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Meeting Report: Vitamin E Satellite Symposium (VESS) associated to the Annual Meeting of the SFRR-Europe, Rome, 26 August, 2009

After 5 years from the "Vitamin E and Health Conference" at Boston, which was the last meeting entirely devoted to vitamin E, scientists actively involved in the field met to discuss some of the recent findings and also future lines of research on the occasion of the Satellite Symposium on Vitamin E.

This scientific event held on August 26th before the opening of the annual meeting of Society for SFRR-Europe at Rome, has been organized on the initiative of some members of this society that has sponsored the Symposium together with the host, IUSM - University of Rome Foro Italico, and the "Società Italiana di Nutrizione Umana".

More than 90 participants registered to this Satellite including several PhD and post-graduate students beside some of the most established scientists in the field.

The scientific program was set with the original formula of a series of short brain-storming oral communications followed by a final general discussion. A total of twenty-two talks by young researchers and expert scientists were divided in thematic sessions chaired by Angelo Azzi, Regina Brigelius-Flohé, Lars Gille, Francesco Galli, and Luigi Iuliano. The scientific topics were: metabolism and transport, signalling and genes, intervention studies and protective functions, synthetic analogues and pharmacological applications, and general topics concerning plant metabolism and antioxidant activity.

The final discussion coordinated by Francesco Galli has seen the participation of the Chairs and from the audience of Alberto Boveris, David Muller, Jan-Marc Zingg, and the members of the organizing committee Marc Birringer and Francesco Mazzini.

During this discussion Regina Brigelius-Flohé, presented an editorial plan to publish the most relevant communications together with some invited review papers by some experts on the physiologic functions, nutritional aspects and biological roles of vitamin E.

Lars Gille discussed perspectives in the field of vitamin E derivatives and their possible pharmacological applications, which was the subject of several communications in this symposium. In this respect he laid emphasis on the need to focus on the question of how can we extrapolate from the derivatives to biological functions of α-tocopherol. He pointed out that there are now promising vitamin E derivatives with pharmacological activity for anticancer and antiparasitic applications. Although some of these have been clearly demonstrated to act as mitocans, the role of mitochondria in these pharmacological activities requires further clarification. In addition, the problem of vitamin E supplement-drug interaction was addressed. Regina Brigelius- Flohé highlighted the fact that beyond the investigation of nutritional and health properties there is need for more information about the interaction of vitamin E with drug and xenobiotic metabolism that remains an aspect so far poorly understood.

Luigi Iuliano addressed issues regarding the possible clinical applications of vitamin E supplements in humans, highlighting the absence of sufficient experimental evidence for its application in the majority of so-called oxidative stress-related conditions.

The absence of success for the majority of the secondary prevention trials on cardiovascular disease and more recently of the largest trial on prostate cancer SELECT interrupted after 7 years, were also discussed by the participants together with the issue of possible toxicity of high doses of vitamin E in some groups of patients. This lack of success and the general precaution principle in medicine are aspects that have to be taken into due consideration in planning further intervention trials.

According to the contribution of Dr Michele Betti, Francesco Galli highlighted that the risk of toxicity by high doses of vitamin E could be particularly high during intrauterine life. Actually, the supplementation with high dose of vitamin E usually applied during pregnancy might expose the fetus to high levels of this vitamin in the circulation, which could result in significant toxicity in the presence of limited efficacy of the detoxification machinery expressed by the fetal liver. This risk could be further exacerbated by a defective placental barrier or other pregnancy-associated conditions that need to be further investigated.

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Angelo Azzi agreed with the observation by Dr Iuliano, adding a comment on the need for more convincing studies on the biological and molecular properties of this vitamin in all its forms before planning other extensive clinical trials, which are obviously expensive and at a high risk of failure. The canonical antioxidant properties of vitamin E, often accounted for as putative therapeutic mechanism for this vitamin, have created false expectations to cure advanced symptoms of chronic and degenerative conditions.

He commented also on the absence of evidence for the use of vitamin E in disease states such as micro-angiopathy and other complications of diabetes, preclampsia, neurodegeneration and other conditions that are sustained by microinflammation and possibly tissue oxidative damage, and said that "other situations that might deserve further investigation for a prevention intervention with vitamin E could be identified in some diseases associated with a defective metabolism and tissue distribution that may mimic the condition of AVED, such as a large number of ataxias of unknown pathogenesis".

On the side of clinical applications of vitamin E, Regina Brigelius-Flohé mentioned that it is hard to predict a beneficial outcome and/or an explanation of missing or unexpected effects of vitamin E supplementation without knowing what the biological function of vitamin E really is.

Other comments from the audience pointed out the need for more basic research on the side of expected therapeutic effects and disease mechanisms, and also on more careful clinical and laboratory evaluation of patient populations to eventually identify responsive subjects. The need of further investigation about clinical and laboratory biomarkers found general consensus between the participants. Marc Birringer and others in the audience suggested that the application of supranutritional doses of the vitamin in clinical trials should be regarded as pharmacological intervention and investigated as such. He commented also on the importance of better understanding vitamin E metabolism that needs also be accounted for in clinical trials where analytical methods should be developed in order to investigate treatment compliance, pharmacokinetics and metabolic transformation at the individual level. In this perspective, alpha-tocopheryl phosphate, formerly studied by the group of Zingg and Azzi, as well as long-chain metabolites will play a key role in future investigations since they provide additional properties of the vitamin.

Concluding remarks by Angelo Azzi considered that, based on recent literature and also on several interesting communications in this symposium, biological mechanisms alternative to the antioxidant role of tocopherols have to be taken into consideration, including the most recent evidence on signaling effects and gene regulation by the different tocopherols and tocotrienols; they unquestionably deserve more attention in identifying research priorities and planning future studies.

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