A Symposium on

AMINO ACID METABOLISM

Edited by

William D. McElroy and Bentley Glass

A Symposium on

AMINO ACID METABOLISM

Sponsored by

THE

McCOLLUM–PRATT INSTITUTE

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Edited by

WILLIAM D. McELROY AND H. BENTLEY GLASS

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PREFACE

A Symposium on Amino Acid Metabolism was held at The Johns Hopkins University under the sponsorship of the McCollum-Pratt Institute on June 14-17, 1954. This volume consists of the papers and discussions presented at these meetings.

In planning the symposium an effort was made to select one or two participants who would summarize our present knowledge of the metabolism of a group of closely related amino acids. The book is arranged according to these various groups and in the order in which they were presented at the symposium. As has been done in previous years, short contributions by other participants follow the major papers. Unfortunately, it was not possible to cover adequately all aspects of amino acid metabolism in one meeting. We hope, however, to cover other phases of nitrogen metabolism in future symposia; in particular, the incorporation of inorganic nitrogen into the amino acids and other nitrogen containing compounds.

The participants and members of the Institute contributed their time generously in the planning of the symposium. Dr. S. P. Colowick helped in editing the transcription of the discussion and also in the preparation of the summary. In addition it is a pleasure to acknowledge the important contributions of the following moderators: Dr. I. C. Gunsalus (Part 1), Dr. P. P. Cohen (Part 2), Dr. H. K. Mitchell (Part 3), Dr. Vincent Du Vigneaud (Part 4), Dr. H. G. Wood (Part 5) and Dr. Roger Stanier (Part 6).

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Part I

GENERAL CONSIDERATION OF AMINO ACID METABOLISM

GENERAL REACTIONS OF AMINO ACIDS

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THE METABOLISM OF amino acids may be considered in terms of at least three types of reactions: (1) reactions leading to the synthesis of amino acids; (2) reactions which result in the combination of amino acids to form protein; and (3) reactions which involve the conversion of amino acids to other products, e. g., (a) formation of urea, uric acid, allantoin, creatine, and products which also arise in the course of the metabolism of fats and carbohydrates; (b) conversion of one amino acid to another; and (c) utilization of amino acids for the synthesis of peptides (e. g., glutathione, carnosine), vitamins (e. g., pantotothenic acid, folic acid, nicotinic acid), and many other compounds (e. g., melanin, porphyrin, nucleic acid, histamine).

In 1912, Kossel (1), referring to the problem of the structure of proteins, stated: "We can obtain some idea of the possible variety in the combinations of the protein Bausteine by recalling the fact that they are as numerous as the letters in the alphabet which are capable of expressing an infinite number of thoughts." The metabolic versatility of the amino acids, and the fact that more than 50 amino acids are now known to occur in nature, suggests that this statement may be applicable also to the metabolic transformations of amino acids.

Although it is obvious that the available information on the biological reactions of amino acids cannot be expressed exclusively in terms of a few generalizations, there are at least several categories of reactions in which a number of amino acids participate, and which may therefore be considered as "general reactions." These include:

(1) Deamination

(2) Decarboxylation
(3) Transamination
(4) Peptide and protein synthesis

It is anticipated that the formidable problem of protein synthesis will be considered by other speakers at this symposium. The present discussion will therefore be limited mainly to recent developments concerning the first three of these topics. It is necessary to treat only cursorily some aspects of these fields, and it is expected that these and related subjects will receive additional attention during the discussion.

DEAMINATION

D-*Amino Acid Oxidase.*

The first definitive enzymatic studies on the deamination of amino acids were carried out by Krebs (2, 3), who observed oxidation of both D- and L-amino acids by kidney and liver preparations. These reactions were shown to be catalyzed by separate optically specific enzyme systems. The D-amino acid oxidase of kidney has been purified, extensively investigated (4), and shown to require flavin adenine dinucleotide as a coenzyme (5). The oxidation may be considered to take place in accordance with three reactions, of which only the first is enzymatic:

$$\mathrm{RCH(NH_2)COOH} + \mathrm{O_2} \rightarrow \mathrm{RC(=NH)COOH} + \mathrm{H_2O_2} \qquad (1)$$

$$\mathrm{RC(=NH)COOH} + \mathrm{H_2O} \rightarrow \mathrm{RC(=O)COOH} + \mathrm{NH_3} \qquad (2)$$

$$\mathrm{RC(=O)COOH} + \mathrm{H_2O_2} \rightarrow \mathrm{RCOOH} + \mathrm{CO_2} + \mathrm{H_2O} \qquad (3)$$

As yet, unequivocal evidence for the formation of the intermediate imino acid has not been obtained. In the presence of catalase, reaction (3) does not take place, and the products include the analogous α-keto acid and ammonia. A large body of evidence regarding the specificity of D-amino acid oxidase has accumulated,