

Exercise walk-through

2.7

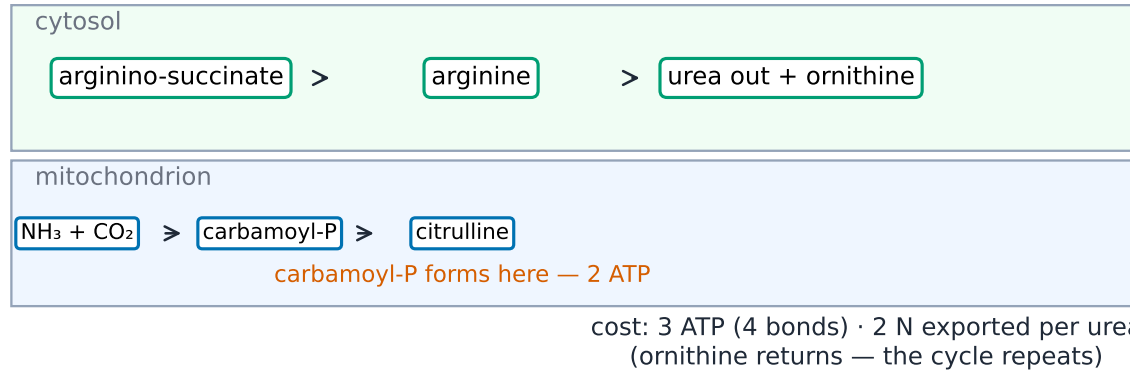
Nitrogen metabolism and the urea cycle

University Medicine

Nitrogen metabolism: two nitrogens, one ticket

- 1 **Funnel Transamination** moves amino groups onto α -ketoglutarate as glutamate; brain and muscle taxi N as glutamine and alanine.
- 2 **Cycle** Liver, 2 compartments, 5 enzymes: $\text{NH}_3 + \text{CO}_2 \rightarrow \text{carbamoyl-P} \rightarrow \text{citrulline} \rightarrow \text{arginine} \rightarrow \text{urea} + \text{ornithine back}$.
- 3 **Cost** 3 ATP (4 high-energy bonds) per urea, exporting 2 N; $\sim 30 \text{ g urea/day} \approx 14 \text{ g N}$ ✓ matches the diet.

The urea cycle across two compartments



Mitochondrial carbamoyl-P and citrulline, cytosolic arginine: five enzymes, 3 ATP, 2 N exported per urea.

Exercises 2.1-2.3

2.1 Which molecule carries nitrogen from brain to liver? [3]

2.2 How many nitrogens does one urea carry, and from which sources? [3]

2.3 Why is ammonia toxic at micromolar levels? [3]

Exercises 2.1-2.3

2.1 Which molecule carries nitrogen from brain to liver? [3]

2.1

- Glutamine (the ammonia taxi).
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2.2 How many nitrogens does one urea carry, and from which sources? [3]

2.2

- Two: one from free NH_3 (carbamoyl phosphate), one from aspartate.
-

2.3 Why is ammonia toxic at micromolar levels? [3]

2.3

- The brain lacks the urea cycle and ammonia drains into glutamate $\rightarrow$ glutamine, depleting intermediates and osmotic balance (astrocyte swelling).

Exercise 3.1

3.1 A (fictional) patient eats 90 g protein/day.

Compute the nitrogen intake (assume 16 % N by mass). Compute the urea excreted if all N leaves as urea. Verify the ATP cost of that urea per day. [7]

Exercise 3.1

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3.1

- $90 \times 0.16 = 14.4$ g N/day.
- Urea: $14.4 \div (28/60) = 30.9$ g urea/day ✓.
- Moles: $30.9/60 = 0.515$ mol $\times 3$ ATP = 1.5 mol ATP/day $\approx$ ordinary liver expenditure.

Exercise 3.2

3.2 (Fictional newborn) coma after first feeds; ammonia high, orotic acid in urine.

Localise the block to OTC deficiency. Explain the orotic acid. Explain why the brain, having no cycle, suffers first. State two management levers implied by the mechanism. [8]

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3.2

- OTC: carbamoyl phosphate cannot enter the cycle; it spills to cytosolic pyrimidine synthesis → orotate.
- Brain has no urea cycle → ammonia accumulates locally, glutamine pools swell → oedema and encephalopathy.
- Levers: limit nitrogen intake; scavenge/alternatives (benzoate/ phenylbutyrate) and feed arginine/citrulline.