VITAMIN E

Its Usefulness in Health and in Curing Diseases

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Commemorating the 70th Anniversary of the Discovery of Vitamin E and the 50th Anniversary of the Founding of Eisai Co., Ltd.

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Preface

This “International Symposium on Vitamin E” is the fourth that has been held in Japan. The year 1991 was the 70th anniversary of the discovery of vitamin E by Drs. H.M. Evans and K.S. Bishop; this was a new vitamin, the inadequacy of which resulted in fetal death and resorption in rats. This was also the 50th anniversary year of the founding of Eisai Co. The symposium was thus organized to commemorate both events. Among the naturally occurring compounds with vitamin E activity, alpha-tocopherol is the most important known and the most active form biologically; it is localized in biological membranes and acts as an important chain-breaking antioxidant. The biological functions of vitamin E that were deduced from basic chemical and biochemical studies are now being confirmed by an increasing amount of epidemiologic evidence with respect to the role of aging in various diseases including cancer and ischemic heart disease. It also appears that many problems of “old age” are probably related to free radical pathology. Thus, vitamin E is thought to be a very important compound for patients with chronic health problems, however, this concept remains to be definitely proven. On the other hand, the problem of oxidant injury has been raised in association with the use of high concentrations of oxygen for the treatment of neonates. A trial of therapy with a high dose of vitamin E was undertaken in the U.S.A. and Europe, but it was associated with unexpected deaths in premature
infants. Due to hazards related to the use of large doses of the vitamin, the Committee of the Fetus and Newborn of the American Academy of Pediatrics subsequently recommended the withdrawal of vitamin 1 preparations for intravenous use. In the pediatric field, the clinical usage of vitamin E also remains uncertain. A recent topic of research has been the discovery of vitamin E deficiency in humans with neurological symptoms. After discovery of this same deficiency in infants with fat malabsorption, the deficiency was also found in patients with neurocerebellar ataxia, despite the lack of any abnormalities of fat metabolism. Such deficiency is called “isolated vitamin E deficiency.” Although investigation of these clinical problems related to vitamin E is progressing on chemical, biochemical, biological, and nutritional bases, there are a number of disagreements among the different research fields. In addition, the physiologic behavior of vitamin E in humans, including its bioavailability, tissue distribution and nutritional effects, all remain unclear at present. The purpose of this symposium was to allow critical review highlighting the bridges between the basic, epidemiologic and clinical research fields. Several previous international meetings on Vitamin E held in Japan, the United States and Europe have been gratifyingly successful. This meeting was also fruitful, and its success was, of course, due to the participants themselves.

This volume consists of the majority of papers presented during the oral portion of the symposium, followed by selections contributed regarding topics raised at the meeting. All chapters not only report the author’s own research data, but also include a review of the subject matter in each research area. In this sense, the book is not literally the “proceedings” of the meeting.

I wish to take this opportunity to express my thanks to Professors H.J. Kaydon from New York, AT. Diplock from London and II. Nakamura from Tokorozawa for their helpful advice as members of the organizing committee. I also wish to thank Professor O. Iuarashi, the secretary of the committee, and the other domestic executive members. Professors E. Niki, F. Umemeda, and T. Yoshikawa for their valuable assistance. This symposium held in Gifu was supported by the Eisai Co. of Japan, and I wish to sincerely thank Mr. Haruo Naito President, and other staff of the Eisai Co. for their generous financial support and warm hospitality.
In this 70th anniversary year of the discovery by Herbert Evans of the lipid-soluble substance he called ‘vitamine E’ that prevented resorption of gestation in female rats and testicular atrophy in males, it is entirely fitting that the occasion should be marked by an International Symposium. It is an exceedingly happy coincidence that this anniversary coincides with the celebration of the 50th anniversary of the founding of the Eisai Company, a company whose development has been so intimately bound up with the history of vitamin E research. On behalf of all the participants in the symposium may I congratulate the Chairman, President and Directors of the Eisai Company on their past success and wish them great good fortune in the future. It is also appropriate that I express the gratitude of the scientific community to Eisai for their generous sponsorship of this Symposium under the auspices of the Vitamin Society of Japan.

My own interest in and research on vitamin E began 35 years ago and I was fortunate in meeting, and in some instances getting to know well, several of the early pioneers in this fascinating field. It became apparent to me that these were men and women of remarkable scientific ability who had succeeded in identifying a lipid-soluble factor, initially shown to be present in lettuce leaves and later in wheat germ, that was capable of preventing reproductive failure in rats. These discoveries were of course made with the very limited facilities of the day, which makes the achievement even more remarkable. The particular gifts of Herbert Evans himself are apparent to anyone who takes the trouble to look at the classical monograph (1) that he published summarising his
work; the micrographs are a model of clarity that would do credit to someone working today with modern superior optical techniques. But with what I was told was characteristic humility, he dismissed these early successes by saying that “good fairies attended every phase of the advent and early history of vitamin E” (2). Among the early pioneers one person stands out as a remarkable example of what a scientist should be, namely Karl Mason, who made such a striking and important contribution to early knowledge about vitamin E. Karl Mason was a man of great charm and exceptional humility for whom the pursuit of knowledge was an all-embracing endeavour. On the several occasions when it was my privilege to stay with him and his wife, Pearl, at their home near Washington DC, it was fascinating to hear him speak of his personal knowledge of several of the early workers, who to me were familiar names in reference lists, and to begin to put a human face to those who had contributed to the early days of vitamin E research. Karl also showed me some of the original microscope slides that derived from his efforts to elucidate the nature of the lesion, both in the gravid rat uterus and in the mate testis, that was caused by the absence of vitamin E. Again, I was struck by the superlative quality of the work.

In more recent times, the past decade has seen a massive growth in interest in vitamin E. The elucidation of the biological consequences of uncontrolled proliferation of free radical-initiated or -mediated reactions has been a major preoccupation of research scientists from many different disciplines, and the central role of vitamin E as a free radical scavenger among membrane polyunsaturated fatty acids has led to an upsurge in interest in vitamin E. Much progress has been made in understanding the manner in which vitamin E functions in living systems, and the localization of the vitamin in biological membranes and its relationship to other lipids and membrane proteins have been of particularly absorbing interest. Vitamin E has also gained much attention from clinicians as the potential for protection by the vitamin against human diseases, such as cardiovascular disease and certain forms of cancer have become apparent. Prospective epidemiological trials, begun ten to fifteen years ago, are now coming to fruition and the association of a high intake of the vitamin, or of high serum levels, with lower subsequent incidence of disease, have become a proven reality. In this connexion vitamin E is seen as one member of a panoply of protective agencies, which includes selenium, vitamin C and beta
carotene, that keeps a tight control on free radical-initiated or mediated-processes in the aetiology of disease.

The present International Symposium provides a timely opportunity for scientists from many parts of the world who have an interest in vitamin E to get together to exchange information about their research. The wide differences in research fields among the participants in the Symposium reflects the diversity of interest that vitamin E engenders today. The occasion thus provides an excellent opportunity for basic scientists to get together with clinicians, and those of us responsible for planning the programme have been at pains to attempt to deal with all aspects of interest in vitamin E in the Symposium. We have divided the proceedings into six sections covering aspects of biochemistry, physiology and deficiency of vitamin E, followed by a consideration of the impact of free radical damage in the environment, in pharmacology and in diseases such as cardiovascular disease, cancer, neuropathy, and diabetes mellitus, and in ischaemia-reperfusion injury, and of the potential for protection by vitamin E in them. Thus, the first section deals with the membrane function and localisation of tocopherol, and with the biodiscrimination between the various forms of the vitamin. The absorption, metabolism and excretion of vitamin E, and its lipoprotein transport, receive attention in the physiology section, and a number of important nutritional aspects concerning the human requirement for the vitamin, means of assessment of vitamin E status and safety of supplements are covered in the next section. The theme then changes to a consideration of the possible protection by vitamin E against atmospheric pollutants, the adverse effects of alcohol abuse and radiation damage followed by a section dealing with the effects of the vitamin on the arachidonic acid cascade, in immunity and on macrophages. The clinical aspect occupies a considerable part of the Symposium and is concerned with detailed consideration of the relationships of vitamin E to the diseases mentioned above. At the end of the Symposium, the Co-Chairman Dr. Herbert Kayden summarises the proceedings and draws out the perspectives as to the likely future of vitamin E research.

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