A Summary of Amino Acid Metabolism Based on Amino Acid Structure

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A difficult pedagogic problem in Biochemistry is teaching amino acid metabolism. The names of amino acids and the names of the Krebs-cycle intermediates, pyruvate and/or acetyl CoA to which the amino acids are first metabolized are often presented to summarize these catabolic pathways (Fig 1).[1–5] However, this approach does not reinforce learning of the structures of the compounds involved nor does it encourage students to recognize the relationships between structures of compounds in a metabolic pathway. Thus, students may memorize the names of amino acids and the names of selected compounds to which these substances are converted in order to pass an exam, but it is unlikely that they will retain this information after the examination period.

We have devised a method for summarizing catabolism of amino acids to intermediates of the Krebs cycle, pyruvate and/or acetyl CoA based on the structures of these compounds. This method seems to help students understand the underlying relationships between biochemicals and remember the structures of related compounds.

The method is based on three basic concepts. First, part or all of the carbon skeleton of six of the amino acids coded for in DNA must be metabolized to acetyl CoA in mammals. These six amino acids can be considered to be

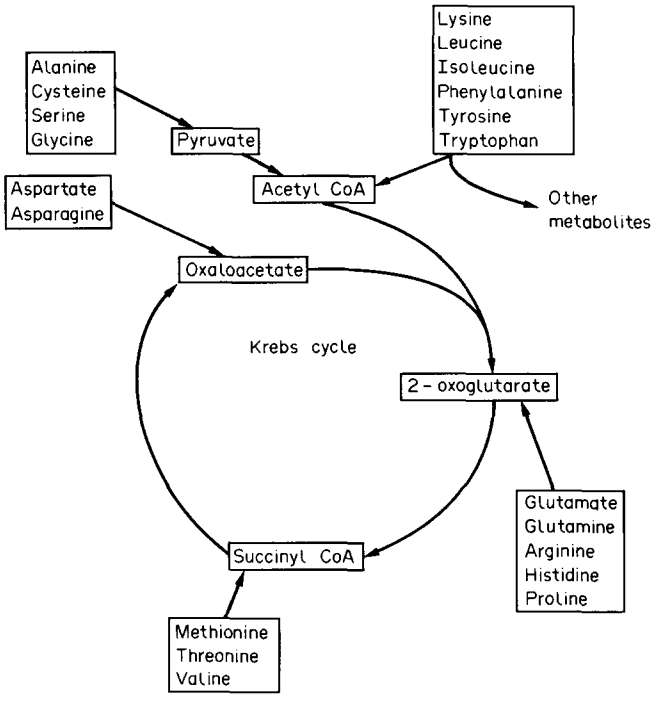

Figure 1 Summary of conversion of amino acids to intermediates of the Krebs cycle, pyruvate and/or acetyl CoA

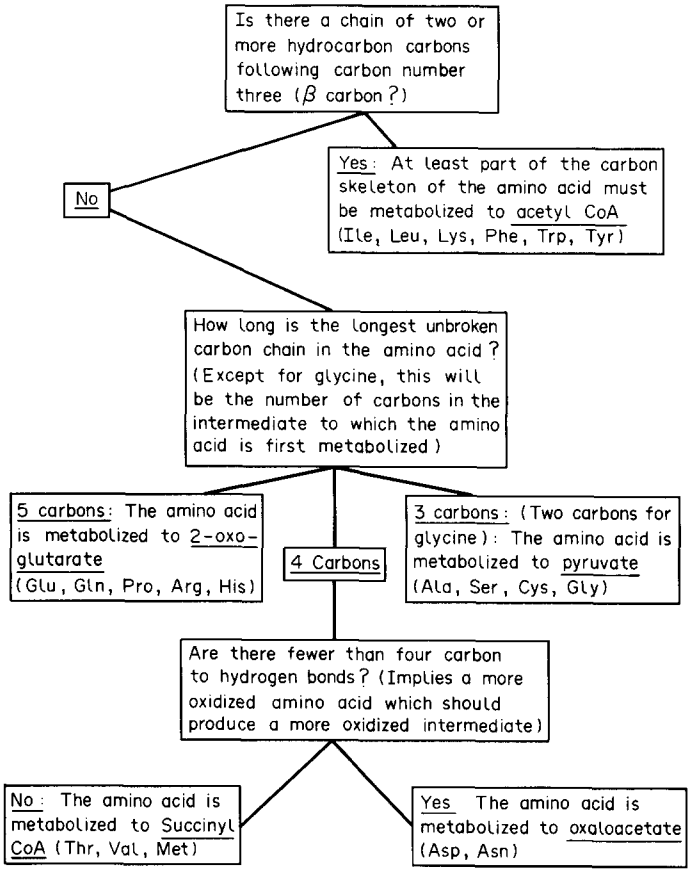

Figure 2 Structural basis of metabolism of the twenty amino acids coded for in DNA to intermediates of the Krebs cycle, pyruvate or acetyl CoA via major pathways found in mammals

partly or entirely 'ketogenic' in that the portion of their carbon skeleton which must be metabolized to acetyl CoA cannot be used for net glucose synthesis. The six partly or wholely 'ketogenic' amino acids are also the amino acids which are most 'fatty acid-like'[5] in that they contain a chain of three or more hydrocarbon carbons beginning with the β carbon (carbon number 3) (Figs 1, 2 and 3*a*). Beta-oxidation of fatty acids, which usually have a predominately hydrocarbon structure, must, for the most part, also produce acetyl CoA.

The carbon skeletons of the other 14 amino acids coded for in DNA can be used to synthesize glucose. Each of these carbon skeletons can be converted, via major mammalian metabolic pathways, to a particular intermediate of the Krebs cycle or to pyruvate before being metabolized to other compounds. For these pathways, the intermediate in which the carbon from the amino acid first appears, contains the same number of carbon atoms as the longest unbroken chain of carbon atoms present in the amino acid (Figures 1, 2 and 3*b*); glycine is the only exception to this rule. Five amino acids contain five carbons in a row and are converted to 2-oxoglutarate, three amino acids contain three carbon atoms and are metabolized to pyruvate (as is glycine) and five amino acids contain an unbroken chain of four carbons and can lead initially to the net production of either succinyl CoA or oxaloacetate.

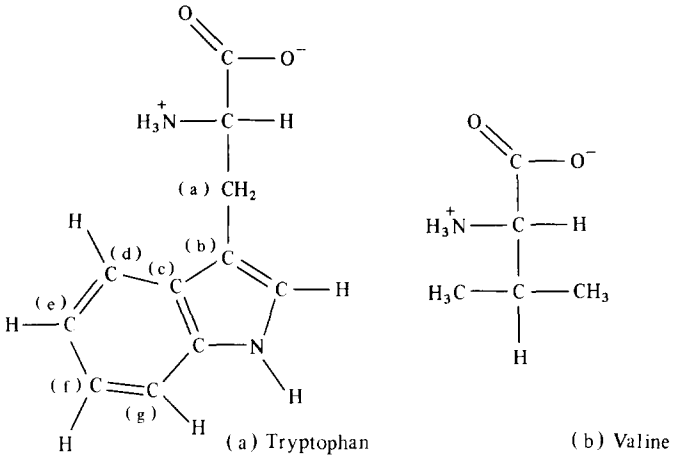

Figure 3 Examples of the relationship between amino acid structure and metabolism
(a) Tryptophan has at least three hydrocarbon carbons in a row beginning with the β carbon (carbon 3) and thus must be converted, at least in part, to acetyl CoA (hydrocarbon carbons are labeled a, b, c, d, e, f, and g)
(b) Valine has (a) only two hydrocarbon carbons in a row beginning with the β carbon (b) an unbroken chain of four carbons and (c) a total of more than four carbon to hydrogen bonds. Thus, it is metabolized to succinyl CoA before it is converted to any other intermediate of the Krebs cycle, pyruvate or acetyl CoA

Whether an amino acid with four carbons in a row is first catabolized to oxaloacetate or succinyl CoA also relates to the structure of the amino acid. The more reduced of these amino acids contain more than four carbon to hydrogen bonds and are catabolized to the more reduced 'four-carbon' intermediate, succinyl CoA (Figs 1, 2 and 3*b*). In contrast, the more oxidized of these amino acids contain fewer than four carbon to hydrogen bonds and are converted to the more oxidized Krebs cycle intermediate, oxaloacetate. Because of these logical relationships between the structures of amino acids and the four-carbon intermediates to which they can be catabolized, the principles of biological oxidation-reduction, important to understanding the Krebs cycle, electron transport and oxidative phosphorylation, are reinforced when summarizing amino acid metabolism.

We believe that summarizing amino acid metabolism in the manner described above is superior to simply presenting a summary of the names of the amino acids and selected intermediates to which the amino acids are metabolized. The method summarized in Fig. 2 not only presents an overview of amino acid metabolism, but also reinforces important biochemical concents and emphasized biochemical relationships. In these ways students are encouraged to understand rather than memorize biochemistry.

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Recent Books on Virology

Comprehensive Virology, Volume 18 (Virus-Host Interactions)

Edited by H Fraenkel-Conrat and R R Wagner. pp 200. Plenum Press, New York. 1983. $32.50.

ISBN 0–306–41158–X

The Herpes Viruses, Volumes 1 and 2

Edited by B Roizman. pp 445 and 439. Plenum Press, New York. 1983. $39.50/$42.50.

ISBN 0–306–409224–4 and ISBN 0–306–41083–4

The writing and publishing of research books in virology has become a hazardous business. Indeed the dissemination of virology research in book form has become a victim of virology's (especially molecular virology's) own success. The series 'Comprehensive Virology' is an illustrative case. The present volume under review (volume 18) is perhaps the penultimate volume in a series which began in 1974 with the laudable aim of providing a 'horizontal' treatment of virology, namely to collect several articles on different virus systems together in single volumes under a general title. Volume 18, 'Virus-Host Interactions', contains diverse chapters on cellular receptors for picornaviruses, persistent infection of mice with lymphocytic choriomeningitis (LCM) virus, and two chapters on 'slow' virus diseases, subacute sclerosing panencephalitis (SSPE) and progressive multifocal leukoencephalopathy. I particularly appreciated the chapters on LCM virus and SSPE. Lehmann-Grube *et al* provide a fascinating insight into the complex interaction of LCM virus with the host immune system and provide an extremely interesting account of a virus from a rarely considered genus of viruses, the arenaviruses. Ter Meulen *et al* provide a clearly written and truly comprehensive chapter on SSPE viruses and their interesting relationships to measles virus. My main caveat about this whole series is that of rapid obsolescence. I think that this worry is less likely to be fulfilled in the case of the present volume, however libraries with limited funds would do well to consider their purchases of virology books, especially those in long series, with great care.

Perhaps with such factors in mind, the editors have decided to initiate a new series of books rather than revising past volumes in the Comprehensive Virology series. This new series will adopt a 'vertical' approach to virology, focusing on particular virus families. The first two volumes deal with herpes viruses and look certain to be standard works for researchers in this rapidly-advancing field. Volume 1 is concerned with primate and avian herpes viruses, preceded by a chapter on taxonomy and classification. Volume 2 deals with cytomegaloviruses, varicella-zoster virus and a variety of herpes viruses infecting hosts from reptiles to horses. Departments with a strong interest in this area will certainly want to have these volumes in their library. There is a uniformly high standard of treatment of topics with reference to published work up to 1983. The notable omission is the herpes simplex viruses. No doubt this will be reserved for a suitably bulky volume in the future.

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