Arginine Metabolism: Enzymology, Nutrition, and Clinical Significance

Introduction to the Symposium Proceedings[1]

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Since the initial characterization of its structure around the beginning of the 20th century, studies of arginine over the past 100 years or so have proceeded through multiple phases, including elucidation of its roles in the urea cycle, synthesis of creatine, nutritional requirements, endogenous synthesis, and synthesis of nitric oxide (1). Although much is known about each of these aspects of arginine metabolism and regular meetings have been held for many of the individual topic areas, integration of this information remains relatively limited because researchers in each of these areas seldom meet together in a common venue. Thus, for many researchers the situation has been somewhat akin to that of the 3 blind men who are asked to describe an elephant: the first feels the trunk and states that the elephant is like a snake, the second feels a leg and asserts that the elephant is like a tree, and the third feels the tail and notes that the elephant is like a rope. To biochemists and nutritionists working in the field, arginine has a complex metabolism, serving as a so-called semiessential or conditionally essential amino acid that, by definition, requires exogenous repletion in states of stress. To nitric oxide biologists, arginine is simply the substrate that the nitric oxide synthases convert to citrulline and nitric oxide. Clearly, the latter view is excessively oversimplified, betraying the consequences of the complex metabolism of arginine that can affect nitric oxide production. Similarly, biochemists have often focused more on the metabolic pathways of arginine than on their regulation or phenotypic consequences for cells or organisms. It is with this background in mind that the late Vernon Young had the insight and prescience to organize this symposium so that researchers could gain a more comprehensive perspective on the elephant that is arginine metabolism in all its aspects.

Accordingly, this unique symposium brought together for the first time investigators with overlapping, but distinct, interests. Over the course of 2 intense days of presentations and discussions, the investigators whose lectures are summarized in this supplement identified areas of mutual interest and highlighted areas for future investigation in the field of arginine metabolism. The symposium was organized into 5 sessions: I) basic aspects of arginine metabolism, II) physiology of arginine metabolism, III and IV) arginine and pathophysiology, and V) therapeutic aspects and supplementation. Session I reviewed the properties and functions of nitric oxide synthases, arginases, and transporters of arginine metabolism. Session II dealt with in vivo measurement of arginine metabolism, consequences of genetic disorders that influence arginine metabolism, arginine nutrition in neonatal pigs, and renal arginine metabolism. Complementing these presentations, Sessions III and IV focused on determinants of arginine metabolism that affect various diseases, including cardiovascular disease, hypertension, and renal disease; neurologic disorders; asthma; infection and inflammation; catabolic disease states; cancer; and the roles of asymmetric dimethylarginine in disease. Session V discussed fermentative production of arginine; roles of arginine metabolism in sexual function; and roles for dietary supplementation with arginine, creatine, or ornithine α-ketoglutarate in vascular health, capacity for exercise, and enhancement of immune function. Therapeutic targets and treatment approaches for a wide variety of disorders were discussed, including endothelial dysfunction in atherosclerosis and hypertension, male erectile dysfunction and female sexual arousal disorder, and immune reconstitution in burn and trauma patients.

This symposium was sponsored by Ajinomoto USA, Inc. Members of the organizing committee included Drs. Dennis M. Bier (Baylor College of Medicine), Joseph Loscalzo (Boston University School of Medicine), Sidney M. Morris, Jr. (University of Pittsburgh School of Medicine), Wiley W. Souba (Pennsylvania State University School of Medicine), and Vernon R. Young (Massachusetts Institute of Technology). The committee wishes to express their gratitude to the following individuals of the Ajinomoto company for their invaluable support, encouragement, and assistance in planning and running the symposium: Mr. Takuzo Kitamura, Dr. Ryuji Yamaguchi, Mr. Yoichi Kobayashi, Mr. Hiroyuki Miyake, Mr. Kazuhiro Shimotori, Mr. Kazunori Mawatari, and Dr. Junichiro Kojima. The editorial assistance of Dr. D'Ann Finley is gratefully acknowledged. In gratitude for intellectual leadership and enthusiasm of Dr. Vernon R. Young, who initially organized this symposium and served as chair of the organizing committee until only a few months prior to the symposium, the organizing committee and symposium attendees respectfully dedicate the symposium and its proceedings to his memory.

Overall, the symposium was judged a success by all participants and set the stage for future collaborations and investigative strategies among investigators in these rapidly evolving fields. We trust readers of these proceedings will likewise find the information useful and stimulating.

LITERATURE CITED

1. Wu, G. & Morris, S. M., Jr. (1998) Arginine metabolism: nitric oxide and beyond. Biochem. J. 336: 1–17.

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