READING GUIDE

AMINO ACID DEGRADATION AND SYNTHESIS

Objectives

1. Describe the role of folic acid in amino acid metabolism
2. Diagram and describe how the different classes of amino acids are metabolized and what occurs (at the biochemical level) when there are defects in amino acid metabolism
3. Define nonessential amino acids and describe their synthesis

Read Chapter 20.

THE CARBON SKELETON OF AMINO ACIDS IS BROKEN DOWN TO GLUCOGENIC AND KETOGENIC COMPOUNDS

Big picture

What does the body do with the breakdown products of the carbon backbone of amino acids?

What's the definition of a glucogenic amino acid?

What is the definition of a ketogenic amino acid?

Can an amino acid be both glucogenic and ketogenic?

What is the definition of an essential amino acid?

If you understand and reproduce the figure on the previous page, you can answer all the following questions:

Which amino acids are glucogenic? (Fig. 20.2)

Which amino acids are ketogenic?

Which of the 20 amino acids incorporated into protein are considered essential amino acids?

Which amino acids degrade to oxaloacetate?

Which amino acids degrade to a-ketoglutarate?

Which amino acids degrade to pyruvate?

Which amino acids degrade to fumarate?

Here's a tricky question. Which essential amino acid, in addition to threonine, ultimately degrades to pyruvate?

Which amino acids break down to acetoacetate?

Which amino acids break down to acetyl-CoA?

Which amino acids breakdown to both acetyl-CoA and acetoacetate?

Breakdown (and resynthesis) of methionine

The metabolism of methionine is important because of its role in the generation of S-adenosylmethionine (SAM), a potent methyl donor molecule, and the production of homocysteine.

How is methionine converted to homocysteine?

Into what two primary products can homocysteine converted?

Which amino acid is converted to cysteine when synthesized from cystathionine? Homocysteine or serine?

What two conditions, named in Harvey's, are associated with elevated circulating homocysteine levels?

What kind of deficiencies could lead to elevated homocysteine?

The branched chain (essential) amino acids

These amino acids are deaminated by the same branched chain-aminotransferase and then decarboxylated by the same branched-chain α-keto acid dehydrogenase complex.

Which of the branched chain amino acids is only glucogenic?

Which of the branched chain amino acids is only ketogenic?

What enzyme deficiency leads to maple syrup urine disease?

Why does the urine smell like maple syrup?

THE SYNTHETIC IMPORTANCE OF FOLIC ACID

(Fig. 20.11)

Why is folate (specifically tetrahydrofolic acid; THF) important (big picture question)?

How does folate deficiency often present?

THE SYNTHESIS OF NONESSENTIAL AMINO ACIDS

These are the 11 amino acids mainly from the upper part of the figure on page 2. Their synthesis is straight forward, compared to their degradation. The figure on the following page contains most of the details you'll need to know. Notice the central role played by glutamate in the synthesis of several amino acids. Some of this you've already seen before (i.e. amidation of asp and glu).

Which amino acids are ultimately made from α-ketoglutarate?

What other amino acids are directly or indirectly synthesized from intermediates of metabolism?

Which amino acids are made from essential amino acids?

METABOLIC DISEASES CAUSED BY METABOLIC DEFECTS IN AMINO ACID METABOLISM

They are rare but there are a lot of them. They can be devastating and usually need to be diagnosed early to optimize the outcome for the patient.

Phenylketonuria (PKU) (Fig. 20.15,17)

What causes PKU?

What other reactions involving amino acids are inhibited with BH_4 deficiency? (Fig. 20.16)

What happens to patients with untreated PKU?

Why are PKU patients usually light colored?

When is the newborn screening for PKU done and why?

Can PKU be diagnosed prenatally? How about pre-implantation?

How is PKU treated?

When does treatment for PKU need to begin to avoid irreversible damage? (Fig. 20.18)

How long does treatment need to be continued? (Fig. 20.19)

Can maternal PKU affect a normal fetus?

Albinism (Fig. 20.20)

What is the general cause of albinism?

Besides lack of pigmentation in the hair, skin, and eyes, what other symptoms are routine in albinism?

Alkaptonuria (Fig. 20.22)

What causes alkaptonuria?

What are the symptoms of alkaptonuria?

What is the onset of symptoms in alkaptonuria?

Maple syrup urine disease (MSUD)

What causes MSUD?

What are the symptoms of MSUD?

What is the treatment for MSUD?

Homocystinuria (Fig. 20.21)

What causes homocystinuria?

What are the symptoms of homocystinuria?

What is the treatment for homocystinurea?

SUMMARY

Metabolic diseases associated with amino acid metabolism (Fig. 20.14)

This is a very nice figure to review and get a sense of how all these metabolic diseases of amino acid metabolism relate to the larger metabolic picture. You do not, however, need to memorize this figure. Just remember the basics of the metabolic diseases related to amino acids that we have discussed here.