

# Supplement for MD

---

- Metabolic acidosis
- Ammonia intoxication
- Carbamoyl-P synthetase I
- Urea cycle defect
- Vit B<sub>12</sub> and folate
- H<sub>4</sub>-biopterin

# Metabolic acidosis (p. 681)

- Kidney extracts little Gln from bloodstream normally
- Acidosis increases glutamine processing in kidney
  - ✓  $\text{NH}_4^+$  + metabolic acids  $\rightarrow$  salts (excreted in urine)
  - ✓  $\alpha$ -ketoglutarate  $\rightarrow$  bicarbonate ( $\text{HCO}_3^-$ , buffer)

In kidney

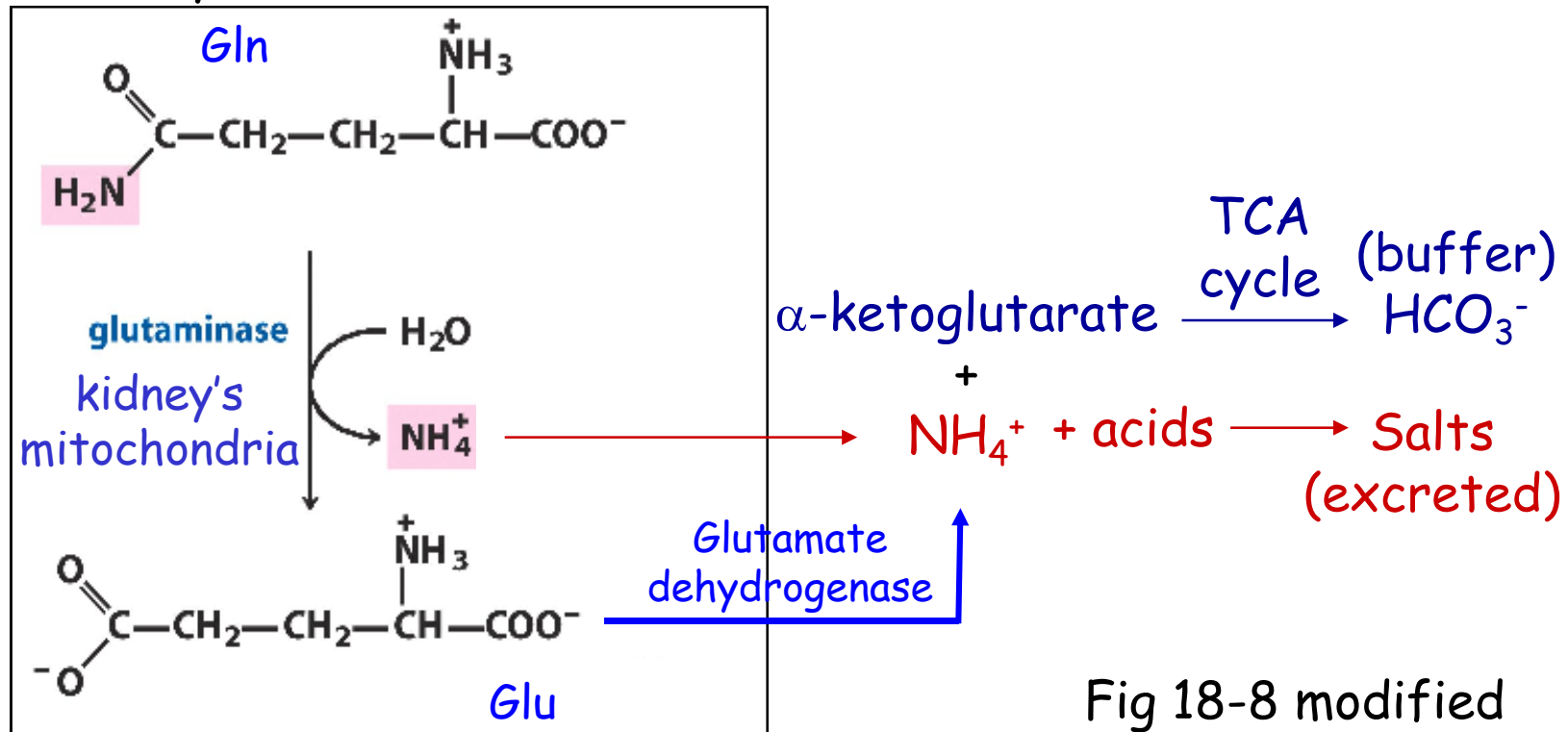


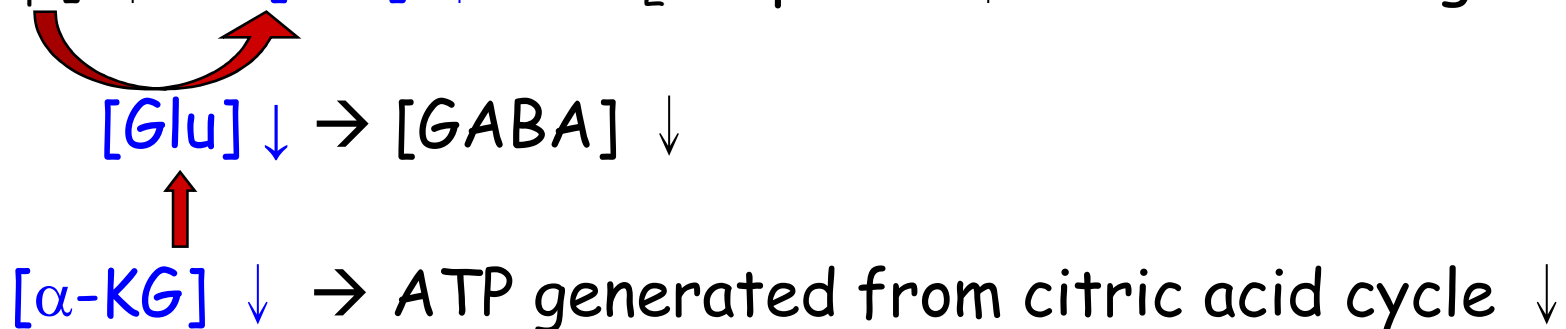
Fig 18-8 modified

# NH<sub>4</sub><sup>+</sup> intoxication

(p.681-682)

- Symptoms
  - ✓ Coma
  - ✓ Cerebral edema
  - ✓ Increase cranial pressure
- Possible mechanisms
  - ✓ Depletion of ATP in brain cells
  - ✓ Changes of cellular osmotic balance in brain
  - ✓ Depletion of neurotransmitter
- Remove excess NH<sub>4</sub><sup>+</sup>
  - ✓ Glutamate dehydrogenase: NH<sub>4</sub><sup>+</sup> + α-KG → Glu
  - ✓ Glutamine synthetase: NH<sub>4</sub><sup>+</sup> + Glu → Gln

[NH<sub>4</sub><sup>+</sup>] ↑ → [Gln] ↑ → H<sub>2</sub>O uptake ↑ → cell swelling



# Defect in urea cycle enzymes

---

- Build-up of urea cycle intermediates
- Treatments
  - ✓ Strict diet control and supplements of essential a.a.
  - ✓ With the administration of :
    - Aromatic acids (Fig 18-14)
      - Lower  $\text{NH}_4^+$  level in blood
        - Benzoate + Gly + ... → hippurate (left)
        - Phenylbutyrate + Glutamine + ... → phenylacetylglutamine (right)
    - Carbamoyl glutamate (N-acetylglutamate analog)
      - Deficiency of N-acetylglutamate synthase
    - Arginine
      - Deficiency of ornithine transcarbamoylase
      - Deficiency of argininosuccinate synthetase
      - Deficiency of argininosuccinase

# Vit B<sub>12</sub> and folate (p. 691)

- Met synthesis in mammal
  - ✓ N<sup>5</sup>-methyl H<sub>4</sub> folate as C donor
    - C is transferred to cobalamin derived from Vit B<sub>12</sub>
    - Vit B<sub>12</sub> as the final C donor
- Vit B<sub>12</sub> deficiency
  - ✓ Q: 18-12, 13 and 22-8
  - ✓ H<sub>4</sub> folate is trapped in N<sup>5</sup>-methyl form
  - ✓ N<sup>5</sup>-methyl H<sub>4</sub> folate is formed irreversibly (Fig 18-17, top)
  - ✓ Available folate ↓
    - e.g. pernicious anemia
      - Biosynthesis of Gly → porphyrin → Hb

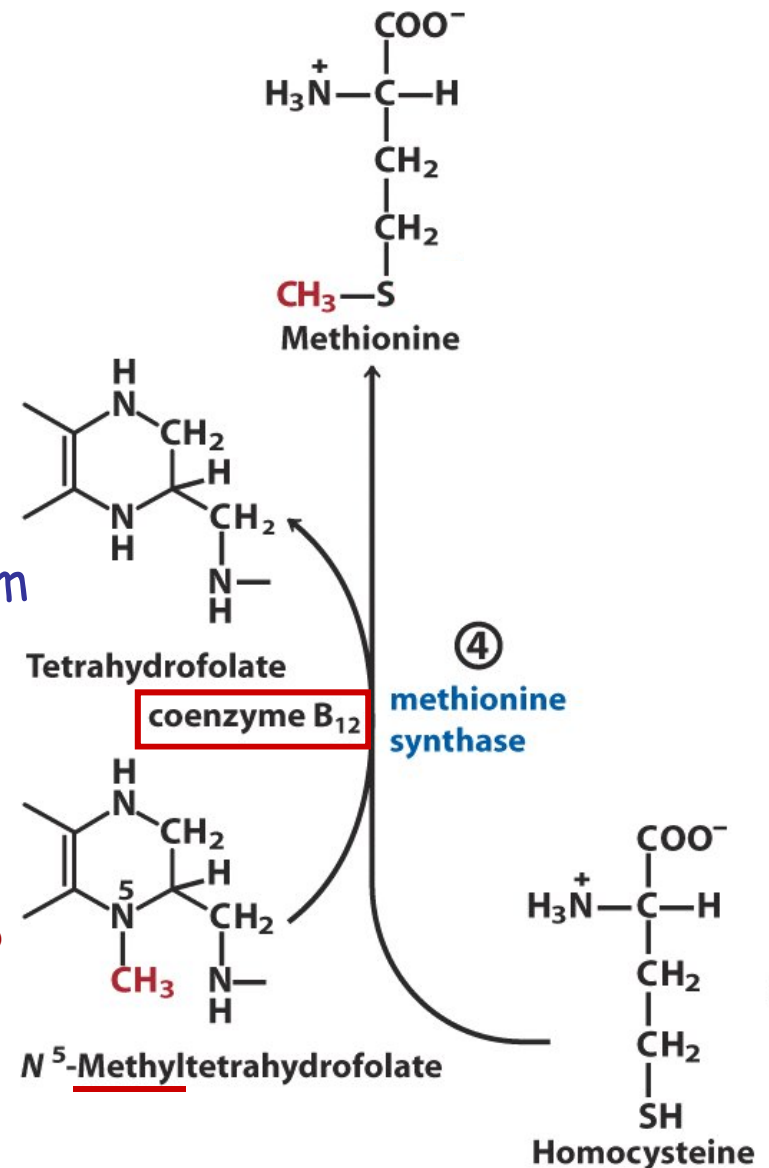


Fig 18-18 left

# H<sub>4</sub> biopterin (p. 697)

- Dihydrobiopterin reductase is required to regenerate H<sub>4</sub> biopterin
  - ✓ Defect in dihydrobiopterin (H<sub>2</sub> biopterin) reductase
    - PKU, norepinephrine, serotonin, L-dopa deficiency, ...
    - Supplement with H<sub>4</sub> biopterin, as well as 5-OH-Trp and L-dopa

Fig 18-24

