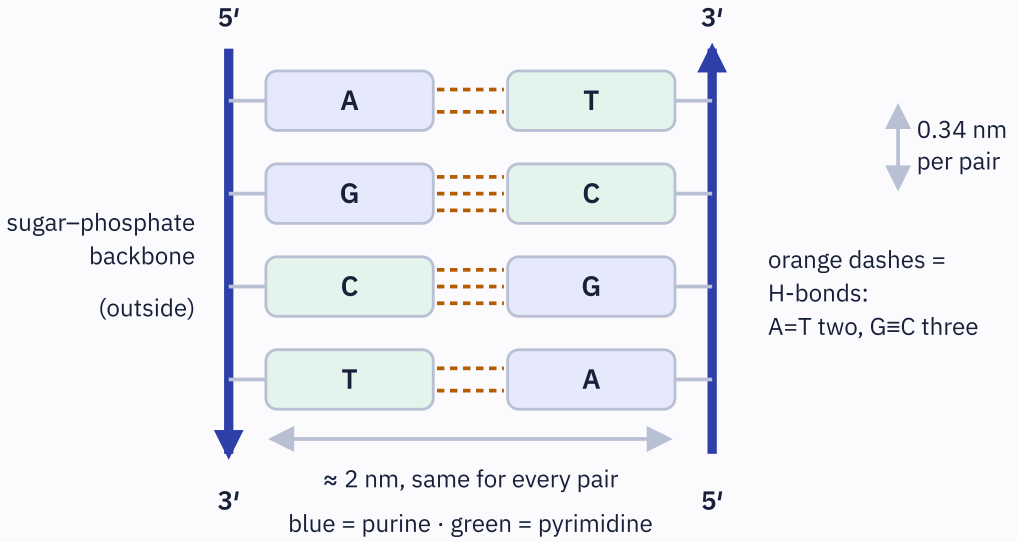


Figure 4.3.1 The double helix unwound into a ladder. Arrows show the antiparallel strands; every rung is a purine (blue) paired with a pyrimidine (green), so all rungs have the same length. Count the dashes: two for A=T, three for G≡C.

What holds the helix together, and how it melts

Hydrogen bonds give **specificity**: only A–T and G–C fit the geometry. Most of the **stability**, however, comes from base stacking, the van der Waals and hydrophobic contacts between neighbouring flat pairs. Positive ions (Na^+, Mg^{2+}) shield the repulsion between the negative phosphates.

Heating separates the strands. This is **denaturation** or melting, and the temperature at which half the DNA is single-stranded is the **melting temperature, Tm**. As the bases unstack, absorbance at 260 nm rises; this is the **hyperchromic effect**. DNA with more G–C pairs has a higher Tm, because G–C pairs have three hydrogen bonds and stack more strongly. On slow cooling, complementary strands find each other again (renaturation or annealing), which is the basis of PCR and of hybridisation probes.

WORKED EXAMPLE

Question (8 marks). (a) A double-stranded DNA contains 22% adenine. Find the percentage of the other bases. (b) In one strand of a DNA duplex, (A + G)/(T + C) = 0.6. What is this ratio in the complementary strand and in the whole duplex? (c) The *E. coli* K-12 genome is about 4.64×10^6 base pairs of B-DNA. Find its length and the number of helical turns, using 0.34 nm per pair and 10.5 pairs per turn.

1. (a) A = T, so T = **22%**. A + T = 44%, leaving 56% for G + C. G = C = **28%** each.
2. (b) Each A in strand 1 faces a T in strand 2, and each G faces a C. So (A + G) of strand 1 = (T + C) of strand 2, and the ratio in strand 2 is the inverse: 1 ÷ 0.6 = **1.67**.
3. In the duplex, purines equal pyrimidines, so the ratio is **1.0**.
4. (c) Length = $4.64 \times 10^6 \times 0.34$ nm = 1.58×10^6 nm = **1.58 mm**, roughly a thousand times longer than the bacterium itself (about 1–2 µm).
5. Turns = $4.64 \times 10^6 \div 10.5$ = **4.4×10^5 turns**.

EXAM TRAPS

- Chargaff says A = T and G = C, not A = G. And (A + T)/(G + C) varies between species; it is not 1.
- The rules apply to double-stranded DNA only; do not use them for RNA or single-stranded DNA.
- Hydrogen bonds explain which bases pair; stacking explains most of the helix's stability. Examiners like this distinction.
- The strands are antiparallel, and the complementary strand of 5′-ATGC-3′ is 5′-GCAT-3′, not 5′-TACG-3′.
- Higher GC content means higher Tm; the hyperchromic effect is a rise, not a fall, in A260.

CHECK YOURSELF

– REMEMBER **State Chargaff's rules.** 3 marks

In double-stranded DNA, A = T and G = C, so purines = pyrimidines; composition varies between species but is constant across tissues of one species and is not changed by age, diet or environment.

– REMEMBER **How many hydrogen bonds are there in an A–T pair and in a G–C pair?** 1 mark

Two in A–T; three in G–C.

– UNDERSTAND **Why is the diameter of the double helix constant along its length?** 2 marks

Each rung is one two-ring purine plus one one-ring pyrimidine, so every pair spans the same width (about 2 nm). Purine–purine pairs would be too wide and pyrimidine–pyrimidine pairs too narrow.

– UNDERSTAND **What is the hyperchromic effect?** 2 marks

The rise in UV absorbance at 260 nm when double-stranded DNA is denatured, because unstacked bases absorb more light than stacked ones.

– APPLY **A DNA sample has 35% G. Find A, T and C.** 2 marks

C = 35%; G + C = 70%; A + T = 30%, so A = T = 15%.

– APPLY **Write the complementary strand of 5′-AGGTCA-3′ in the 5′ → 3′ direction.** 2 marks

Pair each base and reverse: 3′-TCCAGT-5′ becomes **5′-TGACCT-3′**.

– ANALYZE **DNA X has Tm 72 °C and DNA Y has Tm 88 °C in the same buffer. Which has more A–T pairs, and why?** 3 marks

X. Lower Tm means the helix is less stable, which follows from fewer G–C pairs (three hydrogen bonds and stronger stacking), so X has more A–T pairs.

BEYOND THE SYLLABUS

The same pairing rules let engineers design DNA origami, where a long strand is folded by short “staple” strands into shapes a few nanometres across, used in drug delivery and nanoscale sensors. Not all DNA is a simple double helix: guanine-rich sequences such as telomeres can fold into four-stranded G-quadruplexes, now studied as drug targets. The history of the structure, including the role of Franklin’s Photograph 51, is retold in many accounts worth reading. Search “DNA origami” and “G-quadruplex”. This is not for the exam.

4.4 Forms of DNA: A, B and Z

The Watson–Crick helix is one shape DNA can take, not the only one. The same double strand can be squeezed into a shorter, wider right-handed **A form** when water is scarce, or twisted into a thin left-handed **Z form** by certain sequences.

You need: the B-form dimensions and grooves from Chapter 4.3.

Why DNA changes shape

The backbone has several rotatable bonds, and the sugar ring can pucker in two main ways: C2′-endo (C2′ bent out of the ring plane toward C5′) or C3′-endo. The base can also turn about its glycosidic bond, into the **anti** position (base away from the sugar, the usual case) or the **syn** position (base over the sugar). Change the pucker and the base rotation, and the whole helix changes its width, rise and handedness. Water, salt, sequence and supercoiling decide which shape wins.

The three forms compared

Values differ slightly between textbooks and crystal structures, so learn the approximate numbers and, above all, the direction of each difference.

FEATURE	A-DNA	B-DNA	Z-DNA
Handedness	Right	Right	Left
Base pairs per turn	11	10.5 (10 in fibres)	12 (6 dinucleotide repeats)
Rise per base pair	≈ 0.23–0.26 nm	≈ 0.33–0.34 nm	≈ 0.37–0.38 nm
Pitch (one turn)	≈ 2.8 nm	≈ 3.4 nm	≈ 4.5 nm
Diameter	≈ 2.3–2.6 nm (widest)	≈ 2.0 nm	≈ 1.8 nm (thinnest)
Base pairs relative to axis	Strongly tilted, pushed off the axis	Nearly perpendicular, on the axis	Slightly tilted
Sugar pucker	C3′-endo	C2′-endo	Alternates: C2′-endo at C, C3′-endo type at G

FEATURE	A-DNA	B-DNA	Z-DNA
Glycosidic bond	Anti	Anti	Anti at pyrimidines, syn at purines
Grooves	Major narrow and deep; minor wide and shallow	Major wide and deep; minor narrow	Major almost flat; minor narrow and deep
Favoured by	Low humidity (dehydrated fibres); also RNA–RNA and DNA–RNA duplexes	High humidity; normal cell conditions	Alternating purine–pyrimidine (e.g. CGCGCG), high salt, cytosine methylation, negative supercoiling

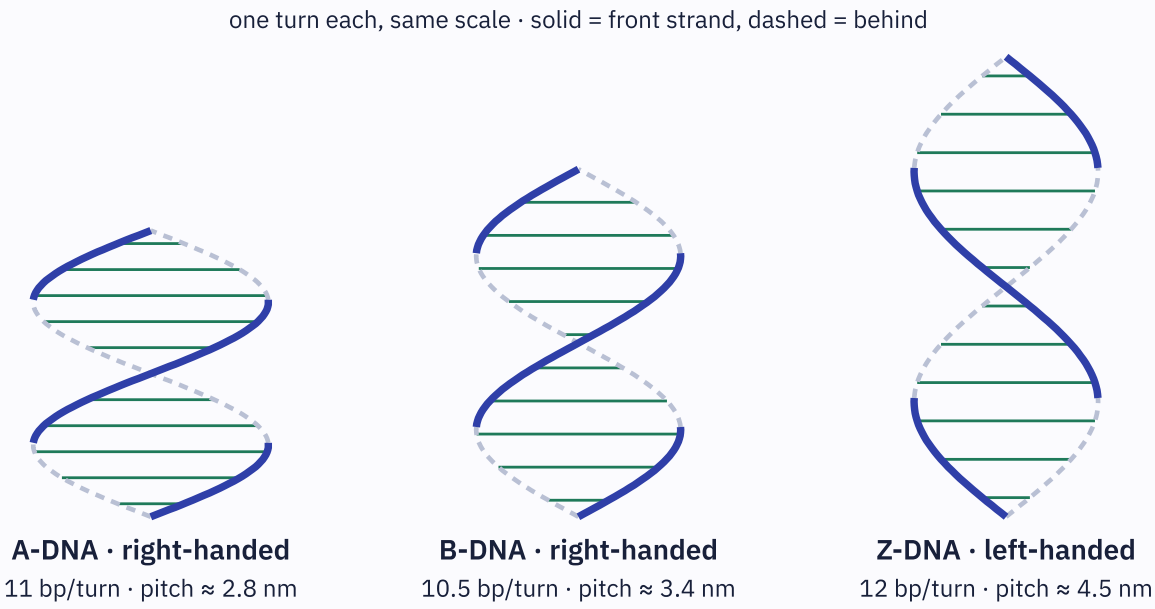


Figure 4.4.1 One helical turn of each form drawn to the same scale from the approximate pitch and diameter in the table (green rungs are base pairs). Notice that A is short and wide, Z is long and thin, and the front strands of Z slope the opposite way because it is left-handed.

Where each form matters

B-DNA is the form of almost all DNA in cells. **A-form** geometry matters mainly for RNA: double-stranded RNA and DNA–RNA hybrids cannot take the B form, because the 2′-OH of ribose favours the C3′-endo pucker, so they adopt an A-like helix. **Z-DNA** was discovered in 1979 when Alexander Rich's group solved the crystal structure of the short sequence CGCGCG. Its backbone zigzags, which gave it the name. In cells, short Z stretches form behind a moving RNA polymerase where the DNA becomes negatively supercoiled, and some proteins bind Z-DNA specifically.

WORKED EXAMPLE

Question (5 marks). A 120-bp segment of DNA is converted from B to A form and, separately, to Z form. Using rises of 0.26, 0.34 and 0.37 nm and 11, 10.5 and 12 bp per turn for A, B and Z, find the length and number of turns in each form.

1. A form: length = 120 × 0.26 = **31.2 nm**; turns = 120 ÷ 11 = **10.9** (right-handed).
2. B form: length = 120 × 0.34 = **40.8 nm**; turns = 120 ÷ 10.5 = **11.4** (right-handed).
3. Z form: length = 120 × 0.37 = **44.4 nm**; turns = 120 ÷ 12 = **10** (left-handed).
4. So the same molecule is about 24% shorter in A form and about 9% longer in Z form than in B form (31.2/40.8 = 0.76; 44.4/40.8 = 1.09).

EXAM TRAPS

- Only Z is left-handed; A and B are both right-handed.
- A-DNA is the widest and shortest per turn; Z-DNA is the thinnest. Students often swap A and Z.
- Z-DNA needs an alternating purine–pyrimidine sequence; a random sequence does not form it easily.
- In Z-DNA the purines are syn and the pyrimidines anti; in A and B every base is anti.

CHECK YOURSELF

– REMEMBER **Which DNA form is left-handed, and who described it first?** 1 mark

Z-DNA; Alexander Rich and colleagues, 1979, from crystals of CGCGCG.

– REMEMBER **Give the sugar pucker of A- and B-DNA.** 1 mark

A: C3′-endo. B: C2′-endo.

– UNDERSTAND **Why do double-stranded RNA molecules form an A-like helix rather than a B helix?** 2 marks

The 2′-OH of ribose clashes with the C2′-endo pucker that B form needs, so ribose stays C3′-endo, which gives A-form geometry.

– APPLY **How many turns does a 360-bp Z-DNA stretch make?** 1 mark

360 ÷ 12 = **30 left-handed turns**.

– ANALYZE **A DNA fibre gives a wider, shorter helix when dried and returns to the usual shape when humid. Identify the two forms and explain the role of water.** 3 marks

Dry fibre: A form; humid: B form. Water hydrates the backbone and the grooves; removing it lets the sugars switch to C3′-endo and the pairs tilt and move off the axis, giving the shorter, wider A helix.

BEYOND THE SYLLABUS

Proteins with a Zα domain, such as the RNA-editing enzyme ADAR1 and the immune sensor ZBP1, bind Z-shaped DNA and RNA, and research links them to antiviral defence and inflammation. Other non-B structures, such as triplexes, cruciforms and G-quadruplexes, form at special sequences and can cause genome instability. Search “Z-DNA binding proteins” and “non-B DNA”. This is not for the exam.

4.5 Types of RNA: mRNA, tRNA and rRNA

RNA is the working copy of genetic information. It is a single strand made with ribose and uracil, and it folds back on itself into hairpins and loops. Three kinds of RNA build every protein: **messenger RNA** carries the gene’s message, **transfer RNA** brings the matching amino acid, and **ribosomal RNA** forms the core of the ribosome and actually joins the amino acids.

You need: ribose, uracil and the phosphodiester bond from Chapter 4.2; base pairing from Chapter 4.3.

How RNA differs from DNA

- **Sugar and base:** ribose instead of deoxyribose, uracil instead of thymine.
- **Strands:** usually a single strand that pairs with itself in short stretches (A–U, G–C, and also G–U “wobble” pairs), giving A-form hairpins (Chapter 4.4). Chargaff’s rules do not apply.
- **Stability:** broken down by alkali and by many ribonucleases; most RNAs live minutes to hours, not a lifetime.
- **Catalysis:** some RNAs are enzymes, called **ribozymes**.

In a typical cell, rRNA is by far the most abundant (roughly 80% of total RNA), tRNA comes next (about 15%) and mRNA is a small fraction (about 5%), although mRNA has the most different sequences.

Messenger RNA (mRNA)

mRNA is copied from a gene by RNA polymerase and is read by the ribosome three bases at a time; each triplet is a **codon**. Reading starts at the start codon AUG and ends at a stop codon (UAA, UAG or UGA).

- **Prokaryotic mRNA** is often *polycistronic* (one mRNA codes for several proteins), has no cap or long poly(A) tail, and has a ribosome-binding **Shine–Dalgarno sequence** a few bases before each start codon. It is translated while still being made.
- **Eukaryotic mRNA** is usually *monocistronic*. It is made as a longer precursor (pre-mRNA, also called hnRNA) whose introns are removed by splicing. The finished molecule has a **5′ cap** of 7-methylguanosine joined through an unusual 5′–5′ triphosphate bridge, a 5′ untranslated region (UTR), the coding region, a 3′ UTR, and a **poly(A) tail** of tens to a few hundred adenylates. The cap and tail protect the mRNA from exonucleases and help ribosomes start translation.

Transfer RNA (tRNA)

tRNA is the adaptor between a codon and an amino acid. Each tRNA is small, about 73–93 nucleotides, and is rich in modified bases (Chapter 4.1). Drawn flat, it looks like a cloverleaf with four arms; in three dimensions the arms stack into an **L shape**, with the anticodon at one end and the amino-acid site at the other.

1. **Acceptor stem:** the paired 5′ and 3′ ends. The 3′ end always finishes in **CCA**; the amino acid is attached to the terminal A by an ester bond, made by an aminoacyl-tRNA synthetase.
2. **D arm:** its loop contains dihydrouridine; it helps the tRNA fold.
3. **Anticodon arm:** its loop carries the three-base **anticodon**, which pairs antiparallel with the mRNA codon. The first anticodon base (5′ end) can “wobble”, so one tRNA can read more than one codon; inosine in that position pairs with U, C or A.
4. **Variable arm:** its length differs between tRNAs.
5. **TψC arm:** named for ribothymidine, pseudouridine and cytidine in its loop; it helps the tRNA bind the ribosome.

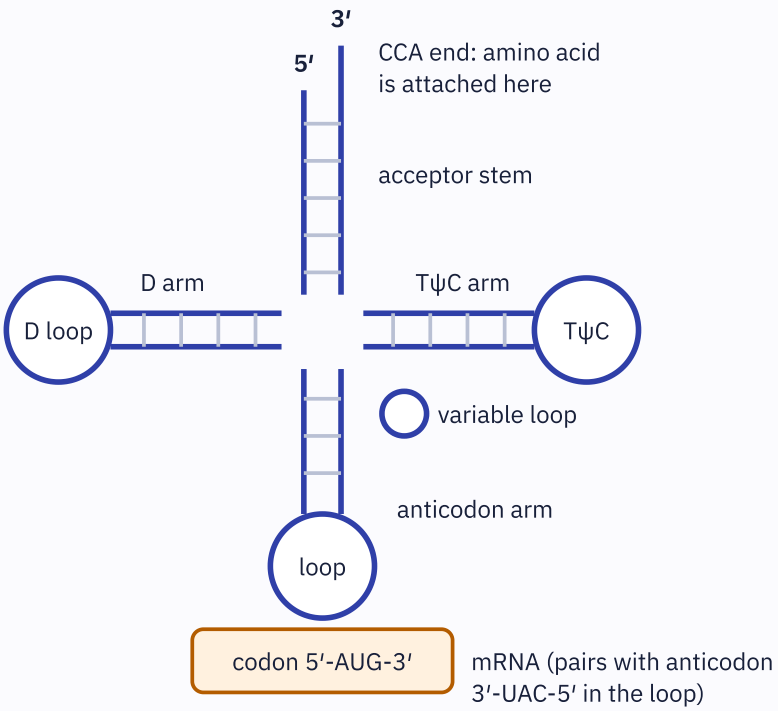


Figure 4.5.1 The tRNA cloverleaf. Grey rungs are paired bases in the stems; circles are unpaired loops. Notice the two business ends: the CCA 3′ end that carries the amino acid, and the anticodon loop that reads the mRNA codon.

Ribosomal RNA (rRNA)

A ribosome is two subunits, each made of rRNA and proteins. Their sizes are given in Svedberg units (S), which measure how fast a particle sediments in a centrifuge. Because sedimentation depends on shape as well as mass, S values do not add.

RIBOSOME	SMALL SUBUNIT	LARGE SUBUNIT
Prokaryotic 70S	30S: 16S rRNA + 21 proteins	50S: 23S and 5S rRNA + over 30 proteins
Eukaryotic 80S (cytoplasm)	40S: 18S rRNA + proteins	60S: 28S (in mammals), 5.8S and 5S rRNA + proteins

rRNA is not just scaffolding. The 16S rRNA pairs with the Shine–Dalgarno sequence to place the start codon, and the 23S rRNA of the large subunit catalyses peptide-bond formation: the **peptidyl transferase** centre is made of RNA, so the ribosome is a ribozyme.

Other RNAs, in one line each

snRNA splices pre-mRNA; snoRNA guides chemical modification of rRNA; microRNA (miRNA) and small interfering RNA (siRNA) switch genes off by pairing with mRNA; long non-coding RNAs

regulate chromatin and transcription. These are covered in molecular biology courses.

WORKED EXAMPLE

Question (6 marks). An mRNA reads 5′-AUG UUC GGA UAA-3′. (a) How many amino acids does it code for, and which? (b) Write the anticodon of each tRNA used, 5′ → 3′. (c) Write the DNA template strand, 5′ → 3′.

1. (a) Codons: AUG (Met), UUC (Phe), GGA (Gly), UAA (stop). So **3 amino acids**: Met–Phe–Gly. A stop codon has no tRNA; a release factor reads it.
2. (b) Anticodons pair antiparallel. AUG ↔ 3′-UAC-5′ = **5′-CAU-3′**; UUC ↔ 3′-AAG-5′ = **5′-GAA-3′**; GGA ↔ 3′-CCU-5′ = **5′-UCC-3′**.
3. (c) The template is complementary to the mRNA, with T for U: 3′-TAC AAG CCT ATT-5′, which written 5′ → 3′ is **5′-TTATCCGAACAT-3′**. The coding strand has the mRNA sequence with T: 5′-ATGTTCGGATAA-3′.

EXAM TRAPS

- 30S + 50S makes 70S, not 80S; Svedberg values are not additive.
- The amino acid attaches to the 3′ CCA end of tRNA, not to the anticodon.
- Write anticodons 5′ → 3′ unless the question shows the direction; AUG's anticodon is 5′-CAU-3′, not 5′-UAC-3′.
- Cap and poly(A) tail belong to eukaryotic mRNA; prokaryotic mRNA has a Shine–Dalgarno sequence instead.
- rRNA is the most abundant RNA, mRNA the least; but mRNA is the most varied.

CHECK YOURSELF

– REMEMBER **Name the four arms of the tRNA cloverleaf.** 2 marks

Acceptor stem, D arm, anticodon arm, TψC arm (plus a variable arm/loop).

– REMEMBER **Which rRNAs are in the prokaryotic 50S subunit?** 1 mark

23S and 5S rRNA.

– UNDERSTAND **What are the functions of the 5′ cap and poly(A) tail?** 3 marks

Both protect the mRNA from exonucleases; the cap is recognised when translation starts and the tail helps it, so they raise the stability and translation of the mRNA. The cap also helps export from the nucleus.

– UNDERSTAND **Why is the ribosome called a ribozyme?** 2 marks

Peptide bonds are formed at the peptidyl transferase centre, which is made of rRNA (23S in bacteria), not protein. So the catalyst is RNA.

– APPLY **A tRNA has the anticodon 5′-GAA-3′. Which codon does it read?** 1 mark

Pair antiparallel: codon **5′-UUC-3′** (Phe).

– APPLY **An mRNA codes for a 150-amino-acid protein. Find the minimum number of nucleotides in its coding region including the stop codon.** 2 marks

(150 + 1) × 3 = **453 nucleotides**.

– ANALYZE **A cell contains about 80% rRNA but thousands of different mRNAs make up only about 5%. Explain both facts.** 4 marks

A cell needs very many ribosomes, all with the same few rRNAs, so rRNA mass is large. Each gene makes its own mRNA, so mRNA has many sequences, but each is short-lived and present in few copies, so its total mass is small.

BEYOND THE SYLLABUS

mRNA vaccines deliver a capped, poly(A)-tailed, chemically modified mRNA in lipid nanoparticles so that cells make a viral protein for a while. Cryo-electron microscopy now shows ribosomes and spliceosomes at near-atomic detail. Sequencing of 16S rRNA genes is the standard way to identify bacteria and to profile the gut microbiome, which links this chapter to microbiology. Search “16S rRNA sequencing” and “mRNA vaccine design”. This is not for the exam.

4.6 Water-soluble vitamins: B complex and C

A **vitamin** is an organic compound the body needs in small amounts but cannot make in enough quantity, so it must come from food. The water-soluble vitamins are the eight B

vitamins and vitamin C. Almost every B vitamin is turned into a **coenzyme**, a small helper molecule that an enzyme needs to do its chemistry. Learn each vitamin as a chain: vitamin → coenzyme → reaction type → deficiency disease. That chain is what examiners ask for.

You need: the nucleotide coenzymes NAD^+, FAD and CoA from Chapter 4.2. The pathways where these coenzymes work are in Unit 5 (Bioenergetics and carbohydrate metabolism).

Common features

- They dissolve in water, are absorbed directly into blood, and any excess is mostly lost in urine. So the body stores little of them and needs a regular supply. Vitamin B12 is the exception: the liver stores enough for years.
- Many are lost in cooking water, and some are destroyed by heat (vitamin C, thiamine) or light (riboflavin).
- Toxicity is uncommon, because the excess is excreted.

The B vitamins and vitamin C, vitamin by vitamin

VITAMIN	ACTIVE (COENZYME) FORM	WHAT IT DOES	DEFICIENCY
B1 thiamine	Thiamine pyrophosphate (TPP)	Oxidative decarboxylation of α-keto acids (pyruvate dehydrogenase, α-ketoglutarate dehydrogenase); transketolase of the pentose phosphate pathway	Beriberi (dry: nerve damage; wet: heart failure and oedema); Wernicke–Korsakoff syndrome in alcoholism
B2 riboflavin	FMN, FAD	Carry two hydrogens in redox reactions (succinate dehydrogenase, Complex I)	Angular stomatitis, cheilosis, glossitis
B3 niacin (nicotinic acid, nicotinamide)	NAD^+, $NADP^+$	Carry a hydride ion in dehydrogenase reactions; NADPH for biosynthesis	Pellagra: dermatitis, diarrhoea, dementia, and death if untreated
B5 pantothenic acid	Coenzyme A; acyl carrier protein	Carry acyl groups through a thiol (–SH) end, as in acetyl-CoA	Rare; “burning feet” syndrome

VITAMIN	ACTIVE (COENZYME) FORM	WHAT IT DOES	DEFICIENCY
B6 pyridoxine, pyridoxal, pyridoxamine	Pyridoxal phosphate (PLP)	Amino acid reactions: transamination, decarboxylation (making GABA, serotonin, histamine); haem synthesis; glycogen phosphorylase	Peripheral neuropathy, convulsions in infants, microcytic anaemia; caused by the TB drug isoniazid
B7 biotin	Biotin bound to a lysine of the enzyme	Carries CO_2 in carboxylases (pyruvate carboxylase, acetyl-CoA carboxylase, propionyl-CoA carboxylase)	Rare; dermatitis and hair loss; induced by eating much raw egg white (avidin binds biotin)
B9 folic acid	Tetrahydrofolate (THF)	Carries one-carbon units (formyl, methylene, methyl) for purine synthesis and for making dTMP	Megaloblastic anaemia; neural tube defects in the baby if low in early pregnancy
B12 cobalamin (contains cobalt)	Methylcobalamin; 5′-deoxyadenosylcobalamin	Methionine synthase (homocysteine → methionine, freeing THF); methylmalonyl-CoA mutase (→ succinyl-CoA)	Megaloblastic anaemia with nerve damage; pernicious anaemia when intrinsic factor is missing
C ascorbic acid	Ascorbate itself (a reducing agent)	Keeps the iron of prolyl and lysyl hydroxylases reduced, so collagen is hydroxylated; antioxidant; helps absorb dietary iron	Scurvy: bleeding gums, poor wound healing, bleeding under the skin

Four links examiners like

1. **One enzyme, many vitamins.** The pyruvate dehydrogenase complex, which joins glycolysis to the citric acid cycle, needs TPP (B1), lipoic acid, CoA (B5), FAD (B2) and NAD^+ (B3). So a shortage of thiamine first harms tissues that burn glucose fastest: nerves and heart (Figure 4.6.1).
2. **Niacin from tryptophan.** The body can make niacin from the amino acid tryptophan, roughly 1 mg of niacin from 60 mg of tryptophan, which is why intake is counted in **niacin equivalents**. Pellagra appeared in people living mostly on maize, whose niacin is bound and poorly available, and has been linked in India to diets based on jowar (sorghum), which is rich in leucine.

3. **Folate and B12 work together.** Methionine synthase moves a methyl group from N^5-methyl-THF to homocysteine using methylcobalamin. Without B12, folate is "trapped" as methyl-THF, DNA synthesis slows, and both deficiencies give the same large, immature red cells (megaloblastic anaemia). Only B12 deficiency also damages nerves. B12 is made only by microbes and comes from animal foods, so strict vegetarians, common in India, are at risk; it is absorbed in the ileum only when bound to intrinsic factor from the stomach.

4. **Vitamin C and collagen.** Humans, unlike most animals, cannot make ascorbic acid, because they lack the enzyme L-gulonolactone oxidase. Without it, prolyl hydroxylase cannot keep working, collagen triple helices are weak, and blood vessels and gums bleed. Amla (Indian gooseberry), guava and citrus are rich sources.

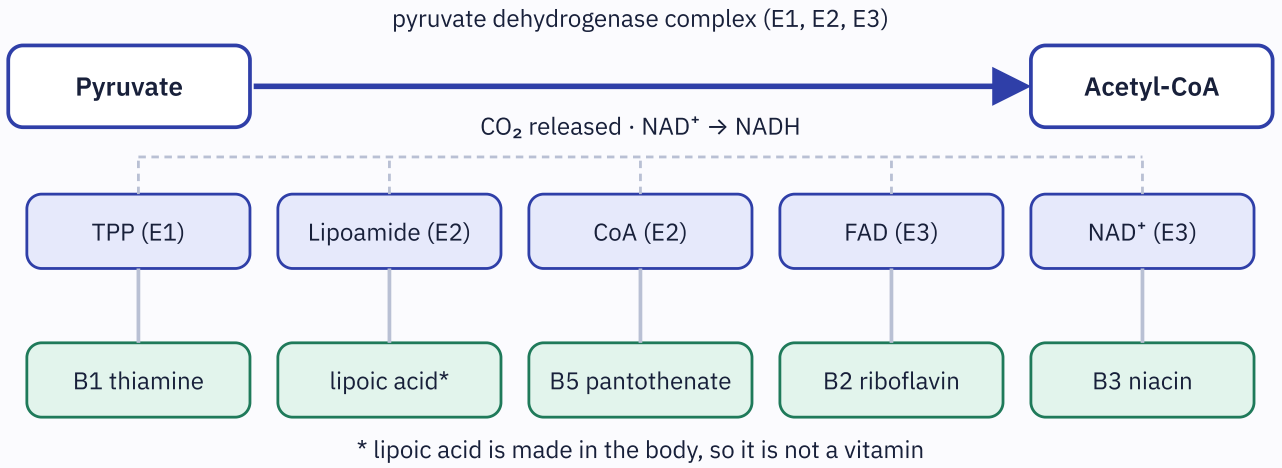


Figure 4.6.1 One reaction, four B vitamins. The coenzymes (blue) of the pyruvate dehydrogenase complex each come from a vitamin (green). A shortage of any of B1, B2, B3 or B5 slows the conversion of pyruvate to acetyl-CoA; that is why thiamine deficiency raises blood pyruvate and lactate.

WORKED EXAMPLE

Question (6 marks). (a) A day's diet supplies 9 mg of preformed niacin and 780 mg of tryptophan. Taking 60 mg tryptophan = 1 mg niacin, find the niacin equivalents (NE). (b) A 45-year-old strict vegetarian has tiredness, tingling in the feet, large red cells on a blood smear and raised methylmalonic acid in urine. Which vitamin is deficient? Give the reasoning.

1. (a) Niacin from tryptophan = 780 ÷ 60 = 13 mg.
2. NE = preformed niacin + niacin from tryptophan = 9 + 13 = **22 mg NE per day**.
3. (b) Large red cells (megaloblastic anaemia) point to folate or B12 deficiency.
4. Nerve symptoms and raised methylmalonic acid point to B12 only: methylmalonyl-CoA mutase needs adenosylcobalamin, so methylmalonyl-CoA builds up and is excreted as methylmalonic acid.
5. A strict vegetarian diet lacks B12. Answer: **vitamin B12 (cobalamin) deficiency**. Giving folate alone would improve the blood picture but not stop the nerve damage, which is why B12 must be checked.

EXAM TRAPS

- Thiamine coenzyme is TPP; pyridoxine coenzyme is PLP. Do not swap the two "P" coenzymes.
- Pellagra is niacin (B3); beriberi is thiamine (B1); scurvy is vitamin C. Write the 3 Ds for pellagra.
- Both folate and B12 deficiency cause megaloblastic anaemia; only B12 deficiency causes nerve damage and methylmalonic aciduria.
- Biotin carries CO_2 (carboxylation); TPP takes part in decarboxylation. Opposite jobs, similar words.
- B12 contains cobalt; it is the only vitamin with a metal.

CHECK YOURSELF

– REMEMBER **Give the coenzyme form of riboflavin, niacin and pantothenic acid.** 3 marks

Riboflavin: FMN and FAD. Niacin: NAD^+ and $NADP^+$. Pantothenic acid: coenzyme A (and the acyl carrier protein).

– REMEMBER **Name the deficiency disease of thiamine and of vitamin C.** 1 mark

Thiamine: beriberi. Vitamin C: scurvy.

– UNDERSTAND **Why are water-soluble vitamins needed regularly while vitamin A is not?** 2 marks

Water-soluble vitamins are stored little and the excess is lost in urine (B12 aside), so stocks run down in weeks. Vitamin A is fat-soluble and stored in the liver for months.

– UNDERSTAND **Explain the "methyl trap" of folate in B12 deficiency.** 3 marks

N^5-methyl-THF can give up its methyl only to homocysteine, through B12-dependent methionine synthase. Without B12 folate accumulates as methyl-THF, other THF forms run short, purine and dTMP synthesis slow, and megaloblastic anaemia develops.

– APPLY **A diet gives 6 mg niacin and 600 mg tryptophan. Find the niacin equivalents.** 2 marks

6 + 600/60 = 6 + 10 = **16 mg NE**.

– APPLY **A TB patient on isoniazid develops tingling in the hands and feet. Which vitamin should be given, and why?** 2 marks

Vitamin B6 (pyridoxine). Isoniazid reacts with pyridoxal and lowers PLP, which nerves need for neurotransmitter synthesis.

– ANALYZE **Thiamine deficiency raises blood pyruvate and lactate. Analyse why, using the pathway.** 4 marks

Pyruvate dehydrogenase needs TPP. Without it pyruvate cannot become acetyl-CoA, so pyruvate accumulates, and lactate dehydrogenase turns the excess into lactate. Energy supply to nerves and heart falls, giving the symptoms of beriberi.

BEYOND THE SYLLABUS

Antifolate drugs act on these pathways: methotrexate blocks dihydrofolate reductase in cancer cells, and trimethoprim blocks the bacterial enzyme. Food fortification is a public-health tool; India fortifies rice and salt in some programmes and recommends folic acid around pregnancy to prevent neural tube defects. Riboflavin and B12 are made industrially by microbial fermentation, a direct biotechnology application. Search "vitamin fermentation industrial" and "food fortification India". This is not for the exam.

4.7 Fat-soluble vitamins: A, D, E and K

Vitamins A, D, E and K are oily molecules built from isoprene units, so they dissolve in fat, not water. They travel with dietary fat, are stored in the liver and fat tissue, and most of them act less like coenzymes and more like hormones or membrane protectors: A for vision and gene control, D for calcium, E against oxidation, K for blood clotting. Because they are stored, too much can be as harmful as too little.

You need: isoprenoids, cholesterol and steroids from Unit 3 (Lipids); calcium from Chapter 4.8 links to vitamin D.

Common features

- Absorbed in the small intestine inside bile-salt micelles together with fat, then carried in chylomicrons. Any condition that blocks fat absorption (obstructed bile flow, chronic pancreatitis, cystic fibrosis) can cause all four deficiencies.
- Stored: A and D mainly in the liver, E in fat tissue. Deficiency develops slowly; excess builds up, so A and D can be toxic.

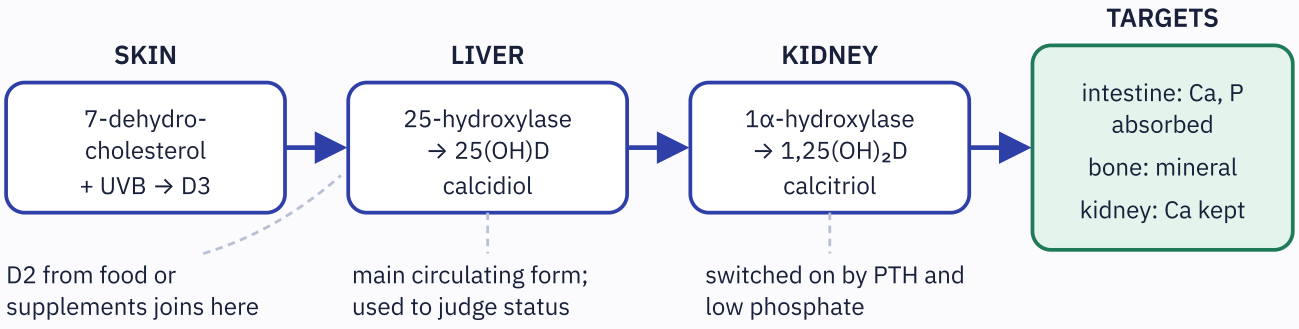
Vitamin A (retinoids)

Vitamin A exists as three related molecules: **retinol** (the alcohol; stored in the liver as retinyl esters), **retinal** (the aldehyde; used in vision) and **retinoic acid** (the acid; controls genes through nuclear receptors, needed for growth and for healthy skin and mucous membranes). Retinol and retinal interconvert, but retinoic acid cannot go back, so it cannot support vision. Plants supply **β-carotene**, a provitamin that the intestine cleaves into retinal.

Vision (Wald's visual cycle). Rod cells contain **rhodopsin**, the protein opsin bound to 11-*cis*-retinal. Light switches 11-*cis*-retinal to all-*trans*-retinal; opsin changes shape, activates the G protein transducin, and a phosphodiesterase lowers cGMP, closing sodium channels and sending a nerve signal. All-*trans*-retinal then leaves opsin and is converted back to the 11-*cis* form before rhodopsin can be rebuilt. In dim light the rods depend on this cycle, so the first sign of deficiency is **night blindness**, followed by xerophthalmia (dry eye), Bitot's spots and keratomalacia, which can blind a child. India runs vitamin A supplementation for young children for this reason. Excess vitamin A is toxic and harms the developing foetus.

Vitamin D (calciferols)

Vitamin D is really a prohormone. **Cholecalciferol (D3)** is made in the skin when ultraviolet-B light opens a ring of 7-dehydrocholesterol; **ergocalciferol (D2)** comes from ergosterol in fungi and yeast. Neither is active until it has been hydroxylated twice.



Calcitriol acts through the nuclear vitamin D receptor, switching on genes such as calbindin, a calcium-binding protein of the gut cell.

Figure 4.7.1 Vitamin D becomes a hormone in three organs. Notice which form is which: calcidiol (25-hydroxy) is the storage and status marker made by the liver; calcitriol (1,25-dihydroxy) is the active hormone made by the kidney under control of parathyroid hormone (PTH).

Calcitriol raises blood calcium and phosphate, mainly by increasing their absorption from the gut. Deficiency gives **rickets** in children (soft, bent bones, bowed legs, a beaded “rickety rosary” on the ribs) and **osteomalacia** in adults. Surveys find vitamin D deficiency common in India despite plentiful sunshine, linked to indoor life, covered skin, pigmentation and air pollution. Excess causes high blood calcium and calcium deposits in soft tissues.

Vitamin E (tocopherols)

Vitamin E is a family of tocopherols and tocotrienols; **α-tocopherol** is the most active. It sits in membranes and lipoproteins and is the main fat-soluble **chain-breaking antioxidant**: it gives a hydrogen atom to a lipid peroxyl radical, stopping the chain reaction that would destroy polyunsaturated fatty acids. The tocopheroxyl radical formed is regenerated by vitamin C. Deficiency is rare and mostly seen in premature babies (haemolytic anaemia, because red-cell membranes break) and in long-term fat malabsorption (nerve and muscle damage). Vegetable oils, nuts and wheat germ are rich sources.

Vitamin K (quinones)

K1 (phylloquinone) comes from green leafy vegetables, K2 (menaquinones) from bacteria including gut bacteria, and K3 (menadione) is synthetic. Reduced vitamin K is the cofactor of **γ-**

glutamyl carboxylase, which adds a carboxyl group to specific glutamate residues, making γ-carboxyglutamate (Gla). Gla residues bind Ca^{2+}, which lets clotting **factors II (prothrombin), VII, IX and X** and proteins C and S attach to phospholipid surfaces where clotting happens. In the reaction vitamin K becomes an epoxide, and the enzyme vitamin K epoxide reductase recycles it. The anticoagulant **warfarin** blocks this reductase. Newborns have little vitamin K (poor transfer across the placenta and a sterile gut), so a vitamin K injection is given at birth to prevent bleeding.

WORKED EXAMPLE

Question (5 marks). (a) A vitamin D3 sachet contains 60,000 IU. Express this in micrograms, given 1 µg = 40 IU. (b) A food label lists 3,000 IU of retinol, and the same food also supplies 6 mg of dietary β-carotene. Using 1 IU retinol = 0.3 µg retinol activity equivalents (RAE) and 12 µg dietary β-carotene = 1 µg RAE, find the total vitamin A activity in µg RAE.

1. (a) 60,000 IU ÷ 40 IU per µg = **1,500 µg** = 1.5 mg of cholecalciferol.
2. (b) Retinol: 3,000 × 0.3 = 900 µg RAE.
3. β-carotene: 6 mg = 6,000 µg; 6,000 ÷ 12 = 500 µg RAE.
4. Total = 900 + 500 = **1,400 µg RAE**. Note that β-carotene counts far less than retinol per microgram, because it is absorbed and converted inefficiently. (These conversion factors are the US ones; check the convention your textbook uses.)

EXAM TRAPS

- Calcidiol is 25(OH)D from the liver; calcitriol is $1,25(OH)_2D$ from the kidney. Calcitriol is the active form.
- Retinoic acid supports growth and gene control but not vision; only retinal works in rhodopsin.
- Vitamin K "K" comes from the German *Koagulation*, not potassium. Warfarin is a vitamin K antagonist.
- Vitamin E is an antioxidant, not a coenzyme; vitamin C regenerates it.
- IU conversions differ between vitamins: 1 µg vitamin D = 40 IU, but 1 IU retinol = 0.3 µg.

CHECK YOURSELF

– REMEMBER **Name the active form of vitamin D and the organ that makes it.** 1 mark

Calcitriol, 1,25-dihydroxycholecalciferol, made in the kidney.

– REMEMBER **List the vitamin K-dependent clotting factors.** 2 marks

Factors II (prothrombin), VII, IX and X (also proteins C and S).

– UNDERSTAND **Why is night blindness the earliest sign of vitamin A deficiency?** 3 marks

Rods, which work in dim light, need a steady supply of 11-cis-retinal to rebuild rhodopsin after each bleach. When vitamin A is short, rhodopsin regenerates slowly, so dim-light vision fails before the other tissues show damage.

– UNDERSTAND **How does vitamin E protect cell membranes?** 2 marks

α-Tocopherol donates a hydrogen atom to lipid peroxyl radicals, ending the chain reaction of lipid peroxidation that would damage polyunsaturated fatty acids.

– APPLY **Convert 25 µg of vitamin D to IU.** 1 mark

25 × 40 = **1,000 IU**.

– APPLY **A patient with blocked bile flow bruises easily. Which vitamin is involved and why?** 2 marks

Vitamin K. Without bile salts fat-soluble vitamins are poorly absorbed, so prothrombin and factors VII, IX and X are not carboxylated and clotting fails.

– ANALYZE **A child with chronic kidney disease develops rickets even with enough sunlight and diet. Explain.** 3 marks

Skin and liver make D3 and 25(OH)D normally, but the damaged kidney cannot carry out 1α-hydroxylation, so calcitriol is low; calcium absorption falls and bone is poorly mineralised. Treatment uses calcitriol or a 1α-hydroxylated analogue, not plain vitamin D.

BEYOND THE SYLLABUS

Golden Rice is a genetically engineered rice that makes β-carotene in its grain, designed for regions with vitamin A deficiency. Retinoic acid derivatives treat severe acne and a form of leukaemia (acute promyelocytic leukaemia), and newer oral anticoagulants act on clotting factors directly instead of on vitamin K recycling. Search “Golden Rice” and “vitamin D receptor gene regulation”. This is not for the exam.

4.8 Macro and micro minerals

Minerals are the inorganic elements the body needs from food. They build bone, carry charge across membranes, hold water in the right compartments, and sit in the active sites of enzymes. They are divided by how much we need: **macrominerals** (major elements) are needed at more than about 100 mg a day, and **microminerals** (trace elements) at less than that. A trace element is needed in small amounts, but it is no less essential; iron and iodine deficiency are among the most common nutritional problems in India.

You need: vitamin D and calcium absorption from Chapter 4.7; B12 (which contains cobalt) from Chapter 4.6.

Macrominerals

MINERAL	MAIN ROLES	TOO LITTLE OR TOO MUCH
Calcium (Ca)	About 99% is in bones and teeth as hydroxyapatite; the rest controls muscle contraction, nerve signalling, blood clotting and acts as a second messenger. Blood level about 9–11 mg/dL, held by PTH, calcitriol and calcitonin.	Low: rickets, osteomalacia, osteoporosis; tetany when ionised Ca falls. High: kidney stones, soft-tissue calcification.
Phosphorus (P)	Bone mineral with Ca; part of ATP, nucleic acids, phospholipids; phosphate buffer	Low: rickets and muscle weakness
Magnesium (Mg)	Binds ATP: kinases use Mg–ATP, not free ATP; muscle and nerve function; bone	Low: tremor and tetany-like spasms
Sodium (Na)	Main cation outside cells; sets extracellular volume and osmotic pressure; nerve impulses	Low: hyponatraemia, confusion. High intake: raises blood pressure
Potassium (K)	Main cation inside cells; resting membrane potential; heart rhythm	Low or high: dangerous heart arrhythmias
Chloride (Cl)	Main anion outside cells; HCl of gastric juice; chloride shift in red cells	Lost with vomiting, giving alkalosis
Sulfur (S)	Taken in as methionine and cysteine; disulfide bonds; part of CoA, biotin and thiamine	No separate deficiency if protein is adequate

Sodium and potassium are kept on opposite sides of the membrane by the **Na^+/K^+-ATPase**, which pumps 3 Na^+ out and 2 K^+ in for each ATP it splits. This gradient drives nerve impulses and the uptake of glucose and amino acids in the gut and kidney.

Microminerals (trace elements)

ELEMENT	WHERE IT WORKS	DISORDER
Iron (Fe)	Haemoglobin, myoglobin, cytochromes, iron–sulfur proteins	Iron-deficiency anaemia; iron overload (haemochromatosis)
Zinc (Zn)	Carbonic anhydrase, alcohol dehydrogenase, carboxypeptidase; zinc-finger DNA-binding proteins; insulin storage	Poor growth, delayed wound healing, loss of taste; acrodermatitis enteropathica (inherited)
Copper (Cu)	Cytochrome c oxidase, Cu/Zn superoxide dismutase, lysyl oxidase (collagen cross-links), ceruloplasmin (oxidises Fe^{2+} for transport)	Wilson's disease (copper builds up in liver and brain); Menkes disease (copper transport fails)
Iodine (I)	Thyroid hormones T3 and T4	Goitre; cretinism in children of deficient mothers
Selenium (Se)	As selenocysteine in glutathione peroxidase, thioredoxin reductase and the deiodinases that activate thyroid hormone	Keshan disease (a heart disease); toxic in excess
Manganese (Mn)	Arginase, mitochondrial superoxide dismutase, pyruvate carboxylase	Deficiency rare
Cobalt (Co)	Only as part of vitamin B12	Seen as B12 deficiency
Molybdenum (Mo)	Xanthine oxidase, sulfite oxidase	Deficiency rare
Fluorine (F)	Forms fluorapatite, which makes enamel resist acid	Low: dental caries. High: dental and skeletal fluorosis, found in areas of India with high-fluoride groundwater

India adds iodine to salt (universal salt iodisation) to prevent goitre, and gives iron and folic acid tablets under the Anaemia Mukt Bharat programme.

Iron: a mineral the body cannot excrete

Iron is the trace element examiners ask about most, because its handling is unusual: the body has **no regulated way to excrete iron**, so the total is controlled at absorption.

1. **In food:** haem iron (meat, fish) is absorbed well. Non-haem iron in plant foods is mostly Fe^{3+} and must be reduced to Fe^{2+}; vitamin C helps, while phytates (cereals), tannins (tea) and calcium hinder it.

2. **Into the gut cell:** Fe^{2+} enters cells of the duodenum through a transporter called DMT1. It is either stored there as **ferritin** or passed out of the cell through **ferroportin**.
3. **In blood:** leaving iron is oxidised to Fe^{3+} by copper-containing ferroxidases (hephaestin, ceruloplasmin) and carried by **transferrin**, two Fe^{3+} per molecule.
4. **Use and storage:** cells take up transferrin through transferrin receptors; bone marrow uses most iron to make haemoglobin. Liver stores iron as ferritin and haemosiderin.
5. **Control:** when iron stores are high, the liver releases the hormone **hepcidin**, which destroys ferroportin and so blocks absorption.

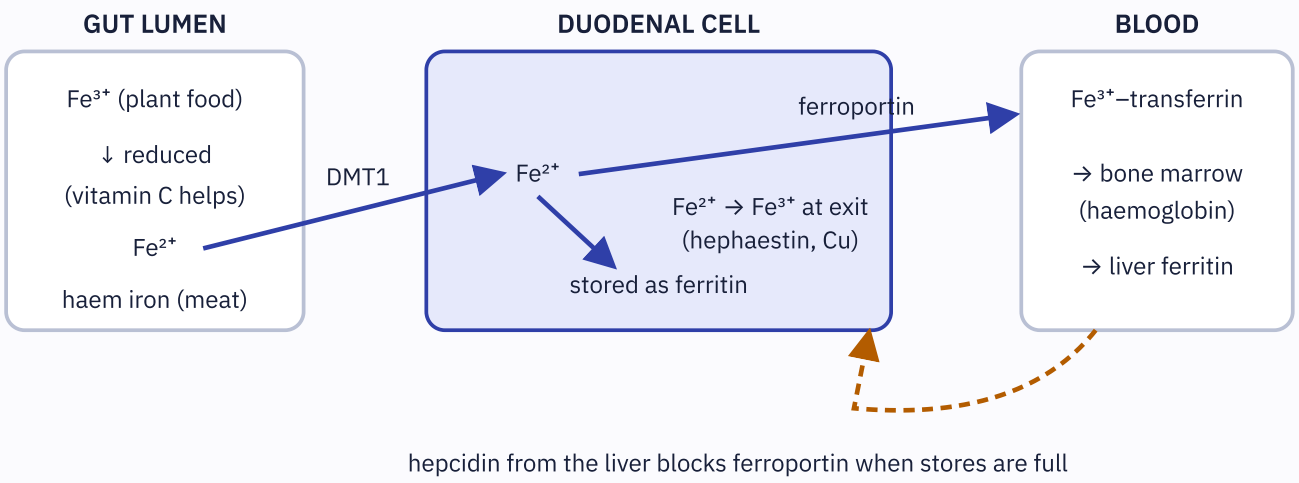


Figure 4.8.1 How dietary iron reaches the blood. Notice the two control points: iron can be locked in the gut cell as ferritin (and lost when the cell is shed), and hepcidin shuts the exit door, ferroportin, when the body has enough.

WORKED EXAMPLE

Question (6 marks). (a) Haemoglobin has a molar mass of about 64,500 g/mol and contains 4 iron atoms (Fe = 55.85 g/mol). Find the iron content in mg per gram of haemoglobin. (b) A woman has 12 g/dL haemoglobin and 4.5 L of blood. How much iron is in her circulating haemoglobin? (c) How many ATP molecules does the Na^+/K^+-ATPase use to move 3,000 Na^+ out of a cell, and how many K^+ come in?

1. (a) Iron per mole Hb = 4 × 55.85 = 223.4 g. Fraction = 223.4 ÷ 64,500 = 0.00346, so **3.46 mg iron per g Hb**.
2. (b) Blood = 4.5 L = 45 dL. Hb mass = 12 g/dL × 45 dL = 540 g.
3. Iron = 540 × 3.46 mg = 1,868 mg ≈ **1.9 g**. This is the largest single pool of body iron, which is why blood loss (heavy periods, hookworm, frequent pregnancies) leads to anaemia.
4. (c) The pump moves 3 Na^+ per ATP: 3,000 ÷ 3 = **1,000 ATP**, bringing in 1,000 × 2 = **2,000 K^+**.

EXAM TRAPS

- The macro/micro division is by daily need (about 100 mg/day), not by importance.
- Iron is absorbed as Fe^{2+} but carried by transferrin as Fe^{3+}; vitamin C helps by reducing Fe^{3+}.
- The body controls iron at absorption, not excretion. Hepcidin lowers absorption.
- Wilson's disease is copper excess in tissues; Menkes disease is copper deficiency. Ceruloplasmin is a copper protein that also oxidises iron.
- Selenium works as selenocysteine in glutathione peroxidase; do not write "selenium is a vitamin".

CHECK YOURSELF

– REMEMBER **List four macrominerals and four trace elements.** 2 marks

Macro: Ca, P, Mg, Na, K, Cl, S (any four). Trace: Fe, Zn, Cu, I, Se, Mn, Co, Mo, F (any four).

– REMEMBER **Name one enzyme each that needs zinc, copper and selenium.** 3 marks

Zinc: carbonic anhydrase. Copper: cytochrome c oxidase. Selenium: glutathione peroxidase.

– UNDERSTAND **Why does drinking tea with a vegetarian meal lower iron absorption, and lemon juice raise it?** 2 marks

Tannins in tea bind non-haem iron into forms that cannot be absorbed. Vitamin C in lemon reduces Fe^{3+} to Fe^{2+}, the form DMT1 carries, and keeps it soluble.

– UNDERSTAND **How does iodine deficiency cause goitre?** 3 marks

Without iodine the thyroid cannot make enough T3 and T4. Low hormone levels raise TSH from the pituitary, which keeps stimulating the thyroid to grow, and the gland enlarges.

– APPLY **A man has 15 g/dL haemoglobin and 5 L of blood. Estimate the iron in his haemoglobin.** 2 marks

Hb = 15 × 50 = 750 g; iron = 750 × 3.46 mg = 2,595 mg ≈ **2.6 g**.

– ANALYZE **A patient with copper deficiency also has anaemia even though iron intake is normal. Explain the link.** 4 marks

Iron leaves the gut cell and the liver as Fe^{2+} and must be oxidised to Fe^{3+} before transferrin can carry it. This is done by the copper-containing ferroxidases hephaestin and ceruloplasmin. With too little copper, iron is trapped in cells, too little reaches the bone marrow, and haemoglobin synthesis falls.

BEYOND THE SYLLABUS

Biofortified crops, such as high-iron pearl millet and high-zinc wheat varieties released in India, aim to raise mineral intake through ordinary food. An often-quoted estimate is that about a third of enzymes need a metal, and metalloprotein design is an active field of protein engineering. Hepcidin-based drugs are being tested for iron-overload diseases. Search “biofortification HarvestPlus” and “metalloenzymes”. This is not for the exam.

Unit summary

KEY TERMS AND FORMULAS

TERM	MEANING OR FORMULA	CHAPTER
Purine / pyrimidine	Two fused rings (A, G) / one ring (C, T, U); sugar at N9 / N1	4.1
Nucleoside	Base + pentose (β-N-glycosidic bond at C1′)	4.2
Nucleotide	Nucleoside + phosphate (usually at 5′)	4.2
Phosphodiester bonds	n nucleotides in a chain → n − 1 bonds; chain written 5′ → 3′	4.2
Chargaff's rules	A = T, G = C, A + G = T + C (double-stranded DNA)	4.3
B-DNA length	length = base pairs × 0.34 nm; turns = bp ÷ 10.5	4.3
A, B, Z DNA	Right, right, left; ≈ 11, 10.5, 12 bp per turn	4.4
Ribosomes	70S = 30S (16S) + 50S (23S, 5S); 80S = 40S (18S) + 60S (28S, 5.8S, 5S)	4.5
Niacin equivalents	NE (mg) = niacin (mg) + tryptophan (mg) ÷ 60	4.6
Vitamin units	1 µg vitamin D = 40 IU; 1 IU retinol = 0.3 µg RAE; 12 µg dietary β-carotene = 1 µg RAE	4.7
Iron in haemoglobin	≈ 3.46 mg Fe per g Hb (4 × 55.85 ÷ 64,500)	4.8
Na^+/K^+-ATPase	3 Na^+ out, 2 K^+ in per ATP	4.8

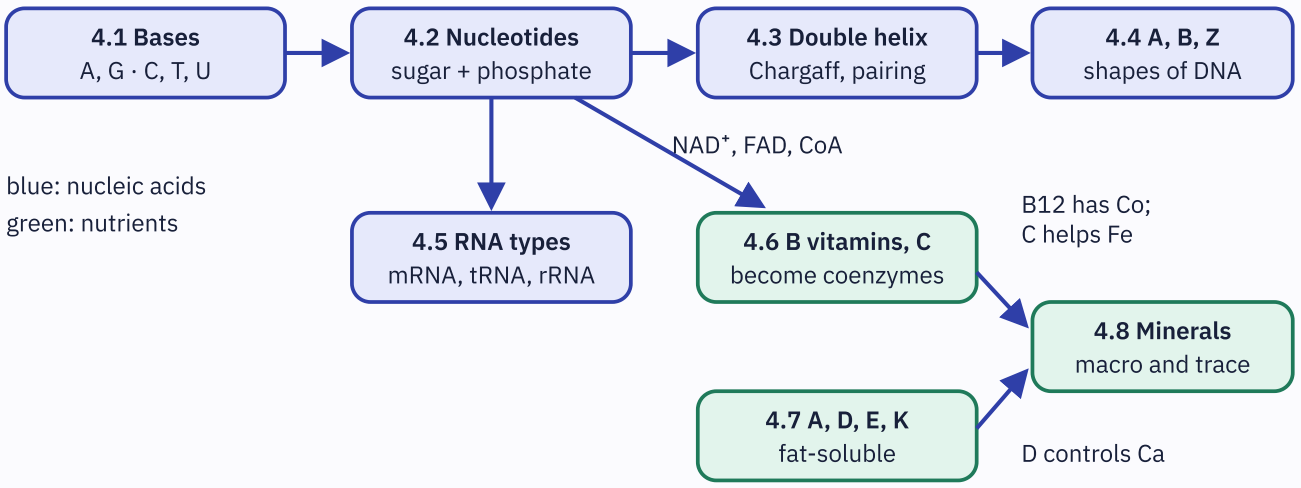


Figure 4.S.1 How the chapters connect. The nucleic-acid chain runs along the top; the nucleotide coenzymes are the bridge to the vitamins, and vitamins C, B12 and D tie into iron, cobalt and calcium.

Takeaways

1. Purines (A, G) have two rings and join the sugar at N9; pyrimidines (C, T, U) have one ring and join at N1. T is 5-methyluracil and is found in DNA.
2. Base + sugar = nucleoside; + phosphate = nucleotide; nucleotides join by 3′,5′-phosphodiester bonds into chains written 5′ → 3′.
3. The 2′-OH makes RNA alkali-labile; its absence makes DNA a stable store. Deoxyribose is what the diphenylamine test detects.
4. Watson–Crick DNA: two antiparallel right-handed strands, bases inside, A=T (2 H-bonds), G≡C (3), 0.34 nm per pair, about 2 nm wide, major and minor grooves. Chargaff's A = T and G = C follow from it.
5. Hydrogen bonds give pairing specificity; stacking gives most of the stability. More GC means a higher Tm.
6. A-DNA is short and wide, B-DNA is the cell's form, Z-DNA is left-handed and forms at alternating purine–pyrimidine sequences.
7. mRNA carries codons, tRNA brings amino acids on its CCA end and reads codons with its anticodon, and rRNA builds the ribosome and forms peptide bonds.
8. B vitamins become coenzymes (TPP, FAD, NAD^+, CoA, PLP, biotin, THF, cobalamin); vitamin C keeps collagen hydroxylases working.
9. A (vision, genes), D (calcium, activated in liver and kidney), E (membrane antioxidant) and K (Gla in clotting factors) are stored and can be toxic in excess.
10. Macrominerals are needed above about 100 mg/day, trace elements below; iron is controlled at absorption by hepcidin.

Exam question bank

Remember and understand

▼ Q1. Draw and number the purine and pyrimidine rings and give the structures of the five bases found in nucleic acids. Mention two unusual bases. (10 marks)

Outline: pyrimidine ring with N1, N3; purine ring with N1, N3, N7, N9 and the shared C4–C5 bond; adenine 6-amino, guanine 2-amino-6-oxo, cytosine 4-amino-2-oxo, thymine 5-methyl-2,4-dioxo, uracil 2,4-dioxo; sugar attachment at N9/N1; keto–amino tautomers; unusual bases such as 5-methylcytosine and pseudouridine with where they occur.

▼ Q2. Distinguish between nucleosides and nucleotides with examples, and list the bonds present in nucleic acids. (8 marks)

Outline: definitions; ribose vs deoxyribose; naming table (adenosine, AMP, dAMP); N-glycosidic, phosphoester, 3′,5′-phosphodiester and phosphoanhydride bonds; hydrogen bonds and stacking between strands; biological roles of free nucleotides (ATP, cAMP, NAD^+, FAD, CoA).

▼ Q3. Describe the Watson–Crick model of DNA and state Chargaff’s rules. Explain how the model accounts for the rules. (12 marks)

Outline: X-ray evidence (Franklin, Wilkins); two antiparallel right-handed strands, backbone outside, bases inside; A=T two, G≡C three hydrogen bonds; 0.34 nm rise, 10 (10.5) bp per turn, 3.4 nm pitch, 2 nm diameter; major and minor grooves; Chargaff’s four rules; complementary pairing makes A = T and G = C; labelled diagram.

▼ Q4. Describe the structure and function of mRNA, tRNA and rRNA, with a labelled cloverleaf diagram. (16 marks)

Outline: general features of RNA; mRNA in prokaryotes (polycistronic, Shine–Dalgarno) and eukaryotes (cap, UTRs, poly(A), splicing); tRNA arms, CCA end, anticodon, modified bases, L shape, wobble; rRNA in 70S and 80S ribosomes, peptidyl transferase as ribozyme; relative abundance.

▼ Q5. Classify vitamins. For any four B vitamins give the coenzyme form, one reaction and the deficiency disease. (12 marks)

Outline: water-soluble vs fat-soluble with properties; four rows such as thiamine–TPP–pyruvate dehydrogenase–beriberi, riboflavin–FAD–succinate dehydrogenase–cheilosis, niacin–NAD^+–dehydrogenases–pellagra, pyridoxine–PLP–transamination–neuropathy; mention niacin from tryptophan.

Apply

▼ Q6. A double-stranded DNA has 18% thymine. Find the other bases. If one strand has (A + G)/(T + C) = 0.8, give the ratio in the other strand and in the duplex. Find the length of a 5,000-bp stretch in B form. (8 marks)

Outline: A = 18%, G = C = 32%; other strand 1/0.8 = 1.25; duplex 1.0; length 5,000 × 0.34 = 1,700 nm = 1.7 μm; about 476 turns at 10.5 bp per turn.

▼ Q7. Explain the principle of the diphenylamine method for DNA estimation. A 200 μg/mL standard gives A = 0.52; an unknown gives 0.39. Find the unknown concentration. (8 marks)

Outline: hot acid releases 2-deoxyribose from purine nucleotides, forming ω-hydroxylevulinyl aldehyde; reaction with diphenylamine gives a blue colour read near 595–600 nm; RNA does not react; standard curve; slope 0.52/200 = 0.0026; unknown 0.39/0.0026 = 150 μg/mL.

▼ Q8. Describe the activation of vitamin D and its role in calcium metabolism. A tablet contains 1,000 IU of vitamin D3; express it in micrograms. (10 marks)

Outline: 7-dehydrocholesterol + UVB → D3; liver 25-hydroxylation → calcidiol; kidney 1α-hydroxylation → calcitriol, controlled by PTH and phosphate; VDR, calbindin, gut absorption, bone, kidney; rickets and osteomalacia; 1,000 ÷ 40 = 25 μg.

▼ Q9. Describe the absorption, transport and storage of iron. Calculate the haemoglobin iron of an adult with 13 g/dL Hb and 5 L blood. (12 marks)

Outline: haem vs non-haem iron; reduction to Fe^{2+}, DMT1, ferritin, ferroportin, hephaestin/ceruloplasmin, transferrin, transferrin receptor, hepcidin; no regulated excretion; deficiency anaemia; 13 × 50 = 650 g Hb × 3.46 mg/g ≈ 2.25 g iron.

Analyze and evaluate

▼ Q10. Compare A-, B- and Z-DNA in a table and explain which conditions favour each form. (10 marks)

Outline: handedness, bp per turn, rise, pitch, diameter, base tilt, sugar pucker, glycosidic conformation, grooves; humidity, salt, sequence, methylation and supercoiling; why RNA duplexes are A-form; schematic diagram.

▼ Q11. “Nucleotides are not only the building blocks of nucleic acids.” Discuss, linking nucleotides to vitamins and metabolism. (12 marks; spans Chapters 4.2 and 4.6)

Outline: ATP and GTP as energy carriers; cAMP and cGMP as second messengers; NAD^+, $NADP^+$, FAD, FMN and CoA each built from a vitamin plus an adenine nucleotide; UDP-glucose, CDP-

choline and S-adenosylmethionine as activated intermediates; pyruvate dehydrogenase as an example that needs four B-vitamin coenzymes.

▼ Q12. Two patients have megaloblastic anaemia; only one has nerve damage and methylmalonic aciduria. Analyse the biochemical basis, and explain how vitamin C and copper status can also affect a patient's blood picture. (14 marks; spans Chapters 4.6 and 4.8)

Outline: folate and B12 roles in one-carbon metabolism; methyl trap; methylmalonyl-CoA mutase needs adenosylcobalamin, so only B12 deficiency gives methylmalonic aciduria and neuropathy; vitamin C reduces Fe^{3+} for absorption; copper ferroxidases are needed to load transferrin, so deficiency of either can add iron-deficiency-type anaemia.

▼ Q13. Evaluate the statement "trace elements are less important than macrominerals", using iron, iodine, zinc and selenium as examples. (10 marks)

Outline: definition by daily need, not importance; iron in haemoglobin and cytochromes, iodine in thyroid hormones, zinc in enzymes and zinc fingers, selenium in glutathione peroxidase; the diseases of deficiency (anaemia, goitre, growth failure, Keshan disease); public-health programmes in India (salt iodisation, iron–folic acid supplementation); conclude that the statement is false.

Glossary

Anticodon	Three bases in the tRNA anticodon loop that pair antiparallel with an mRNA codon.
Base stacking	The van der Waals and hydrophobic contacts between neighbouring flat base pairs; the main stabilising force of the double helix.
Calcitriol	1,25-dihydroxycholecalciferol, the active hormone form of vitamin D, made in the kidney.
Chargaff's rules	In double-stranded DNA, A = T and G = C, so purines equal pyrimidines.
Codon	A triplet of mRNA bases that specifies one amino acid or a stop signal.
Coenzyme	A small organic molecule, often made from a vitamin, that an enzyme needs to catalyse its reaction.
Ferritin	The protein that stores iron inside cells.
Glycosidic bond (N-)	The bond joining C1′ of the sugar to N9 of a purine or N1 of a pyrimidine.
Hepcidin	Liver hormone that lowers iron absorption by destroying ferroportin.
Hyperchromic effect	The rise in absorbance at 260 nm when double-stranded DNA is denatured.

Intrinsic factor	A stomach protein needed to absorb vitamin B12 in the ileum.
Major groove	The wider of the two grooves on the B-DNA helix, where most sequence-reading proteins bind.
Megaloblastic anaemia	Anaemia with large, immature red cells, caused by folate or B12 deficiency.
Melting temperature (Tm)	The temperature at which half of a DNA sample is single-stranded.
Niacin equivalent	1 mg niacin or 60 mg tryptophan; the unit for total niacin intake.
Nucleoside	A nitrogenous base joined to a pentose sugar.
Nucleotide	A nucleoside with one or more phosphate groups on the sugar.
Phosphodiester bond	The phosphate bridge between the 3′-OH of one nucleotide and the 5′-OH of the next.
Poly(A) tail	The run of adenylates added to the 3′ end of most eukaryotic mRNAs.
Retinal	The aldehyde form of vitamin A; 11-cis-retinal binds opsin to form rhodopsin.
Ribozyme	An RNA molecule that acts as an enzyme, such as the 23S rRNA peptidyl transferase.
Svedberg unit (S)	A measure of how fast a particle sediments in a centrifuge; values do not add.
Tautomer	A form of a molecule with a hydrogen atom moved to another position, such as the keto and enol forms of a base.
Trace element	A mineral needed at less than about 100 mg per day, such as iron, zinc or iodine.
Transferrin	The plasma protein that carries iron as Fe^{3+}.
Z-DNA	A left-handed DNA double helix with a zigzag backbone, favoured by alternating purine–pyrimidine sequences.

Sources and further reading

Standard textbooks

- David L. Nelson and Michael M. Cox, *Lehninger Principles of Biochemistry*: the chapters on nucleotides and nucleic acids, and on vitamins as coenzymes (from memory; check the chapter numbers in your edition).
- U. Satyanarayana and U. Chakrapani, *Biochemistry*: the chapters on nucleic acids, vitamins and minerals; widely prescribed in Indian universities (from memory; check).

- Jeremy M. Berg, John L. Tymoczko and Lubert Stryer (later editions with Gregory Gatto), *Biochemistry* (from memory; check).
- Donald Voet and Judith G. Voet, *Biochemistry*: detailed treatment of DNA conformations A, B and Z (from memory; check).

Open web resources

- Wikipedia, “Nucleic acid double helix”, comparison table of A-, B- and Z-DNA geometry: en.wikipedia.org/wiki/Nucleic_acid_double_helix
- NIH Office of Dietary Supplements, “Vitamin A and Carotenoids: Fact Sheet for Health Professionals”, for the IU and RAE conversion factors: ods.od.nih.gov/factsheets/VitaminA-HealthProfessional

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