## **Viewpoint**



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## Dietary Fatty Acids and Cardiovascular Health – An Ongoing Controversy

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In this issue of the journal, a summary is given of the dinner debate that was held during the biennial meeting of the International Society for the Study of Fatty Acids and Lipids (ISSFAL), which was held in Maastricht (the Netherlands) from May 29 to June 2, 2010. The subject of the discussion was 'healthy fats for a healthy heart'. Two important and timely issues related to cardiovascular risk were raised. The first issue was on the importance of saturated fatty acids and the second on the optimal intake of omega-6 polyunsaturated fatty acids.

There is no doubt that a mixture of saturated fatty acids in the diet increases serum LDL cholesterol concentrations as compared to iso-energetic amounts of carbohydrates [1]. A wealth of evidence supports the notion that interventions that lower serum LDL cholesterol result in reduced cardiovascular risk. Amongst other findings, this evidence comes from pharmacological and dietary intervention studies [2, 3], and from genetic studies [4]. Thus, a vast array of evidence from sound science using multidisciplinary approaches underlines the conclusion that LDL cholesterol is a validated biomarker to predict the risk of developing cardiovascular disease. Still, the discussion on the relationship between saturated fatty acids and cardiovascular risk continues.

In this discussion it is important to realize that it is not recommended to avoid all saturated fatty acids from the diet. That is not the debate. The debate centers around at least two important issues: (1) is the intake of saturated fatty acids causally related to cardiovascular disease and (2) are all saturated fatty acids equal?

This discussion is fed by findings from a recent metaanalysis based on prospective cohort studies that did not demonstrate a positive relationship between the intake of saturated fatty acids and cardiovascular disease [5]. Another meta-analysis, however, did show such a relationship, even if the studies used in this meta-analysis were also part of the other meta-analysis [6]. More and more studies are looking for relationships between specific nutrients (for example fatty acids), single food products or food patterns with disease outcome. One important question that needs to be answered is if in these epidemiological studies data on food intake at the individual level has been estimated accurately enough to discern such relationships. May a null relationship not reflect a lack of statistical power, bias or confounding? Are we not making the mistake of relying too heavily on the accurateness of food intake data and on statistical models? These important questions need to be discussed.

Of importance, it is not possible to discuss the effects of any of the macronutrients in isolation. When energy intake does not change, a lower intake of one macronutrient means a higher intake of another macronutrient. The kind of substitution may differently affect cardiovascular risk. Compared with saturated fatty acids, carbohydrates lower both LDL and HDL cholesterol. The total to HDL cholesterol ratio does not change. Then another question emerges: what is the best biomarker for cardiovascular risk? For example, carbohydrates do lower HDL cholesterol compared with a mixture of saturated fatty acids, but is that harmful? Do diet-induced changes in HDL cholesterol truly affect cardiovascular risk? This question is also relevant for the different saturated fatty acids. Compared with myristic and palmitic acids, stearic acid lowers LDL cholesterol, but at the same time also HDL cholesterol. Consequently, these three saturated fatty acids have comparable effects on the total to HDL cholesterol ratio. Also, cardiovascular disease has a multifactorial causality, and different saturated fatty acids may differently affect other cardiovascular risk markers [7]. More research is needed to define these effects. Overall, a reduction of saturated fatty acids is clearly important in the primary prevention of coronary heart disease, but the optimal substitute requires further study.

Similar questions can be raised for the second proposition of this dinner debate on the optimal intake of omega-6 polyunsaturated fatty acids. The evidence to increase the intake of omega-6 polyunsaturated fatty acids seems to be very strongly based on several dietary intervention studies [8]. Results of these studies, however, are difficult to interpret. A decrease in the intake of saturated

fatty acids was accompanied by a decrease in the intake of transfatty acids, and these two types of fatty acids were replaced by various other fatty acids. Also, it is very likely that dietary cholesterol intake was decreased in most of these intervention studies. Ramsden et al. [9] even concluded that specifically increasing the intake of omega-6 polyunsaturated fatty acids (that is, linoleic acid) without a concomitant increase in omega-3 polyunsaturated fatty acids might not reduce, but even increase, cardiovascular risk. If true, this concept has many important implications. For example, it means that linoleic acid-induced decreases in LDL cholesterol do not lower cardiovascular risk or are counteracted by other unbeneficial effects. Challenging, but is there any evidence for that? These, and undoubtedly many other questions, can only be answered by well-controlled dietary intervention studies with cardiac endpoints. In these studies, it is important not only to differentiate between the effects of omega-6 and omega-3 polyunsaturated fatty acids, but also to take into account chain length of these fatty acids (linoleic acid vs. arachidonic acid and  $\alpha$ -linoleinic vs. EPA vs. DHA). Further, these studies also need to address metabolic and mechanistic questions to better understand the effects observed.

But what should we do in the meantime? Are current dietary guidelines not evidence based? Of course they are, but science progresses and current concepts need to be challenged. That is the only way to make a sensible step forwards and open scientific discussions based on facts, such as those held during this dinner debate, should, therefore, be intensified.

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