

Amino Acid Metabolism

Where nitrogen comes from, where it goes, and everything the 20 amino acids build along the way — from the urea cycle to serotonin, melanin, and the one-carbon units that write DNA.

Transamination

Deamination

Urea Cycle

Nitric Oxide

Specialised Products

Inborn Errors

One-Carbon Metabolism

AA Pool

NPN

Trans/Deamination

N Excretion

Individual AAs

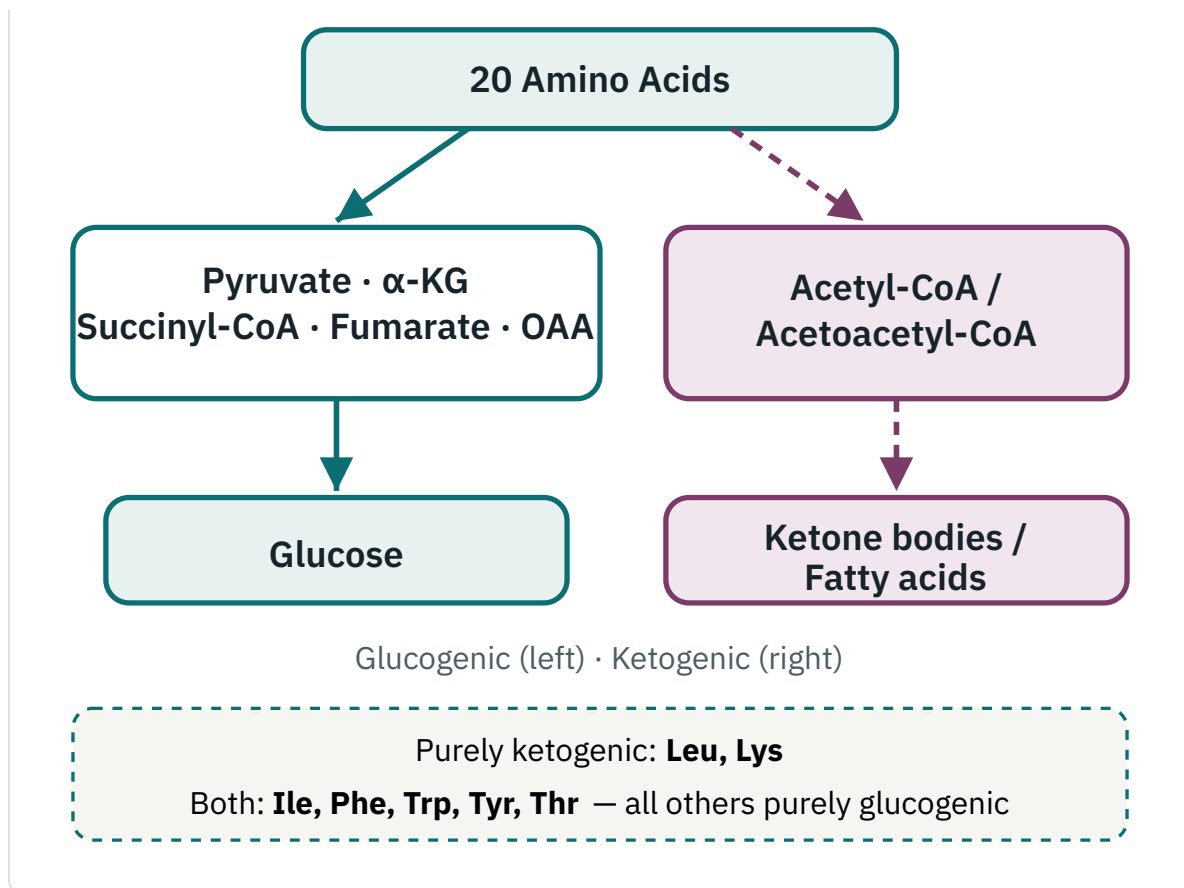
Specialised

1 Amino Acid Pool & Glucogenic/Ketogenic AAs

The body's dynamic, ~100 g free-amino-acid reservoir

The **amino acid pool** is fed by dietary protein digestion, tissue protein turnover, and de-novo synthesis of non-essential amino acids — and drained by protein synthesis, oxidation for energy, conversion to nitrogenous products, and nitrogen excretion.

Where amino acid carbon skeletons re-enter central metabolism



NON-PROTEIN NITROGEN PREVIEW

Only two amino acids — leucine and lysine — are purely ketogenic; five more are dual (glucogenic + ketogenic); the remaining thirteen are purely glucogenic. This single fact underlies a large share of amino-acid exam questions.

2 Non-Protein Nitrogen (NPN)

Nitrogenous compounds in blood that are not proteins

NPN is the filtrate remaining after plasma proteins are precipitated out — historically measured as a single value before individual assays (urea, creatinine, uric acid) became routine.

NPN component	Approx. share	Significance
Urea	~45–50%	End product of protein catabolism; raised in renal failure (azotemia)

Amino acids	~20%	Reflects the circulating amino acid pool
Uric acid	~5%	Purine end-product; raised in gout, renal disease
Creatine + Creatinine	~5–7%	Creatinine reflects muscle mass; used to estimate GFR
Ammonia	<1%	Raised in liver failure/urea cycle defects — neurotoxic

AZOTEMIA

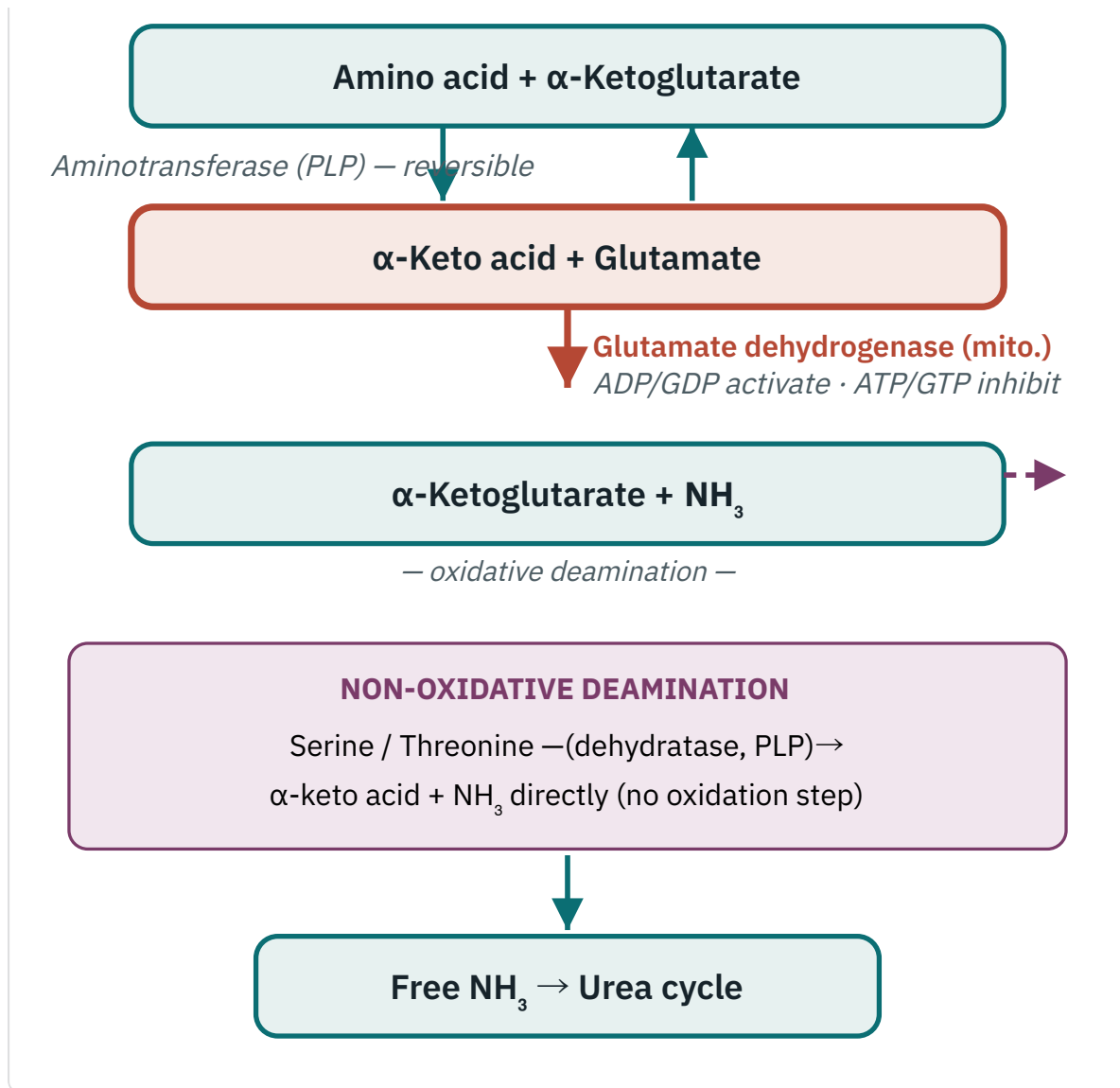
A rising NPN/blood urea signals either reduced renal clearance or increased protein catabolism (fever, trauma, GI bleeding) — the two possibilities that must be distinguished clinically.

3 Transamination & Deamination

Funnelling every amino group toward free ammonia

Before nitrogen can be excreted, it is collected from all twenty amino acids and channelled through glutamate — transamination redistributes it, deamination finally releases it as free NH_3 .

Transdeamination – the funnel to ammonia



4 Ammonotelic, Ureotelic & Uricotelic Organisms

Three evolutionary solutions to the same toxic-waste problem

Type	Excreted as	Organisms	Trade-off
Ammonotelic	Ammonia (NH ₃)	Most bony fish, aquatic invertebrates	No energy cost, but needs abundant water to dilute toxicity
Ureotelic	Urea	Mammals, adult	Moderate energy cost (urea cycle);

		amphibians, terrestrial vertebrates	much less toxic, moderate water need
Uricotelic	Uric acid	Birds, reptiles, insects, land snails	Highest energy cost; non-toxic semi-solid paste — conserves water (essential in shelled eggs)

WHY BIRDS AND REPTILES CHOSE URIC ACID

A developing embryo sealed inside a shell cannot excrete liquid waste into its environment. Uric acid's low solubility lets nitrogenous waste be stored as a solid paste within the egg without poisoning the embryo or dehydrating it.

5 Glycine, Sulphur AAs, Tryptophan & Tyrosine

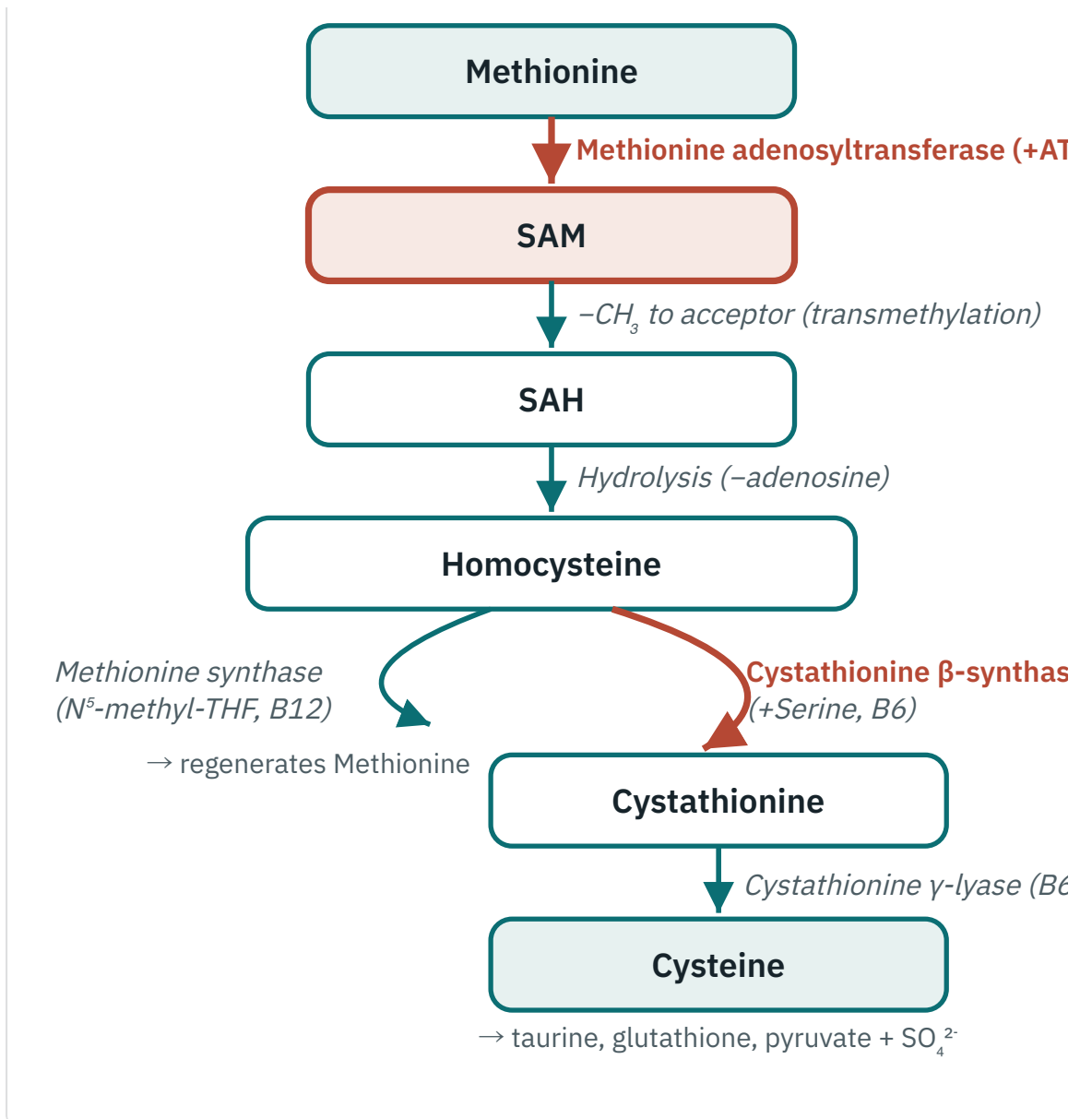
Four amino acids with outsized metabolic importance

Glycine

Made mainly from serine (serine hydroxymethyltransferase, PLP, using THF). Catabolised by the mitochondrial glycine cleavage system (releasing CO₂, NH₃, and one-carbon units). A precursor for **glutathione, haem, purines, creatine**, and bile-salt conjugation. Glycine cleavage system defects cause non-ketotic hyperglycinaemia.

Sulphur-containing amino acids — Methionine & Cysteine

The SAM cycle & transsulfuration

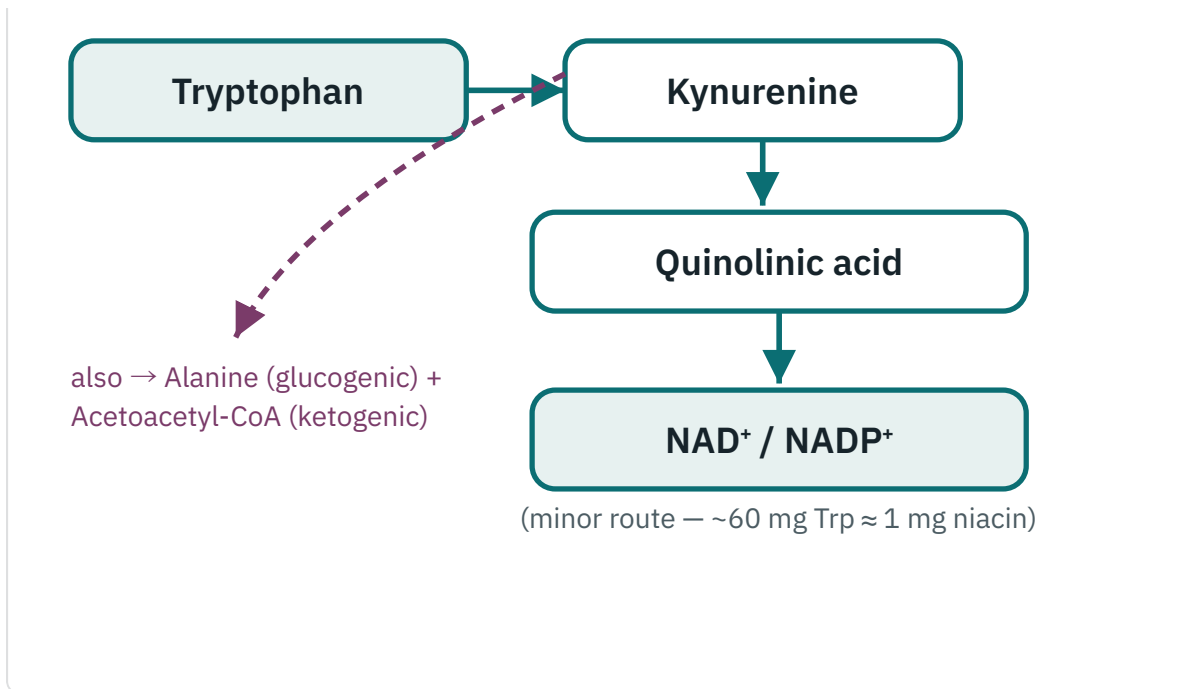


HOMOCYSTINURIA

Most often cystathionine β -synthase deficiency — accumulated homocysteine raises thromboembolic and cardiovascular risk, with Marfanoid habitus and lens dislocation.

Tryptophan

Kynurenine pathway — the major catabolic route

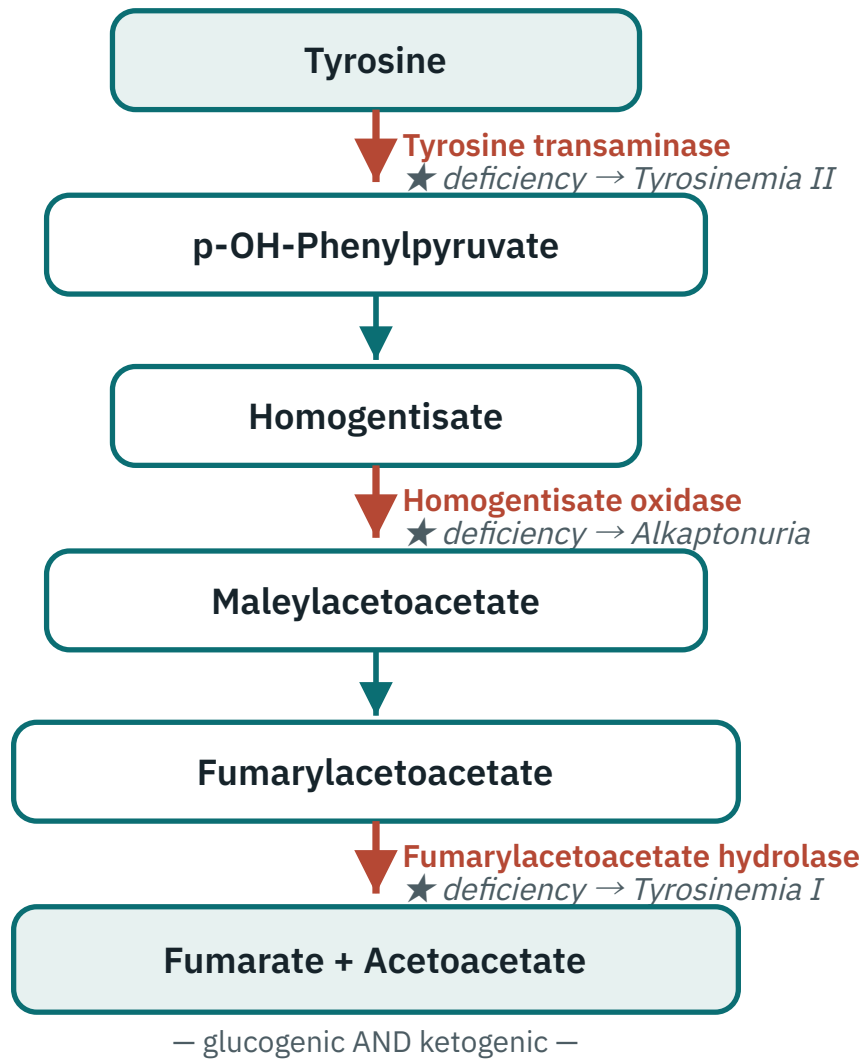


HARTNUP DISEASE

— defective intestinal/renal transport of neutral amino acids (including tryptophan) produces pellagra-like symptoms from functional niacin deficiency, with photosensitive dermatitis and ataxia.

Tyrosine

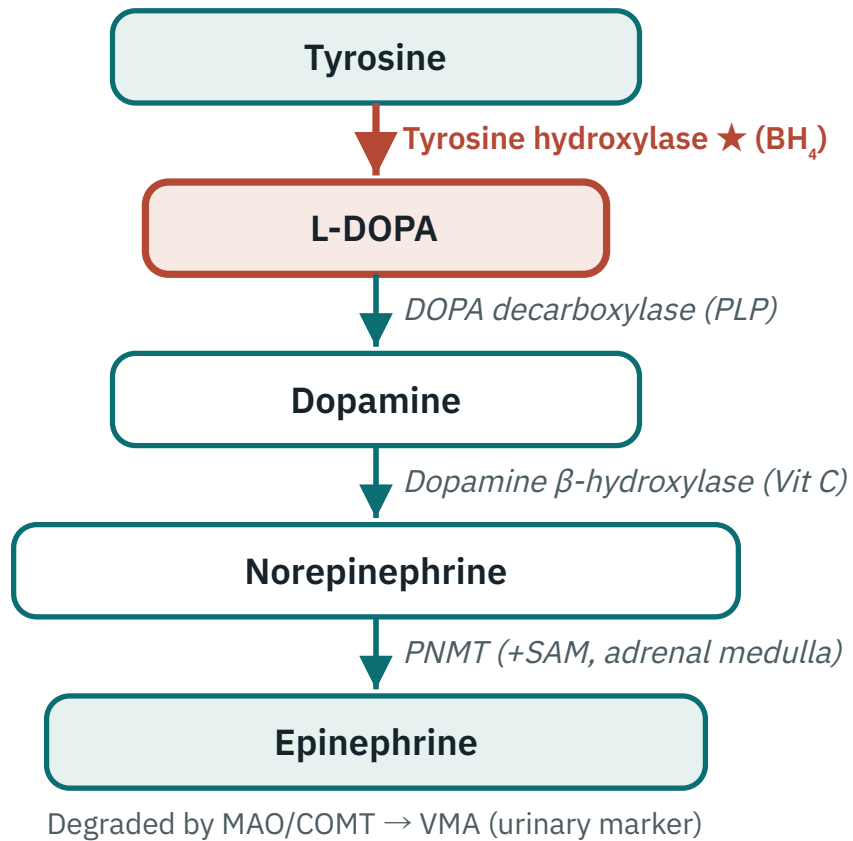
Tyrosine degradation — and where it goes wrong



6 Specialised Products of Amino Acids

Nine small molecules, built directly from amino acid precursors

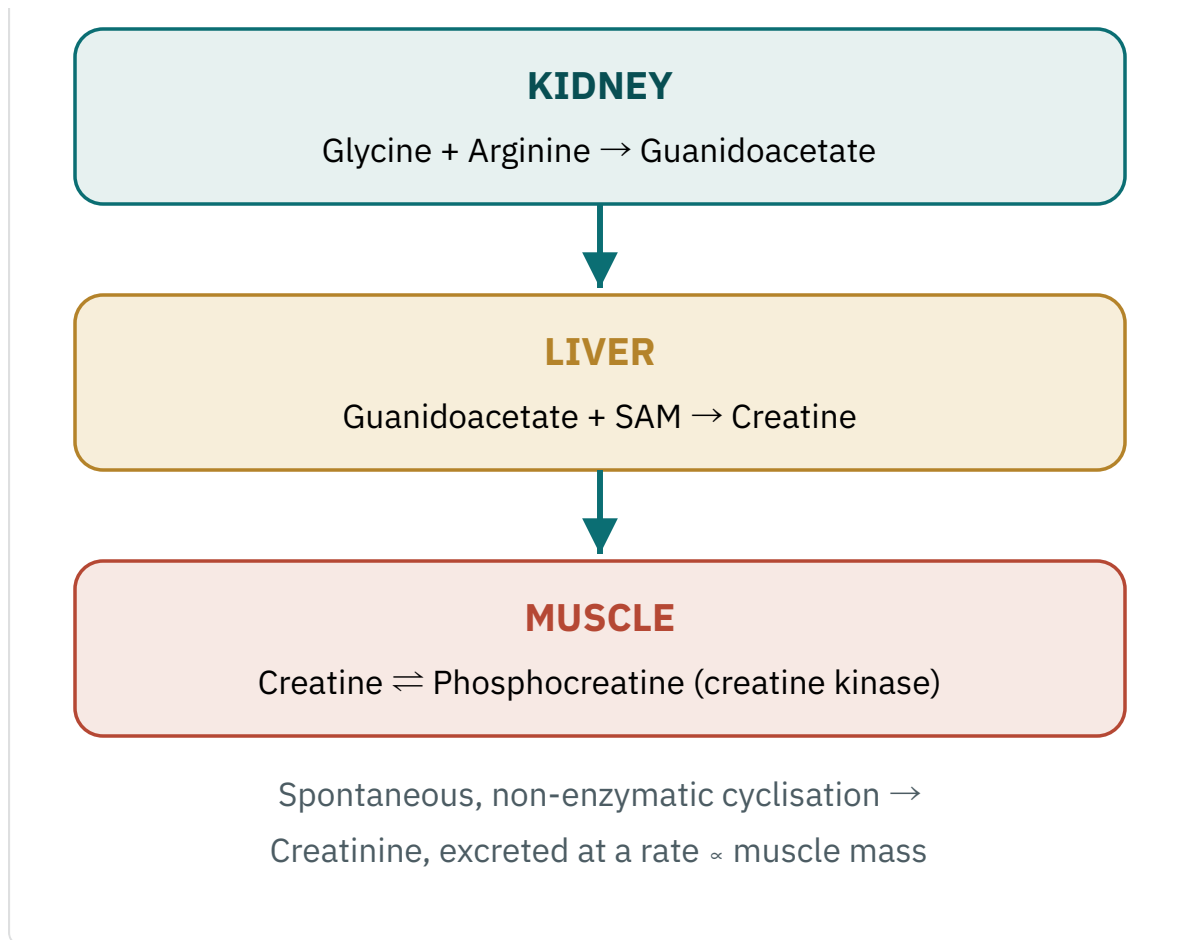
Catecholamine synthesis



CLINICAL LINKS

— Parkinson's disease (dopamine deficiency, nigrostriatal); pheochromocytoma (catecholamine-secreting tumour, ↑ urinary VMA/metanephrines).

Creatine phosphate – a three-organ relay



Product	Precursor AA	Key enzyme	Significance
Serotonin → Melatonin	Tryptophan	Tryptophan hydroxylase; pineal N-acetylation + methylation	Mood, GI motility; melatonin sets circadian rhythm
Histamine	Histidine	Histidine decarboxylase (PLP)	Allergic/inflammatory response, gastric acid secretion
Melanin	Tyrosine	Tyrosinase (via DOPA → DOPAquinone)	Skin/hair pigment; deficiency → albinism
GABA	Glutamate	Glutamate decarboxylase (PLP)	Major inhibitory CNS neurotransmitter
Taurine	Cysteine	Cysteine sulfinic acid → hypotaurine → taurine	Bile acid conjugation, membrane stabilisation
Glutathione	Glu + Cys + Gly	γ -Glutamylcysteine synthetase; GSH synthetase	Major cellular antioxidant; Phase II detoxification

Nicotinamide (NAD ⁺)	Tryptophan	Kynurenine pathway (minor route)	Explains pellagra risk with isoniazid (B6 depletion)
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7 Inborn Errors — Trp, Phe & Tyr

Where the pathways above break down

Disorder	Enzyme deficient	Key features
Phenylketonuria (PKU)	Phenylalanine hydroxylase (or BH ₄)	↑ Phe; musty-odour urine; intellectual disability if untreated; managed with a Phe-restricted diet
Tyrosinemia Type I	Fumarylacetoacetate hydrolase	Liver & kidney failure; cabbage-like odour
Tyrosinemia Type II (Richner–Hanhart)	Tyrosine aminotransferase	Keratitis, palmoplantar keratoderma
Alkaptonuria	Homogentisate oxidase	Urine darkens on standing; ochronosis; arthritis
Albinism	Tyrosinase	Absent pigmentation, photophobia
Hartnup disease	Neutral amino acid transporter	Pellagra-like features from impaired tryptophan uptake

READING THE TYROSINE DIAGRAM AS AN EXAM SHORTCUT

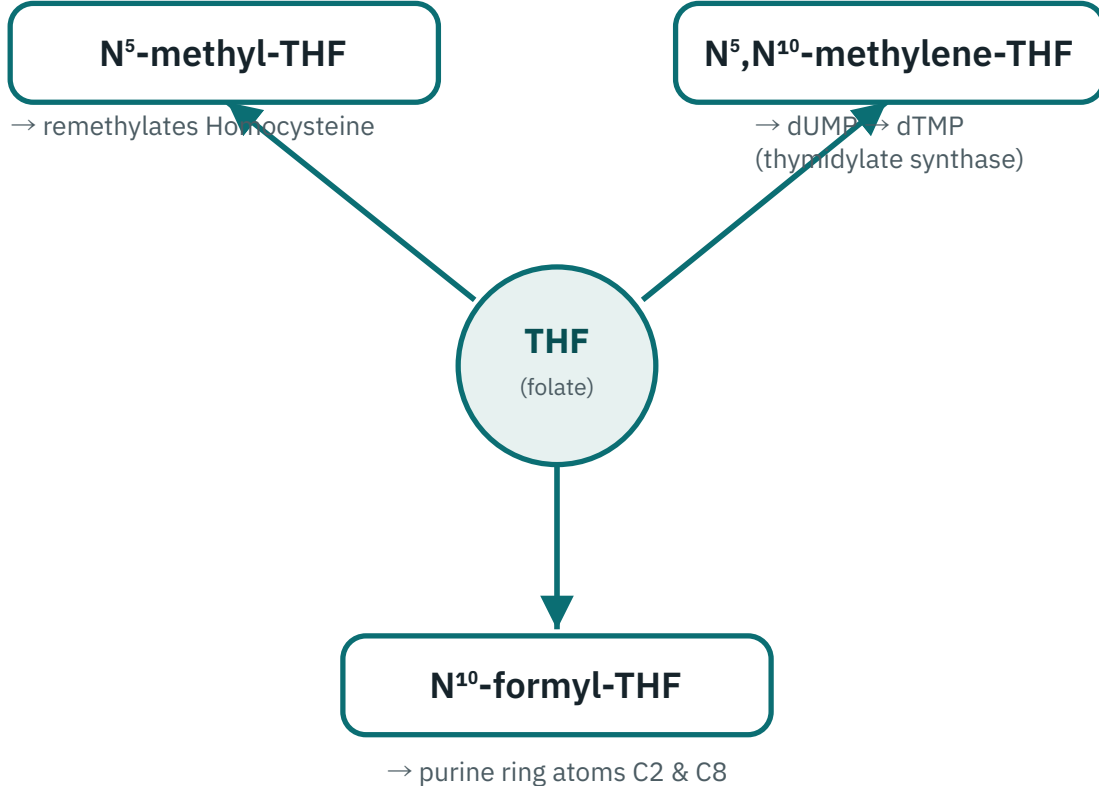
Every enzyme in the tyrosine degradation ladder (Section 5) maps to exactly one disease — transaminase → Tyrosinemia II, homogentisate oxidase → alkaptonuria, fumarylacetoacetate hydrolase → Tyrosinemia I. Learn the pathway once, and the inborn errors table follows for free.

8 One-Carbon Metabolism & Transmethylation

Folate carries the units; SAM delivers the "labile methyl group"

THF – one carrier, several one-carbon forms

from Serine (SHMT)



THE "LABILE METHYL GROUP" & TRANSMETHYLATION

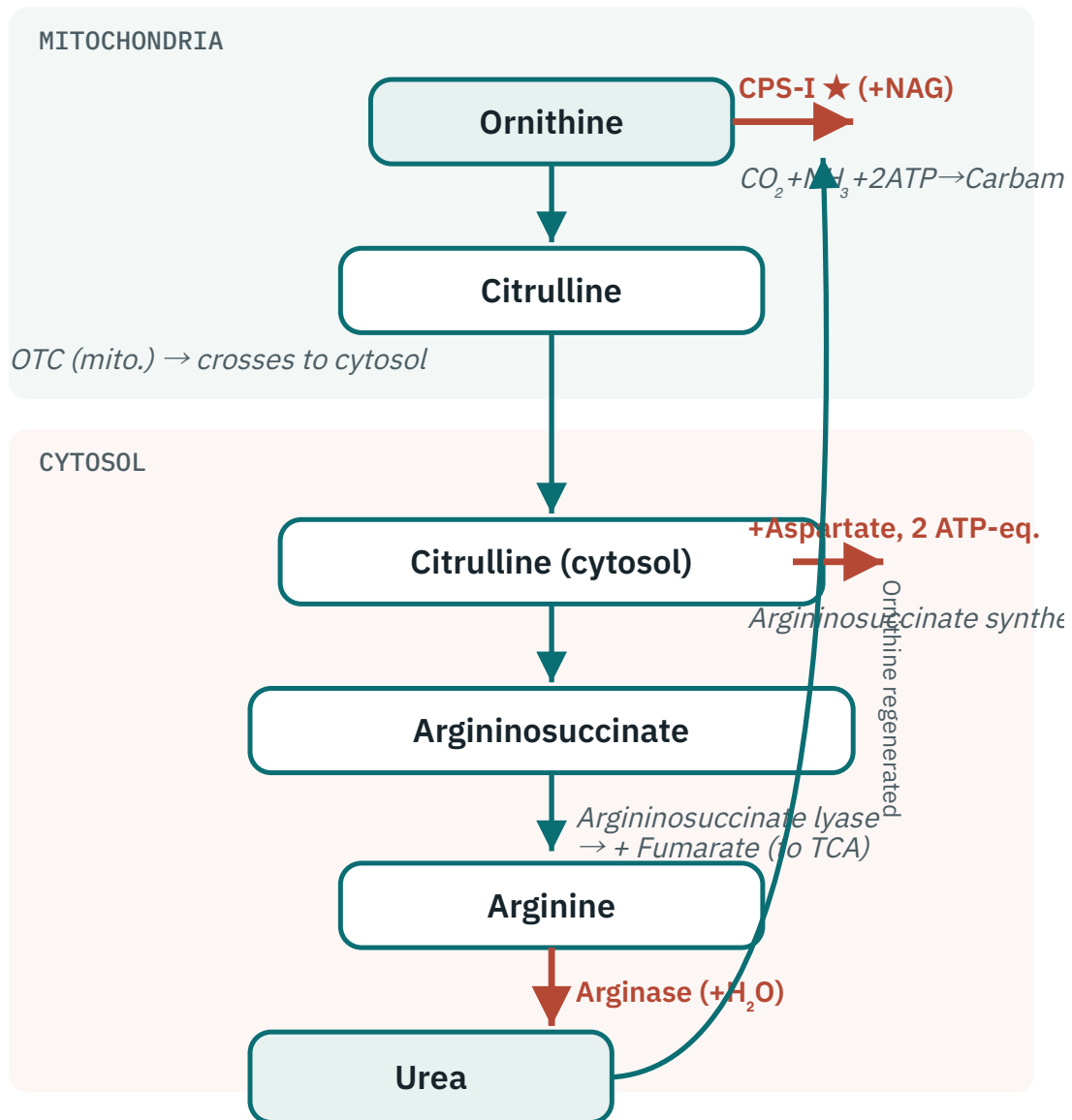
SAM's methyl group (from methionine, Section 5) is called "labile" because it transfers so readily. Its reactions include PE → PC (×3 methylations, PEMT), norepinephrine → epinephrine (PNMT), guanidoacetate → creatine, and nicotinamide → N-methylnicotinamide (an excretion step) — plus DNA/histone methylation.

THE METHYLFOLATE TRAP

B12 deficiency stalls methionine synthase, trapping folate as N⁵-methyl-THF — a form that cannot be converted back to other one-carbon forms. The result is a *functional* folate deficiency (megaloblastic anaemia) even with normal folate stores, plus the neurological signs unique to B12 deficiency.

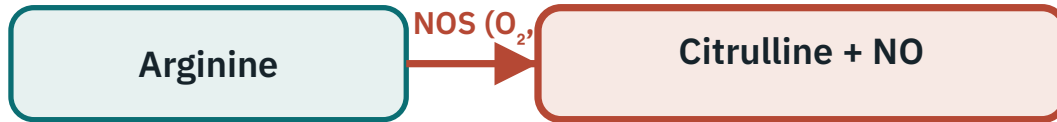
Two very different fates for the same amino acid, arginine

The urea cycle – mitochondria + cytosol



COST & CONTROL

One urea = **4 ATP-equivalents** spent (2 at CPS-I, 2 at argininosuccinate synthetase). CPS-I is rate-limiting and absolutely requires **N-acetylglutamate** (made from acetyl-CoA + glutamate, itself activated by arginine) — linking urea cycle activity directly to amino acid/protein intake.



NO → activates guanylate cyclase → cGMP → smooth-muscle relaxation

eNOS: vasodilation · nNOS: neurotransmission · iNOS: immune/antimicrobial

CLINICAL HOOKS

Nitroglycerin (NO donor) relieves angina; sildenafil blocks cGMP breakdown (PDE5) for erectile dysfunction; excessive iNOS-derived NO drives the hypotension of septic shock.

10 Exam Corner

Practice question set — end-semester format

B.Sc. Biochemistry — End-Semester Examination

Paper: Amino Acid Metabolism

Full Marks: 30

Time: 1.5 Hrs

GROUP A — LONG ANSWER (ANSWER ANY TWO)

1. Describe the urea cycle with a labelled diagram, indicating the compartmentation, the rate-limiting step, and its energy cost. Add a note on nitric oxide synthesis from arginine. **10**
2. Discuss transamination and the two types of deamination, with the role of glutamate dehydrogenase in channelling amino nitrogen to ammonia. **10**
3. Describe the catabolism of tyrosine and correlate each enzymatic step with the inborn error of metabolism that results from its deficiency. **10**

GROUP B — SHORT NOTES (ANSWER ANY TWO)

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|--|---|
| a. Glucogenic and ketogenic amino acids | 5 |
| b. One-carbon metabolism and the labile methyl group | 5 |
| c. Ammonotelism, ureotelism and uricotelism | 5 |