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Metabolism of Proteins

Biochemistry

Amino acid metabolism, transamination, deamination, urea cycle, protein synthesis, nitrogen balance and clinical importance.

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CHAPTER 09

Metabolism of Proteins

Amino acid reactions, urea cycle, synthesis and nitrogen balance

1. Introduction

Dietary proteins and tissue protein turnover supply the amino acid pool. Amino acids support synthesis of proteins, neurotransmitters, haem, creatine and other nitrogenous compounds. Excess amino acids are not stored as such; their nitrogen and carbon components are handled separately.

2. Transamination

Transfer of an amino group from an amino acid to an alpha-keto acid, usually alpha-ketoglutarate, yielding glutamate and another alpha-keto acid. Aminotransferases use pyridoxal phosphate (vitamin B6).

ALT: alanine + alpha-ketoglutarate pyruvate + glutamate.

AST: aspartate + alpha-ketoglutarate oxaloacetate + glutamate.

Transamination redistributes nitrogen without releasing free ammonia directly.

3. Deamination and ammonia transport

Oxidative deamination of glutamate by glutamate dehydrogenase releases ammonium and alpha-ketoglutarate, mainly in mitochondria. Ammonia is neurotoxic at elevated concentrations. Glutamine synthetase incorporates ammonia into glutamine in many tissues; glutamine transports nitrogen to liver and kidney. The glucose-alanine cycle transfers amino nitrogen from muscle to liver while the carbon skeleton supports glucose synthesis.

4. Urea cycle (ornithine cycle)

Occurs in liver, with the first two steps in mitochondria and the remainder in cytosol. Converts toxic nitrogen into urea for renal excretion.

Step	Enzyme and product
1	Carbamoyl phosphate synthetase I (CPS I): ammonia + bicarbonate + 2 ATP -> carbamoyl phosphate; activated by N-acetylglutamate
2	Ornithine transcarbamylase: carbamoyl phosphate + ornithine -> citrulline
3	Argininosuccinate synthetase: citrulline + aspartate + ATP -> argininosuccinate

4	Argininosuccinate lyase: argininosuccinate -> arginine + fumarate
5	Arginase: arginine + water -> urea + ornithine

The two nitrogen atoms come from ammonia and aspartate. Three ATP molecules are used, equivalent to four high-energy phosphate bonds. Fumarate connects the cycle with TCA metabolism. Urea is formed in liver, transported in blood and excreted mainly by kidneys.

5. Fate of carbon skeletons

Glucogenic amino acids produce pyruvate or TCA intermediates for glucose synthesis. Ketogenic amino acids yield acetyl-CoA or acetoacetate; leucine and lysine are exclusively ketogenic. Breakdown may supply energy during fasting or illness.

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6. Protein synthesis and turnover

DNA is transcribed to mRNA; ribosomes translate the codon sequence using aminoacyl-tRNA. Newly synthesized proteins fold, undergo modifications and are targeted to their functions. Ubiquitin-proteasome and lysosomal pathways degrade proteins for recycling. Insulin, amino acids and growth signals promote synthesis; severe illness and stress can increase breakdown.

7. Nitrogen balance

Nitrogen balance = nitrogen intake - nitrogen losses (urine, stool, skin and other routes). Approximate intake: protein grams 6.25, assuming 16% nitrogen content.

State	Example
Positive	Growth, pregnancy, recovery with adequate nutrition
Neutral	Stable healthy adult
Negative	Severe illness, burns, starvation, inadequate protein intake

A full balance assessment requires clinical and dietary expertise; urinary urea nitrogen alone is not total nitrogen loss.

8. Amino acids as precursors

Amino acid	Derived substance
Tyrosine	Catecholamines, thyroid hormones, melanin
Tryptophan	Serotonin and melatonin; contribution to niacin synthesis
Glutamate	GABA and glutathione components
Glycine	Haem, purines and glutathione components
Arginine	Nitric oxide and urea cycle intermediates

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9. Clinical significance and nursing applications

Urea cycle defects or severe liver dysfunction can cause hyperammonaemia and encephalopathy. Renal dysfunction may increase blood urea. Phenylketonuria results from impaired phenylalanine metabolism (Chapter 20). Monitor mental status, dietary intake, weight, renal and liver tests; promptly report unexplained confusion or severe vomiting. Protein restriction is not routine in liver disease and must follow specialist plans.

10. Important Examination Questions

Long Answer Questions

1. 1. Describe the urea cycle and amino acid metabolism.
2. 2. Explain transamination, deamination and ammonia transport.
3. 3. Describe protein synthesis and nitrogen balance with clinical examples.

Short Answer Questions

1. 1. Write a short note on Transamination versus deamination.
2. 2. Write a short note on nitrogen balance.
3. 3. Write a short note on alanine cycle.

Very Short Answer Questions

1. 1. Which vitamin is needed for transamination? - Vitamin B6 (PLP).
2. 2. Which enzyme releases urea from arginine? - Arginase.
3. 3. Name two amino acids that transport nitrogen between tissues. - Glutamine and alanine.
4. 4. What is positive nitrogen balance? - Nitrogen intake exceeds nitrogen loss.

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Additional objective question

Site of urea formation? - Liver.

11. Quick Revision

- Transamination transfers amino groups, commonly using PLP.
- Oxidative deamination releases ammonia from glutamate.
- Urea is synthesized in liver and largely excreted by kidneys.
- Negative nitrogen balance is associated with net protein loss.

Conclusion

Amino acid metabolism links protein turnover, nitrogen disposal and energy metabolism; liver and kidney function are central to safe nitrogen handling.

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Practice questions

Choose one best answer. The answer key and explanations follow the questions.

1. Which vitamin-derived coenzyme is used by aminotransferases?

A. Thiamine pyrophosphate

B. FAD

C. Pyridoxal phosphate

D. Coenzyme A

2. Where does the urea cycle occur?

A. Kidney only

B. Skeletal muscle only

C. Pancreas only

D. Liver, across mitochondria and cytosol

3. Which pair of amino acids is exclusively ketogenic?

A. Leucine and lysine

B. Alanine and glycine

C. Aspartate and glutamate

D. Serine and cysteine

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Answer key and explanations

1. C - Pyridoxal phosphate

Aminotransferases require pyridoxal phosphate derived from vitamin B6.

2. D - Liver, across mitochondria and cytosol

The urea cycle takes place in liver mitochondria and cytosol.

3. A - Leucine and lysine

Leucine and lysine yield ketogenic products without a net glucogenic pathway.

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