

Purine & Pyrimidine, Mineral Metabolism

Two syllabus halves, one note: how the cell builds and recycles its nucleotide bases, and how the body keeps its electrolytes, calcium, and trace elements in balance.

Purine Synthesis

Pyrimidine Synthesis

Salvage & Catabolism

Na/K/Cl

Ca & P

Fe, I, F, Se

Purine De Novo

Purine Salvage

Purine Catabolism

Pyrimidine De Novo

Pyrimi

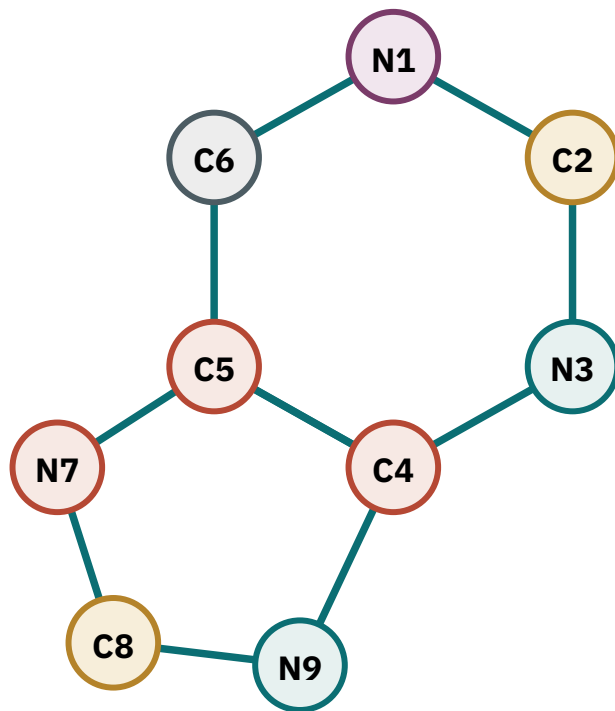
PART A · PURINE & PYRIMIDINE METABOLISM

1 Purine Biosynthesis — De Novo

Liver, cytosol · the ring is built atom-by-atom directly on PRPP

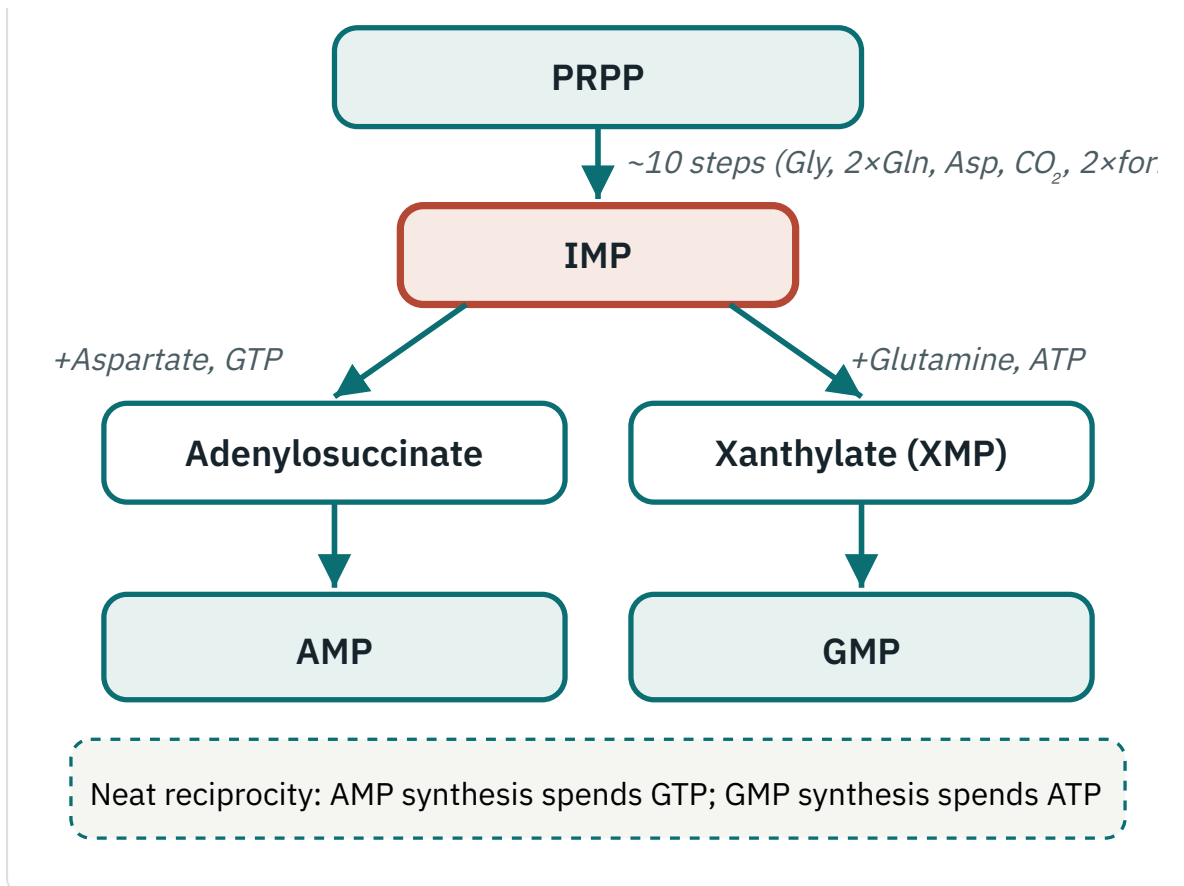
Unlike pyrimidines, the purine ring is assembled piece by piece *on top of* ribose-5-phosphate — there is no free base intermediate until the ring is already complete.

Where each ring atom comes from



- N1 Aspartate
- C2, C8 N¹⁰-formyl-THF
- C4, C5, N7 Glycine
- N3, N9 Glutamine • C6 CO₂

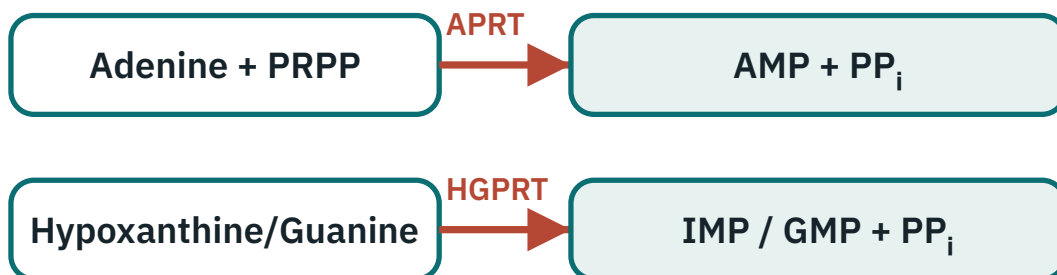
PRPP → IMP → AMP / GMP



2 Purine Salvage Pathway

Recycling free bases — far cheaper than de novo synthesis

Two salvage enzymes cover all three bases



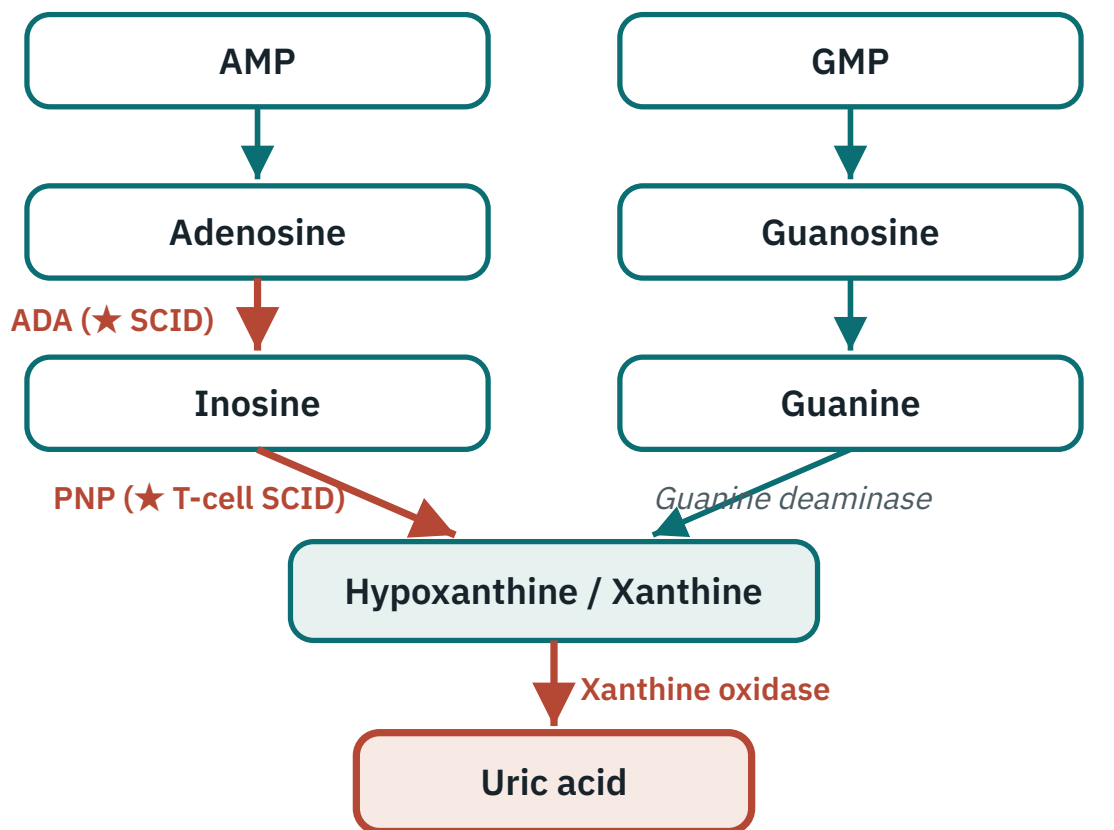
HGPRT DEFICIENCY

Complete: Lesch–Nyhan syndrome — hyperuricemia, gout, self-mutilation, choreoathetosis. Partial: gout only.

3 Purine Catabolism

Every purine converges on uric acid — a peculiarly human problem

AMP & GMP → uric acid



Allopurinol inhibits xanthine oxidase

— first-line gout therapy; humans lack uricase, so uric acid (not soluble at

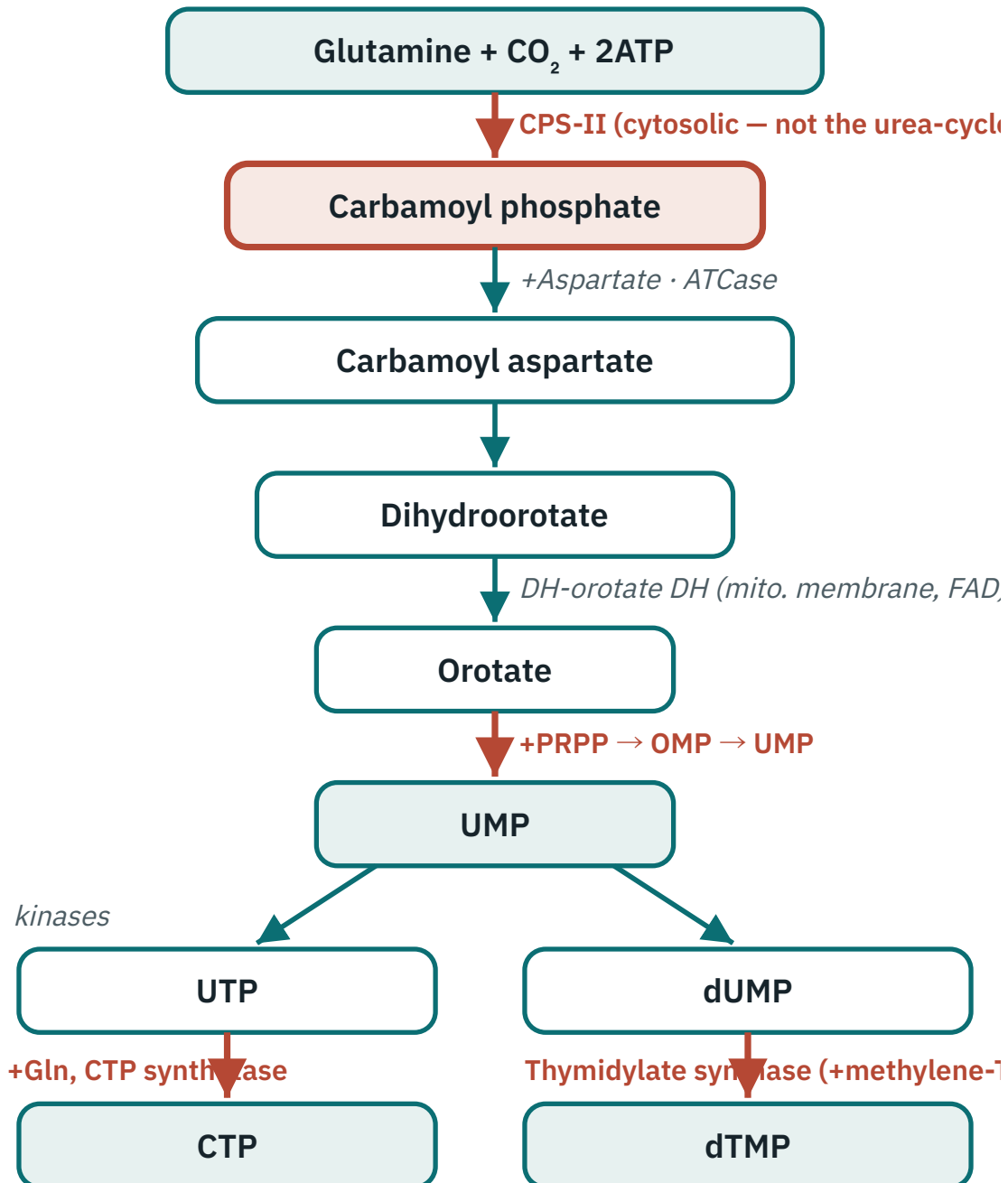
HYPERURICEMIA

Excess uric acid crystallises as monosodium urate in joints (gout — classically the great toe) and can form kidney stones. Overproduction (Lesch-Nyhan, high cell turnover) and underexcretion (renal disease, diuretics) are the two broad mechanisms.

4 Pyrimidine Biosynthesis — De Novo

Ring first, then attached to PRPP — the opposite order to purines

Carbamoyl phosphate → UMP → UTP / CTP, and dTMP



Chemotherapy targets

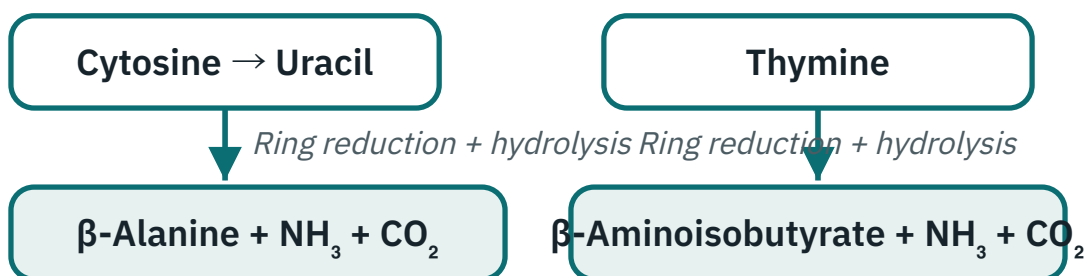
5-FU blocks thymidylate synthase · Methotrexate blocks DHFR (regenerates THF)

5 Pyrimidine Salvage & Catabolism

No "pyrimidine gout" — the end products stay soluble

Pyrimidine salvage is simple — nucleoside kinases (e.g. thymidine kinase salvaging thymidine → dTMP) directly rephosphorylate free nucleosides. Catabolism is where pyrimidines truly diverge from purines.

Catabolism ends in small, soluble molecules



KEY CONTRAST WITH PURINES

Purine catabolism → poorly soluble uric acid → gout risk.
Pyrimidine catabolism → highly soluble β-amino acids that feed ordinary metabolism — no equivalent disease exists.

PART B • MINERAL METABOLISM

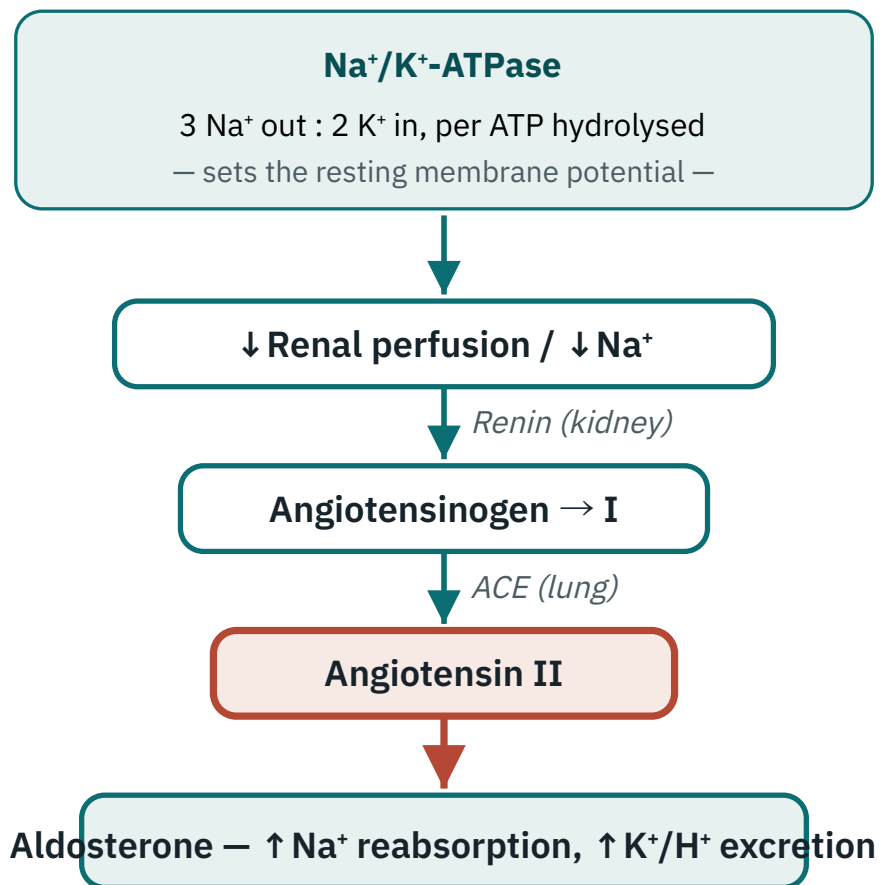
6 Sodium, Potassium & Chloride

The electrolytes that set every membrane potential in the body

Ion	Main location	Normal plasma	Key roles
Sodium	Extracellular	135–145	ECF osmolality/volume, nerve impulse,

(Na ⁺)	(ECF)	mEq/L	acid–base
Potassium (K ⁺)	Intracellular (~98%)	3.5–5.0 mEq/L	Resting membrane potential, cardiac rhythm
Chloride (Cl ⁻)	Extracellular	96–106 mEq/L	Follows Na ⁺ ; gastric HCl; chloride shift (CO ₂ transport)

Na⁺/K⁺-ATPase and the RAAS axis



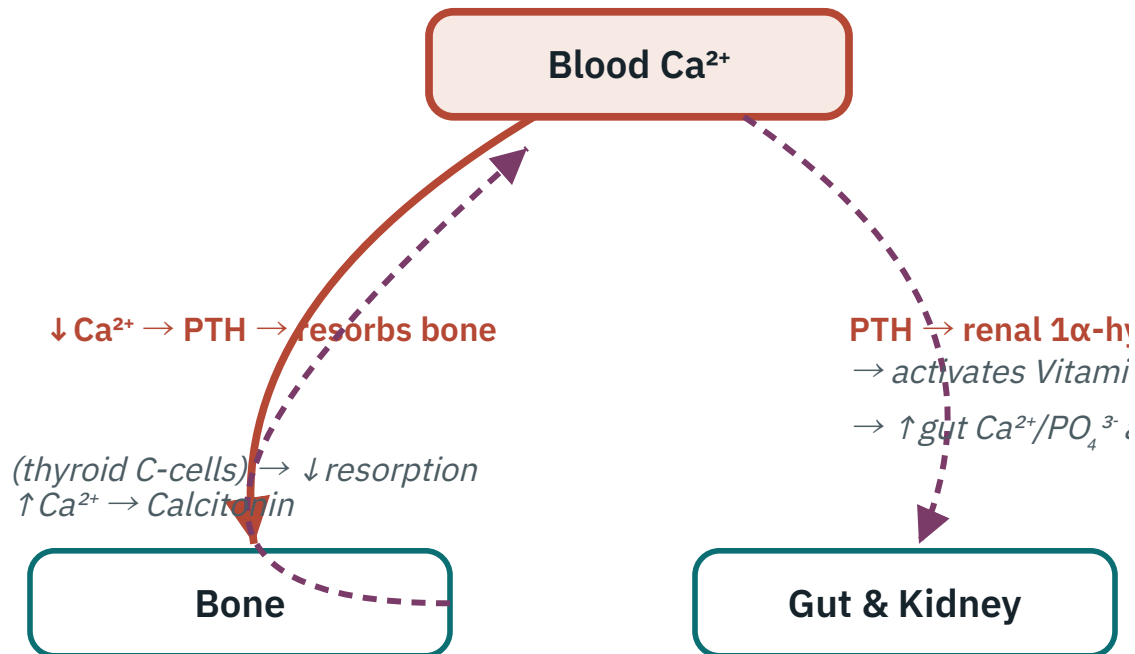
ELECTROLYTE EMERGENCIES

Hyperkalemia → peaked T waves, risk of cardiac arrest; hypokalemia → flattened T waves, muscle weakness, arrhythmia. Chloride tracks sodium in most disturbances but falls disproportionately with vomiting (loss of gastric HCl), producing a hypochloremic metabolic alkalosis.

7 Calcium & Phosphorus

99% locked in bone; the remaining 1% is tightly hormone-controlled

The calcium homeostasis triangle



VITAMIN D ACTIVATION

Skin: 7-dehydrocholesterol $\xrightarrow{\text{UV}}$ Cholecalciferol (D_3)

Liver: 25-hydroxylase $\rightarrow$ 25-OH- D_3 (storage/measured form)

Kidney: 1α -hydroxylase (PTH-driven) $\rightarrow$ 1,25-(OH) $_2$ - D_3 (active)

Active Vit D $\uparrow$ absorbs BOTH Ca^{2+} and phosphate

Hormone	Trigger	Net effect on Ca^{2+}
Parathyroid hormone (PTH)	$\downarrow$ Blood Ca^{2+}	$\uparrow$ (bone resorption, renal reabsorption, activates Vit D)
Calcitriol (active Vit D)	PTH / low Ca^{2+} , PO_4^{3-}	$\uparrow$ (intestinal Ca^{2+} & phosphate absorption)

Calcitonin	↑ Blood Ca^{2+}	↓ (inhibits osteoclasts) — minor role in humans
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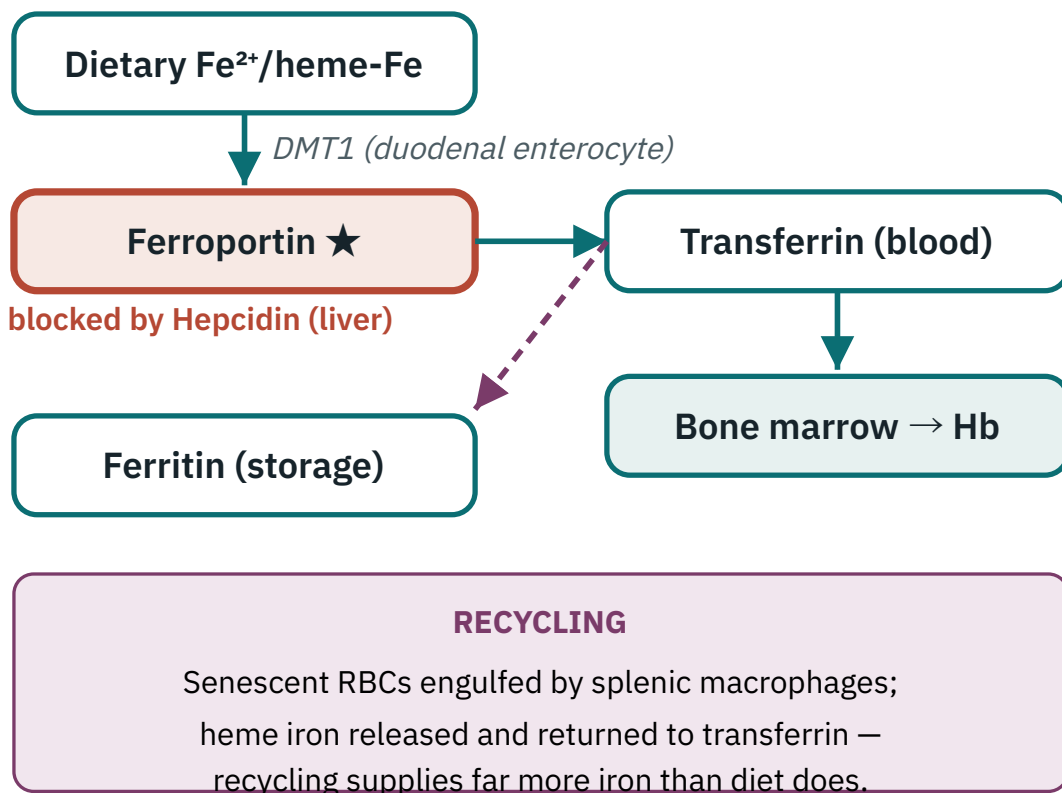
CLINICAL CORRELATIONS

Hypocalcemia → tetany, positive Chvostek's/Trousseau's sign, laryngospasm.
Hypercalcemia → "stones, bones, groans, psychiatric overtones" (renal stones, bone pain, GI upset, confusion). Vitamin D deficiency → rickets (children) / osteomalacia (adults).

8 Trace Elements — Iron

The most tightly recycled mineral in the body

Absorption, transport & storage



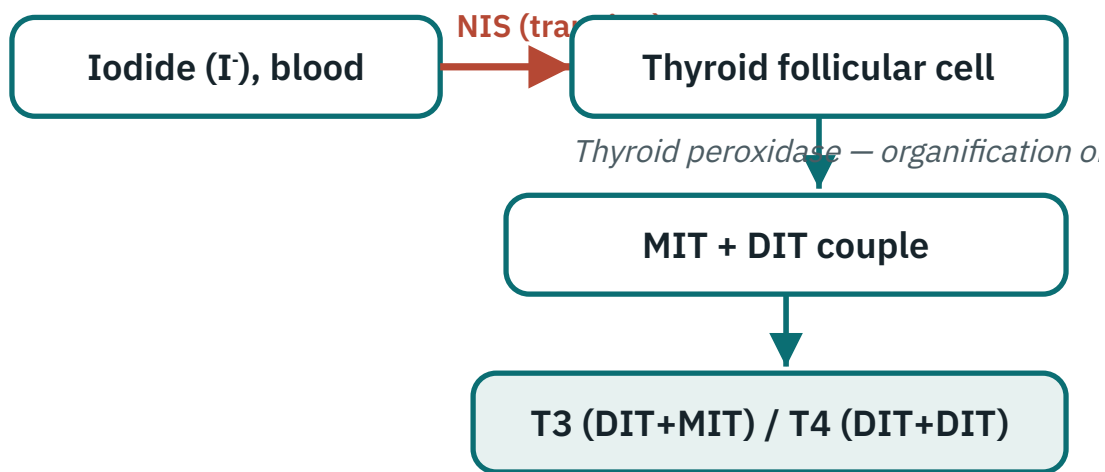
	Cause / feature
Deficiency	Microcytic hypochromic anaemia — commonest nutritional deficiency

	worldwide; blood loss, poor intake, malabsorption, pregnancy
Excess	Hereditary haemochromatosis (HFE mutation) — iron overload, cirrhosis, "bronze diabetes," cardiomyopathy

9 Trace Elements — Iodine, Fluorine & Selenium

Micrograms that make macro differences

Iodine – thyroid hormone synthesis



Element	Function	Deficiency	Excess
Iodine	Thyroid hormone (T3/T4) synthesis	Goitre, hypothyroidism, cretinism (congenital)	Rare — can also cause goitre/hypothyroidism
Fluorine	Forms fluorapatite in bone/teeth	↑ Dental caries	Dental & skeletal fluorosis
Selenium	Selenocysteine in glutathione peroxidase & T4→T3 deiodinase	Keshan disease (cardiomyopathy), Kashin–Beck disease	Selenosis — hair/nail loss, GI upset

IODINE AND SELENIUM ARE LINKED

Converting T4 to the active hormone T3 requires a selenium-dependent

deiodinase — so selenium deficiency can worsen the clinical impact of borderline iodine deficiency, even when iodine intake itself looks adequate.

10 Exam Corner

Practice question set — end-semester format

B.Sc. Biochemistry — End-Semester Examination

Paper: Purine/Pyrimidine & Mineral Metabolism Full Marks: 30 Time: 1.5 Hrs

GROUP A — LONG ANSWER (ANSWER ANY TWO)

1. Describe the de novo biosynthesis of purine nucleotides, indicating the source of each ring atom, and explain the fate of excess purines in the body. **10**
2. Discuss the hormonal regulation of calcium and phosphorus homeostasis, with the synthesis and activation of vitamin D. **10**
3. Describe the absorption, transport, and storage of iron in the body, and discuss the biochemical basis of iron deficiency anaemia. **10**

GROUP B — SHORT NOTES (ANSWER ANY TWO)

- a. Purine salvage pathway and Lesch–Nyhan syndrome **5**
- b. Difference between purine and pyrimidine catabolism **5**
- c. Functions and deficiency manifestations of iodine and selenium **5**