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AND HEALTH
COLLECTION

Lipids from Alpha to Omega

AN INITIATIVE
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INTRODUCTION

The title "lipids from α to ω" does not symbolize the extreme and simplistic positions between organoleptic pleasure in food and lipid excess generating atherosclerosis. Rather, "lipids from α to ω" refers in this volume to the wide range of items to be explored between α-linoleic acid and ω3 (n-3) and ω6 (n-6) fatty acids.

The following text begins with an explanation of background data and of the functional changes that may be generated in cells in relation to the amount and type of dietary fat. The new concept of functional food is presented, and the connection between the consumption of functional fatty acids, development, pathogenesis, and the prevention of cardiovascular and inflammatory diseases, is dealt with. The text also seeks to examine the implications of these scientific findings on public policy. Regulatory aspects are then taken into consideration. Lastly, since quantitative and qualitative determinations have shown the importance of chemical structure on biological properties, and since estimates of intake are often approximations based on limited data and problematic techniques, this volume concludes with recent analytical aspects of fatty acids.

CHAPTER I

PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL ASPECTS

ESSENTIALITY OF FATTY ACIDS

It is well known that fatty acids are associated with energy production and storage. Available data also indicates the importance of polyunsaturated fatty acids (PUFAs) as universal cellular regulators. Indeed, PUFAs are associated with many vital functions, such as membrane lipid structure and physical properties, intracellular signaling, plasma lipid transport, covalent modification of cellular proteins, eicosanoid formation, gene transcription, mRNA stability, and cellular differentiation.

The discovery that fatty acids can affect gene transcription in lipogenic as well as in non-lipogenic tissues, involving both peroxisome proliferator-activated receptors-dependent and -independent pathways (figure 1), thus modulating the cell's metabolic state, is essential to our understanding of responses to dietary changes. This has led to a careful examination of the mechanisms through which PUFAs modulate lipid metabolism and, due to the complexity of the phenomena, for the need to determine the molecules involved.

Saturated and monounsaturated fatty acids are obtained either from diet or by complete synthesis from acetyl CoA. In contrast, (n-3) and (n-6) fatty acids, which represent about one-third of the intracellular fatty acids, cannot be synthesized by humans and are, therefore, essential components of diet (figure 2). This explains why the fatty acid composition of the tissue lipids, including membrane phospholipids, can be modified to some extent by the amount of each class of PUFAs in the diet. This type of nutritional approach has been employed, for example, to make tumor cells grow in culture, such as promyelocytic

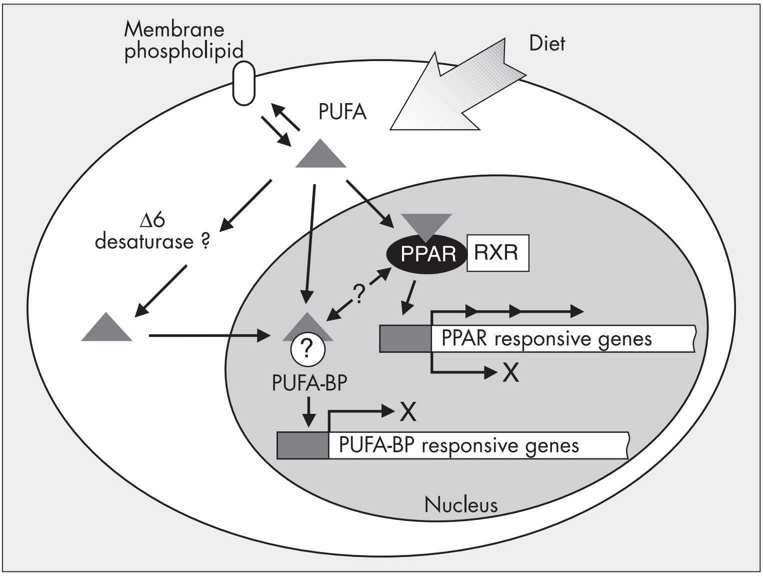

Figure 1. Mechanisms of PUFA control of gene expression: a PUFA-PPAR-dependent mechanism responsible for up-regulation and repression of gene expression, and a PPAR-independent or PUFA-specific mechanism for repression of gene expression. Cross-talk could exist between these two pathways, as well as conversion of the PUFA by a Δ6 desaturase to an active metabolite. Abbreviations: PPAR, peroxisome proliferator activated receptor; RXR, retinoid X receptor; BP, binding protein.
From Sessler and Ntambi, J Nutr 1998 (reproduced with permission).

leukemic HL-60 or retinoblastoma cells, more sensitive to oxidative stress and to therapeutic agents that generate free radicals.

Arachidonic acid, a member of the (n-6) PUFA class, is the substrate for most of the eicosanoids mediators produced by mammalian cells. It is also present in large amounts in phosphatidylinositol, a phospholipid that functions in membrane signal transduction. The requirement for arachidonic acid is probably the main reason why (n-6) PUFAs are essential for optimum health.

Docosahexaenoic acid (DHA), the most abundant (n-3) PUFA ordinarily present in the tissues, is contained in large amounts in retinal and neuronal membrane phospholipids. It is required for optimum development and function of the nervous system, and the need for DHA is doubtless the main reason why (n-3) PUFAs are essential. However, cultured cells of neural origin incorporate the 22-carbon (n-6) fatty acid analogue of DHA ((n-6) DPA [figure 3]) just as readily as DHA. This suggests that the nervous system incorporates DHA because it is more readily available than (n-6) DPA, not because DHA possesses special metabolic properties. In this regard, the main (n-3) product of PUFA metabolism in astrocytes is DHA, whereas the main (n-6) product is arachidonic acid, not (n-6) DPA.

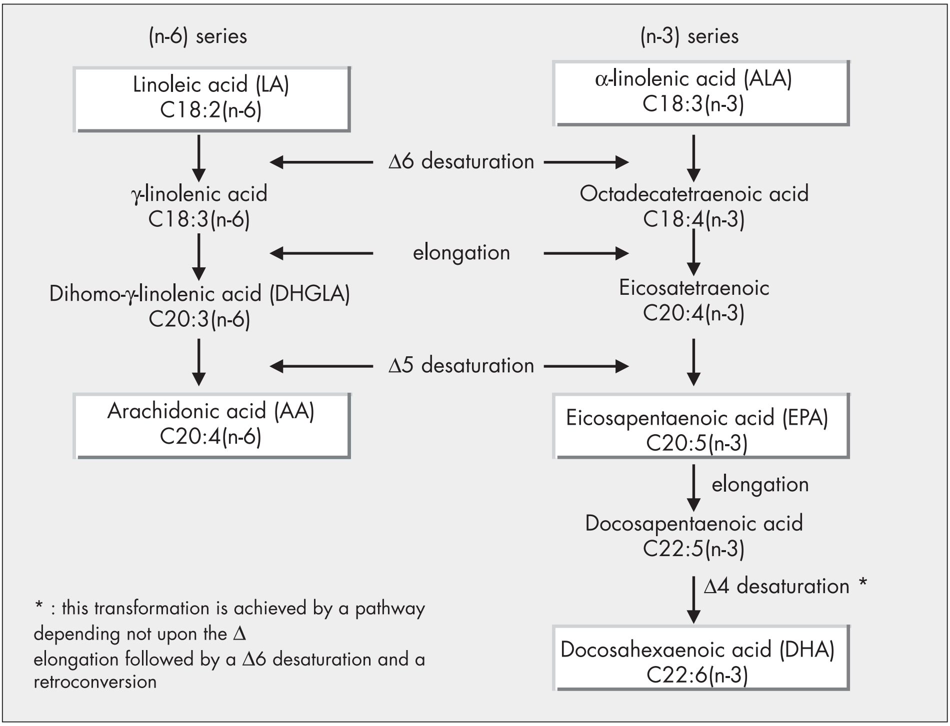

Figure 2. Essential fatty acids and their derivatives.

Therefore, more DHA than (n-6) DPA is available in the brain even though the blood supply provides considerably more 18- and 20-carbon (n-6) PUFA precursors. This difference in availability, due primarily to differences in PUFA metabolism in astrocytes, is probably a major reason why neural membranes accumulate DHA and, consequently, why the retina and brain have evolved to function better with DHA than with (n-6) DPA. These results suggest that (n-3) PUFAs are essential because the PUFA elongation and desaturation pathway does not produce enough of the corresponding 22-carbon (n-6) analogue to satisfy the needs of the nervous system (figure 3).

FATTY ACIDS AND CELL BEHAVIOR

It has become increasingly clear that the amount and type of dietary fat will alter cellular responses. However, fatty acids do not act alone. All PUFAs having the 1,4-cis, cis-pentadiene structure may undergo peroxidation, which can be achieved by cell lipoxygenases and/or cyclooxygenases, depending on the fatty acid type. Further reduction of the hydroperoxide products leads, at least indirectly, to consumption of cell antioxidants, which may subsequently affect the cell's behavior. This finally explains why the effects of fatty acids, while potent, are influenced by other nutrients, in particular vitamins C and E.

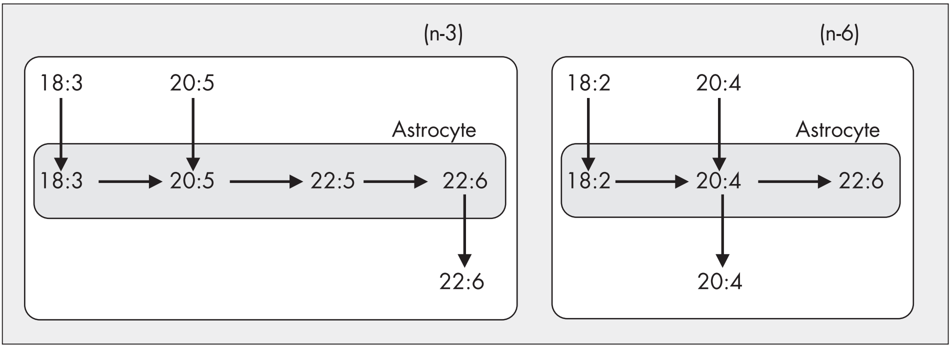

Figure 3. Metabolism of polyunsaturated acids in astrocytes (from A.A. Spector, University of Iowa, USA).

Among PUFAs, those of the (n-3) family are believed to have beneficial effects against atherothrombogenesis, partly in affecting the production of arachidonic acid-derived eicosanoids in blood and vascular cells. However, the high degree of unsaturation of (n-3) fatty acids, especially the long chain ones such as eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids, makes them highly susceptible to peroxidation and to generate potential pro-oxidants (figure 4). Evidence has been provided that EPA and DHA influence the redox status of blood and vascular cells depending on their concentration. In vitro, small concentrations of EPA prevent the lowering of platelet vitamin E content induced by diamide, depressing reduced glutathione. However, high concentrations of EPA or DHA induce an oxidative stress (increase in malondialdehyde and decrease in vitamin E), resulting in an increased expression of the antioxidant enzyme glutathione peroxidase at a posttranscriptional level. In vivo, two studies in an elderly population (aged 70-83 years) who ingested either 100 mg/day for 60 days of EPA at the sn-2 position of pure triglycerides in the first study, or 150 mg DHA plus 30 mg EPA/day in triglycerides for 42 days in the second, have shown decreased oxidative stress in platelets, and a significant reverse of the lower vitamin E content observed in comparison with young adults. In bovine vascular endothelial cells, EPA and DHA may also affect the antioxidant status, with high concentrations stimulating the expression of glutathione peroxidase, and decreasing the expression of the constitutive form of prostaglandin H synthase (PGHS-1 or Cox-1), presumably in response to the oxidative stress induced in the course of cell enrichment.

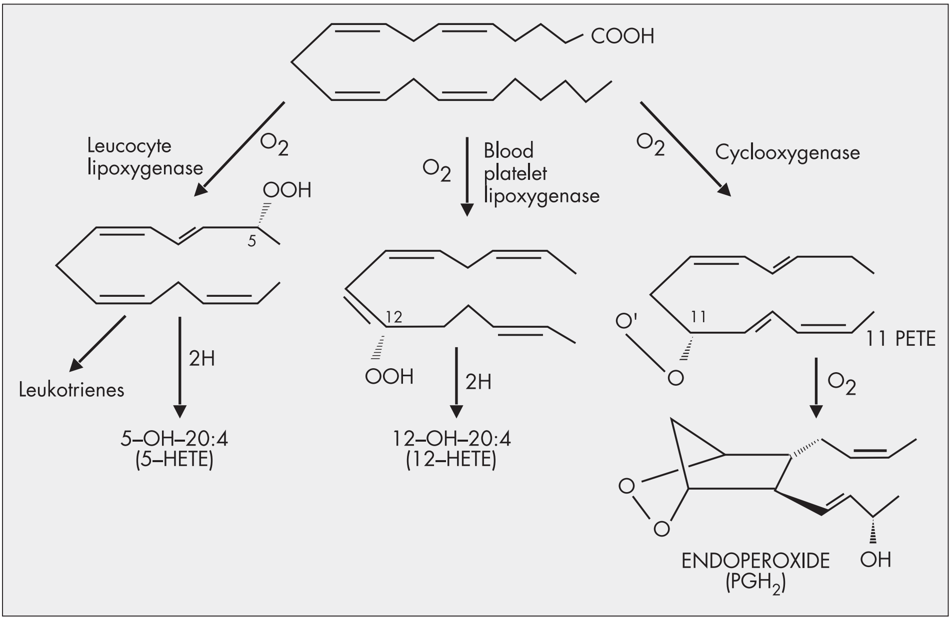

Figure 4. Simplified scheme of the bioconversion of arachidonic acid into various hydroxy fatty acids (PETE: peroxyeicosatetraenoic acid; HETE: hydroeicosatetraenoic acid).

Thus, in addition to exerting competing effects on arachidonic acid metabolism, EPA and DHA may affect, even at small concentrations, the cell redox status which controls this metabolism.

FATTY ACIDS AND CELL MEMBRANE COMPOSITION

Whether the composition of cell membranes is determined by the dietary pattern and/or the genotype is not known. To unravel this question, human twin studies may be performed to assess the influence of genetic factors. Such studies have previously shown intrapair resemblance in the composition of fatty acid in plasma in subjects with schizophrenia and in the fatty acid content of ear cerumen. Genetic influence on fatty acid composition was studied in female obese identical twins. Fourteen pairs of female identical twins concordant for obesity were studied (age, 39.0 ± 1.7 years; BMI, 34.2 ± 1.5). The pattern of intrapair and interpair resemblance in fatty acid composition was described for food, plasma, and adipose tissue after one week of in-patient stabilization. Fasting serum and adipose tissue were obtained for fatty acid examination analysis, using thin layer chromatography fractionation and gas-chromatography. Using food records, intrapair resemblance for energy content, carbohydrates and linoleic acid was found to be significant. No correlation was found between the content of linoleic acid in food and that in serum lipids and adipose tissue triglycerides. Within the lipid fractions in serum phosphatidyl choline, 12 of the 14 fatty acids were found to be similar in intrapair but not in intercomparison. Within the lipid fraction in serum cholesteryl esters and triglycerides and adipose tissue triglycerides, intrapair resemblance was considerable for several saturated and monounsatured fatty acids, but rare for PUFAs. Thus, intrapair resemblance strongly suggests that the genotype contributes to the composition of cell membranes independently of the diet pattern.

TRANS FATTY ACIDS AND ADIPOSE TISSUE CONTENT

The situation regarding the pathogenetic role of trans fatty acids has been much publicized. Some epidemiological studies from estimates of TFAs intake using food-frequency questionnaires have indeed suggested an association between TFA consumption and the incidence of coronary heart disease (CHD). Initial data demonstrated a clear relationship between energy intake from trans 18:1 and LDL-cholesterol concentrations. This trans isomer can also lower HDL-cholesterol concentrations, as opposed to saturated fatty acids, and increase concentrations of triglycerides and lipoprotein. The mechanisms of these effects on the serum lipoprotein profile are still unknown; they may be partially explained by an increase in the activity of cholesteryl ester transfer protein (CETP). The Nurse's Health Study, with findings extending over a total of 14 years of follow-up, suggests that the replacement of 2% of the energy from TFAs with energy from unhydrogenated, unsaturated fats would reduce the risk of CHD by 53%. Epidemiological studies, however, are not conclusive, both in the general population and for individuals at high risk. The discrepancies are partly due to the extreme crudeness of methods for measuring self-reported dietary data, especially in retrospective studies. Thus, research in nutritional epidemiology relies on future dietary survey methods and biochemical markers of long-term fatty acid intake, including the adipose tissue content of fatty acids. In this respect, the type of adipose tissue studied should be taken into consideration, since the fatty acid response of fatty acid synthase and lipoprotein lipase gene expression in adipose tissue is site specific.

A study has been conducted in Aquitaine (France) to examine the relationship between the presence of TFAs in adipose tissue and blood plasma, and LDL- and HDL-cholesterol concentrations, in order to evaluate the associated cardiovascular risk of TFA intake, taking each trans isomer into consideration since each one has its own metabolism with specific consequences. The mean total TFA content of adipose tissue was 2.24% of fatty acids in 71 adults (1.77 in men, 2.38 in non-pregnant women, and 2.17 in pregnant women). The detectable isomers were the trans 16:1, 18:1, 18:2 and 18:3 acids. Based on the trans 18:1 level, the intake of this population is clearly lower than that of other European countries, the USA and Canada. Among the trans 18:1 positional isomers, the Δ11 trans was the most prevalent, as in ruminant fats, suggesting that these are an important dietary source of TFAs in France. In plasma, the average TFA level was about 0.6% of total fatty acids. TFAs were the isomers of the 16:1, 18:1 and 18:2 acids. The trans 18:3 isomers were undetectable.

Having stated the mechanisms by which fatty acids exert their effects, let us now consider their significance on a clinical basis.

CHAPTER II

FUNCTIONAL FOODS

GENERAL CONSIDERATIONS

The function of foods is to supply sufficient nutrients for meeting the substrate needs of the organism as well as to provide satisfaction and well-being through hedonistic features such as taste. In addition, some foods considered as "functional foods" have an added value for health or well-being beyond usual nutritional effects due to nutrient or non-nutrient components that affect specific target functions.

The working definition of the European Concerted Action regards a food as "functional" if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way which is relevant to either the state of well-being and health and/or to the reduction of the risk of a disease. Functional foods must remain foods and they must demonstrate their effects in amounts which can normally be expected to be consumed in the diet. A functional food can be a natural food, a food to which a component has been added, or a food from which a component has been removed by technological or biotechnological means. A functional food can also be a food in which the nature of one or more components has been modified, or in which the bioavailability of one or more components has been modified, or any combination of these possibilities. A functional food might be functional for all members of a population, or for particular groups of the population which might be defined, for example, by age or genetic constitution.

Up to now, the approaches used in functional food science both in Japan and to a lesser extent in the USA have mostly been "food or food component-driven", and they are likely to be very much influenced by local traditional or cultural characteristics. A science-based, "function-driven" approach appears preferable because the functions and their modulation are universal. Functional food science, therefore, refers to the new concepts in the science of nutrition which have stimulated research and led to the development of the functional foods.

The European Concerted Action reviewed the scientific basis of functional foods in Europe with the goals of critically assessing the science required to provide evidence that specific nutrients positively affect functions, examining the available science from a concept-driven point of view rather than a food component-driven one, and reaching consensus on targeted modifications of food and food constituents, as well as options for their application. Reports from groups working on topics have recently been published [August issue of Br J Nutr, 1998].

Development and evaluation of functional foods and their scientific basis are receiving great attention and have been the subject of a recent Concerted Action sponsored by the Commission of the European Union and the International Life Science Institute of Europe. This Concerted Action concludes that we are at a new frontier in nutrition: in the industrialized world, concepts in nutrition are progressing from a concept of adequate nutrition to one of optimal nutrition. We have moved from an early emphasis on survival, through that of hunger satisfaction and food safety, to our present emphasis on the potential of foods to promote health in terms of improving mental and physical well-being as well as reducing the risk of chronic diseases.

FUNCTIONAL FATTY ACIDS

Fatty acids play an important role as functional ingredients of foodstuffs. The following steps need to be considered:

- firstly, biophysical characteristics, such as the length of the carbon chain, the number and nature of C=C double bonds, the distance of the first double bond from the methyl radical, and the position of fatty acids in the triglyceride, that determine the ability to convert into active derivates;
- the proportion of fatty acids among themselves and in the foodstuff, and the physical and chemical environment should also be considered;
- then, these different parameters should be linked to nutritional effects on target functions on the basis of reliable health markers (an example has been provided with the 24-hour heart rate variability, which is a powerful predictor of lethal cardiac arrhythmia). In this respect, defining the target function is critical. For example, if the target is the development of the brain and the retina, it should be reminded that premature infants convert α-linolenic acid to DHA quite poorly. But, considering the cardiovascular system, a high α-linolenic acid intake is associated with a low cardiovascular mortality, either in primary prevention (in Japan, where the amount of α-linolenic acid is very high in the diet, from rapeseed oil) and in secondary prevention (in France, with a Mediterranean α-linolenic acid-rich diet);

- lastly, the above parameters should be linked to an area even broader taking into consideration organoleptic properties, technological constraints for food preparation, oxidation during the shelf life, cost supplies, emotional and cultural aspects.

In conclusion, foods and food components have the potential to modulate target functions in the body that are relevant to well-being and health. Any functional food and claims related to it must be substantiated by sound scientific findings. Concerning fatty acids, this is a real challenge given the great number of fat available for technological utilization.

CHAPTER III

HEALTH IMPLICATIONS

In this vast area, three issues were actively investigated during the workshop: the development in the fetal and neonatal life, the pathogenesis and the prevention of cardiovascular disease, and defense mechanisms.

FETUS AND NEONATAL DEVELOPMENT

We first saw that PUFAs are required for optimum development and function of the nervous system. Since TFAs are incorporated into nearly all lipid classes of various organs, the relation between dietary intake of trans fatty acids (TFAs) and the development was also examined in this workshop.

The metabolism of trans 18:1, the most common TFA in diet, has been studied intensively both in vitro and in vivo in rats, especially to assess its influence on the metabolism of PUFAs. These studies have shown that the trans 18:1 isomers were primarily incorporated into the 1- and 3-positions of triacylglycerols and into the 1-position of both phosphatidylcholine and phosphatidylethanolamine. Numerous experiments have shown that the influence of dietary TFAs is negligible when adequate linoleic acid level is provided in the diet and no tissue degeneration is observed. Therefore, the most common isomer of TFAs may be regarded as an unsaturated fatty acid, no more, no less.

Some trans isomers can be converted by rats to long chain trans PUFAs under conditions of adequate intake of essential fatty acids. Recent studies have shown that they have different effects, when compared with their cis homologues on platelet aggregation and eicosanoid production. In adults, any serious undesirable health hazard has been reported due to the sufficient supply of linoleic acid in a normal diet. However, the fetus is very sensitive to factors which can interfere with metabolism of essential fatty acids. Its need for the arachidonic and DHA acids is extensive. An inverse correlation has been reported in premature infants between the levels of plasma trans octadecenoic acid and the long-chain PUFA level. An inverse correlation was also observed between the TFA level and birth weight in observational studies. These findings suggest that exposure to high levels of TFAs during pregnancy may impair fetus growth.

Isomeric fatty acids have been therefore measured in cord plasma and compared to maternal blood. The trans isomer distribution in cord plasma lipids was different from the maternal distribution. Individual differences were remarkable for isomers of linoleic acid: cord plasma contained three times more of the 9t12c isomer than maternal blood. From the index value of the fatty acid exchange between mother and fetus, it has appeared that the 9t12c isomer was better incorporated into cord plasma. Moreover, an inverse correlation has been observed in cholesterol esters of cord plasma between the content of the 9t12c-18:2 and that of the linoleic acid.

Metabolism of essential fatty acids must be saved from any disruption, in preterm babies as well. The influence of TFAs present in mother's milk on long-chain PUFA deposition in infant erythrocyte lipids has also been studied. Inverse correlations were found in erythrocyte phosphatidylcholine. Presence of TFAs in human milk is based exclusively on the mothers dietary intake. Indeed, the TFAs levels of different populations range according to their TFAs intake rates: 1.22% in Spain, 2.1% in France, 4.0% in Germany, 6.6% in Canada.

To conclude, if long-chain PUFAs and TFAs have been extensively studied, relatively few studies have provided information regarding their impact on development in humans. Recently, it has been reported that 21 infants who had been fed for the first 4 months of their lives with formula supplemented with long-chain PUFAs were found, when tested at 10 months, to have greater problem-solving abilities than infants fed on an unsupplemented formula (problem solving was assessed by an ability to carry out a 3-step procedure to retrieve a hidden toy).

CARDIOVASCULAR DISEASE

This chapter begins with several studies regarding the role of dietary lipids in cardiovascular disease, followed by two studies examining the relationship between blood lipids, lipoproteins and cardiovascular disease.

Dietary lipids and cardiovascular disease

The etiologic role of dietary fat in the development of atherosclerosis and cardiovascular disease, in particular coronary heart disease (CHD), is strongly supported by several sources of evidence. However, there is also an expanding body of evidence indicating that (n-3) fatty acids can favorably influence many of the pathways that are believed to be important in the development of atherosclerosis and its clinical sequelae of ischemia. With the aim of unraveling the complex relation between fatty acids and atherosclerosis, this workshop has brought into focus several properties of these fatty acids that may prevent CHD.

A large number of studies have been done on the potential benefits of dietary (n-3) fatty acids in vascular disease since the original observations in Greenlander and Alaskan Eskimos. Later population studies and observational studies of primary prevention as well as secondary prevention studies in patients with established CHD have supported these classical studies. A close inverse correlation between the consumption of fats and CHD has been observed among Japanese fishermen and farmers. In the Chicago Western Electric Study, where the relationship between base-line fish consumption and the risk of death from CHD was examined over a 30-year period in men aged 40-55 years, the relative risk of non sudden death from myocardial infarction was 0.33 in men who consumed 35 g or more fish daily as compared with those who consumed none, with a graded relation between the relative risk and the strata of fish consumption. In the Lyon Diet Study, which was a prospective randomized double-blind study of secondary prevention, high α-linolenic acid consumption significantly reduced cardiovascular and all-cause mortality, but with the addition of an oleic diet. In contrast, despite the potential advantages of (n-3) fatty acids on platelet aggregation, smooth cell proliferation, monocyte adhesion to endothelial cells, stimulation of the endothelial production of nitric oxide, and neointimal proliferation after vascular injury, large clinical trials with quality-controlled quantitative angiography and biochemical compliance tests showed that re-stenosis after percutaneous coronary revascularization was not prevented by a high-dose supplement of (n-3) fatty acids.

In addition to their antithrombotic effects, antiarrhythmic effects of (n-3) fatty acids have also been considered. Sudden cardiac death is indeed a serious problem in Western countries. About two thirds of patients with CHD die outside of hospital, most of them from malignant ventricular arrhythmia. No improvement in preventing sudden cardiac death in this major proportion of the patients has been noted over the past decades. In fact, clinical trials using antiarrhythmic drugs have been stopped prematurely due to increased mortality among those receiving the active drug. (n-3) fatty acids may thus be an alternative, as several dietary studies have shown a reduced incidence of sudden cardiac death among fish consumers. (n-3) fatty acids have indeed a number of antithrombotic effects of clinical significance, such as inhibition of the synthesis of thromboxane A2 and production of prostacyclin which produces vasodilation and less sticky platelets. Animal studies have convincingly shown an antiarrhythmic effect, EPA and DHA being equally potent. Studies in rats have shown that the most efficient antiarrythmic n-3 fatty acid was α-linolenic acid.

However, with the exception of a randomized placebo-controlled double-blind study showing a 70% reduction in ventricular ectopic beats in subjects with (n-3) fatty acids versus 15% in controls, data on the antiarrhytmic effect of (n-3) fatty acids in humans are sparse. A new intervention trial was therefore undertaken in three different groups: patients with previous myocardial infarction (MI) and left ventricular dysfunction, patients with chronic renal failure (i.e. at high risk for heart disease), and healthy volunteers. The endpoint was the 24-hour heart rate variability (HRV) which is a powerful predictor of mortality and of arrhythmic events in humans. A low HRV indicates a poor prognosis.

Patients with an MI history (n = 55, age 63 ± 7 years) were divided into three subgroups: a) those who never ate fish, b) those who ate fish once a week, and c) those eating fish at least twice a week. The cellular content of (n-3) fatty acids was correlated to both fish intake and HRV. These patients were subsequently randomly allocated to receive either 5.2 g of (n-3) fatty acids daily or placebo oil for 12 weeks: dietary supplementation significantly increased HRV.

Patients with chronic renal failure (n = 29; age, 52 ± 15 years) received 5.2 g of (n-3) fatty acids or olive oil daily for 12 weeks. After dietary supplementation, a close correlation was found between the cellular content of (n-3) fatty acids and HRV.

Lastly, 60 healthy subjects (25 women, 35 men, mean age 38 years) were randomized for 12 weeks to either 2.0 g of (n-3) fatty acids daily, 6.6 g of (n-3) fatty acids daily, or placebo. At baseline, a close correlation was found between (n-3) PUFA in granulocytes and HRV. Subjects with a low HRV at baseline had a dose-dependent increase in HRV after (n-3) fatty acids supplementation.

These three studies suggest an antiarrhythmic effect of (n-3) fatty acids which would explain the low occurrence of sudden cardiac death in subjects who regularly eat fish.

(n-3) fatty acids are not unique in the prevention of CHD. Olive oil, which contains up to 80% of monounsaturated oleic acid, also favorably affects several metabolic processes that aggregate or are singly critical in the initiation and evolution of atherosclerotic events, including the regulation of plasma cholesterol or cholesterol associated to low- and high-density lipoproteins, platelet aggregation, eicosanoid production, monocyte adhesion to endothelial cells, low-density lipoprotein oxidation. To date, dietary trials have demonstrated the major role of oleic acid in primary and secondary prevention of these lipid metabolic disorders. The strategy was largely based on the balance of monounsaturated fatty acids with saturated and polyunsaturated fatty acids. However, this type of management is incomplete, because high-monounsaturated oils containing the same amount of oleic acid do not exert the same biological effects when included in the diet.

It is possible to improve the plasma lipid and lipoprotein profiles in humans through long-term ingestion of olive oil and high-oleic sunflower oil diets, but only olive oil tends to normalize structural and functional properties of membranes in patients at high risk of CHD.

These findings clearly indicate that olive oil is a food with a relevant impact on health not exclusively associated with the content of monounsaturated fatty acids. Rather, it is believed that the distribution of fatty acids into the glycerol backbone as triacylglycerols could be a more important factor during absorption of olive oil (or other fats) and further triacylglycerol-rich lipoprotein particles formation. Olive oil and high-oleic sunflower oil have different triacylglycerols. Therefore, the unique composition of fatty acids and triacylglycerol molecular species in olive oil (together with the supply of natural antioxidants) probably contribute to the well-known effect of Mediterranean diet in lowering incidence of CHD.

Returning to the evidence that saturated fatty acids are pathogenic for CHD, they have however not been studied in detail individually and comparatively to monounsaturated fatty acids. Therefore, the effects of specific saturated fatty acids (medium-chain fatty acids, lauric acid, myristic acid and palmitic acid) were compared with those of a monounsaturated fatty acid (oleic acid) in healthy subjects. In a study with a cross-over design, eighteen women and fourteen men consumed a 6-wk diet enriched in lauric, palmitic or oleic acid (study 1). In a parallel study, thirty-seven women and twenty-three men consumed a 3-wk run-in diet enriched in oleic acid and 6-wk experimental diets enriched in either MCFA, or myristic or oleic acid (study 2). The calculated nutrient composition was the same in each diet, except for 8.5% of the total energy which was provided by lauric, palmitic or oleic acid in study 1, and 10% of the total energy which was provided by either MCFAs, or myristic or oleic acid in study 2. Activated factor VII (factor VIIa), the thrombin generation potential of plasma, the tissue factor pathway inhibitor, factor X activity, antithrombin III, plasminogen activor inhibitor (PAI-1) activity, plasminogen and α2-antiplasmin activities were assessed using chromogenic assays, and prothrombin fragment F1+2 concentrations were assessed using ELISA. Compared with the oleic acid diet, the differences were: a higher concentration (+ 10%) of factor VIIa with lauric acid, myristic acid, and palmitic acid diets in women, but not in men; a higher thrombin generation potential of plasma with the myristic acid diet; a higher PAI-1 activity with the palmitic acid diet. However, there was no significant difference for the other parameters studied. Thus, compared with monounsaturated fatty acids, saturated fatty acids, especially the major dietary fatty acids like lauric, myristic and palmitic acids, have an unfavorable impact on factor VIIa activity in a gender-specific manner and in the plasminogen activator inhibiting capacity of plasma.

Blood lipids, lipoproteins and cardiovascular disease

If cholesterol has become well established as a major risk factor for CHD, the role of triglycerides and the predictive value of apolipoproteins remains controversial. This workshop was an opportunity to report the results of the Caerphilly and Speedwell Studies, extending their findings from 5 to 10 years.

The two cohorts were high response rate samples taken from the general male population, aged 45 to 59 years when first examined. Of the combined cohort of 4,860 men, 4,641 gave a fasting blood sample. At the ten-year follow-up, 571 (12.3%) had developed major CHD. On a univariate analysis, triglycerides were strongly related to incident CHD. However, multivariate analysis showed a major change in the predictive power of triglycerides: the relative odds of incident CHD in the top 20% of the distribution of triglycerides had fallen from 2.24 at 5 years to 1.55 at 10 years, and the standardized relative odds (SRO, i.e. the odds associated with a standard deviation of one) had declined from 1.19 to 1.11 and was no longer statistically significant, even with the much larger number of incident events. It thus appears that triglycerides may only be short-term predictors of CHD.

A second question was whether measurement of plasma apolipoprotein B (apo B), apolipoprotein A-1 (apo A-1), and lipoprotein(a) (Lp(a)) improves the prediction of

CHD provided by total and HDL cholesterol. These lipoproteins were therefore measured in fasting blood samples from 2,398 men aged 49 to 65 years during the second phase of the Caerphilly Study. 282 (12%) men developed major CHD. After adjusting for standard cardiovascular risk factors other than lipids, multiple logistic regression analysis showed that there was a trend (SRO 1.20) for incidence of CHD to increase with apo B. However, on further adjusting for total cholesterol this trend largely disappeared (SRO 1.05). Similarly, a trend for incidence of CHD to increase with decreasing apo A-1 (SRO 1.18) disappeared when HDL cholesterol was added to the model. Incidence of CHD was effectively constant over nearly 90% of the range of Lp(a). Only for the 5% of men with Lp(a) greater than 70 mg/dl was the risk of CHD significantly greater than for men with Lp(a) less than 10 mg/dl.

From this "lipoprotein study", it can be concluded that apolipoproteins B and A-1 do not improve the prediction of risk of CHD provided by total and HDL cholesterol, while Lp(a) may be independently associated with incident CHD among the 5-10% of men with the highest levels.

INFLAMMATORY DISEASES

Preclinical studies have shown that laboratory animals fed with high levels of dietary fat (30% of total energy) have increased susceptibility to infections compared to lower levels of fat (e.g. 15% of total energy). In contrast, numerous studies have shown that long-chain PUFAs, through enzymatic degradation of eicosanoids (figure 5), have beneficial effects on cytokine production, inflammatory reactions, both non-specific and specific immune responses, and infection (figure 6). Feeding laboratory animals diets rich in (n-3) PUFAs (linseed oil, which is rich in α-linolenic acid) or fish oil (rich in EPA and DHA)

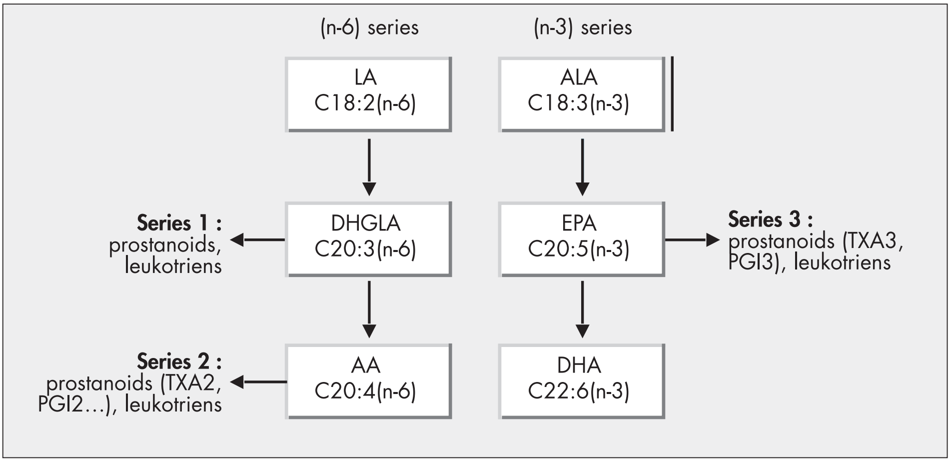

Figure 5. Synthesis of eicosanoids from (n-6) and (n-3) PUFAs.

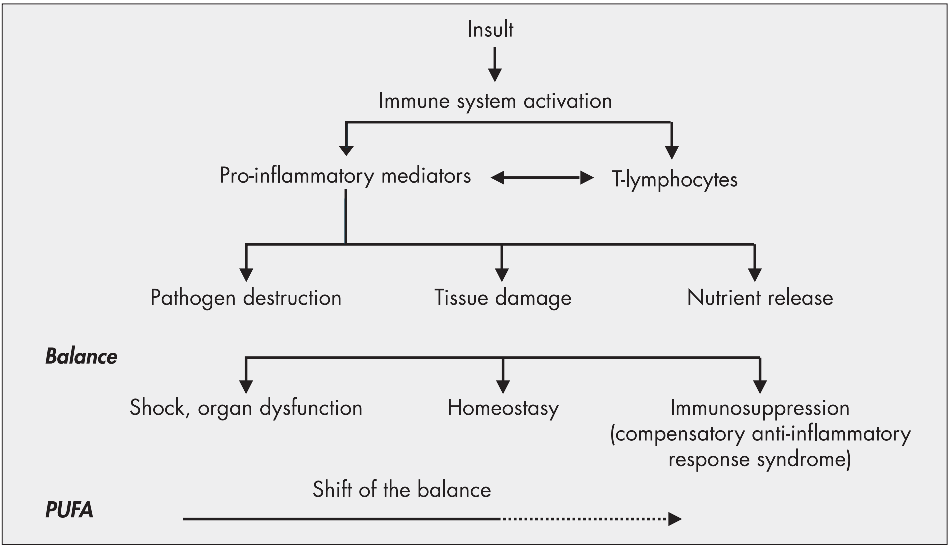

Figure 6. Immune system activation and proposed effects of PUFAs (from P. Calder, Southampton, UK).

decreased lymphocyte proliferation, cytotoxic T cell activity, natural killer cell activity, antigen presentation, and the production of pro-inflammatory cytokines by lymphocytes and macrophages. Investigations which have directly compared the effects of these oils indicate that fish oil is more suppressive than linseed oil, which is, in turn, more suppressive than oils rich in (n-6) PUFAs. Similar observations have been made following diet supplementation (with encapsulated fish oil) in healthy volunteers or in patients with chronic inflammatory diseases. Animal models indicate that fish oil feeding decreases sensitivity to pro-inflammatory cytokines, increases survival following endotoxin administration, and decreases clinical symptoms in animals with autoimmune diseases, thus prolonging their lifespan. It is now apparent that relatively low levels of α-linolenic, EPA, and DHA exert immunomodulatory effects. The relationship between pro-inflammatory cytokine production and the level of (n-3) PUFA incorporation into human mononuclear cells has been reported recently, as have the effects of PUFAs on adhesion molecule expression by a variety of cell types. Recent studies have attempted to examine the effects of EPA and DHA on immune cell function. It appears that EPA is more potent in humans than DHA. In addition to altering the amounts and types of eicosanoids formed, (n-3) PUFAs might affect immune cell function by depleting the antioxidant α-tocopherol, by modulating the generation of intracellular second messengers and/or by influencing the expression of genes for cytokines and adhesion molecules. It is unclear whether (n-3) PUFAs affect intracellular signalling mechanisms directly or via changes in eicosanoid production and/or antioxidant status.

Whatever the mechanism of action, the effects of (n-3) PUFAs suggest that they will be useful as an adjunct to existing therapeutic approaches in not only acute but also chronic inflammation. Indeed, it has been shown in well-controlled clinical studies that dietary interventions with increased amounts of (n-3) fatty acids, often accompanied by decreased total fat in the diet, will alter the development of inflammatory processes (inflammatory bowel disease), autoimmune disorders (rheumatoid arthritis), infection (wound infections, abdominal surgery), allograft rejection (renal transplant), and renal disease (lupus nephritis, IgA nephropathy). When combined with other immunonutrients (arginine and/or glutamine), the beneficial effects of (n-3) PUFAs are improved even more.

Finally, since fish oil may act in synergy with cyclosporin A to induce long-term functional transplant tolerance (unpublished animal studies), manipulation of long-chain fatty acids, especially of the (n-3) series, may now be considered as part of multimodal therapeutic regimen.

CHAPTER IV

NUTRITIONAL RECOMMENDATIONS

This chapter begins with the presentation of recommendations made in Italy, Germany and France, and is followed by an attempt at a consensus with the participants to the panel.

THE ITALIAN POSITION

Fat intake in different populations varies enormously, from less than 10 to over 45% of total energy. The major factors responsible for this marked difference are costs, availability, climate, and dietary habits. For these reasons, global strategies for defining requirements are not easy, and recommendations should initially be targeted to populations in defined geographical areas, where nutritionally homogeneous conditions are present and where information on the relationships between dietary fats and health is available. In addition, requirements for optimal nutrition, rather than for prevention of deficiencies, ought to be considered in defining possible recommendations.

Requirements should therefore be expressed differently for the major fatty acid classes (i.e. as % of total energy) and for the minor essential fatty acids, especially for those in the (n-3) series (α-linolenic, and the long chain fatty acids EPA and DHA), which should be expressed as g or mg/day, and as “ranges” of intake. Assessments of fat intake has been carried out in several Western countries (e.g. USA, UK, France, Belgium, Germany, the Netherlands, Italy, and others), and recommendations have also been provided by various agencies such as the US Research Council (1989), the BNF (1992), and the FAO (1994). While there is substantial agreement on requirements in major fat components (total fat from saturated and monounsaturated fatty acids), there is still some controversy on requirements (and subsequent recommendations) in short and long chain fatty acids. In Italy, where major differences are evident in terms of fat consumption between the North and the South, fat intake increased between the 50s and the 80s, with increments in total fat and in saturated fatty acid intakes, especially in the South, in excess over recommended intake. Some improvement has occurred over the last decade (reduction in total fat and saturates), although fat intake is still in excess.

As to the balance between different fatty acids, data concerning the relative intakes (saturated, monounsaturated, and polyunsaturated fatty acids, i.e. respectively SFAs, MUFAs, PUFAs) and their effects on various physiological variables should be integrated with data from analysis of plasma fatty acids. Correlation between fatty acid classes in plasma lipids of various population groups have been studied, and show some unexpected findings: no correlation between plasma SFAs and MUFAs, a modest negative relationship between SFAs and PUFAs, and a definite inverse relationship between MUFAs and PUFAs. These relationships could be helpful in evaluating metabolic interactions among these classes.

THE GERMAN POSITION

Adequate amounts of dietary fat are essential for health. In addition to its contribution to energy needs, dietary fat must be sufficient to meet requirements for essential fatty acids and fat soluble vitamins. In addition, dietary fat improves the flavor of foods. Minimum intake consistent with health varies throughout a person’s life and among individuals.

Fat intake should not exceed 30% of total energy. Active individuals who are in energy balance may consume up to 35% of their total energy intake from dietary fat if the level of saturated fatty acids does not exceed 10% of the energy.

The saturated fatty acids – lauric, myristic and palmitic – elevate serum cholesterol and LDL levels. Stearic acid does not elevate serum cholesterol or LDL levels; however, other health effects remain undefined. Polyunsaturated linoleic acid reduces serum cholesterol and LDL levels. Monounsaturated oleic acid may be neutral with regard to LDL. Dietary cholesterol elevates serum cholesterol and LDL levels, but the extent of the increase is highly variable. Trans fatty acids elevate serum LDL levels and lower HDL levels. High intakes of trans fatty acids are undesirable.

Intake of saturated fatty acids should provide no more than 10% of energy. Favorable intake of linoleic acid should provide from 7 to 10 percent of energy. Intake at the upper end of this range are recommended when intake of saturated fatty acid and cholesterol are relatively high. Restriction of dietary cholesterol (less than 300 mg/day) is advised.

Substantial evidence indicates that relatively high intake of fruits and vegetables – sources of antioxidants, carotenoids and other components – reduce the risk of coronary heart disease and of some cancers. Specific recommendations concerning the desirable intakes and general health benefits of these substances cannot be made. Food high in PUFAs should contain at least 0.6 mg tocopherol equivalents per gram of polyunsaturated fatty acids to stabilize the double bonds.

The requirement of essential fatty acids must be met with 3% of energy as (n-6) fatty acids and 0.5% of energy as (n-3) fatty acids. The (n-6) and (n-3) fatty acids are of critical importance for the membrane structure and as precursors of eicosanoids. Since they compete for the same enzymes, the balance between the (n-6) and the (n-3) fatty acids in the diet is of considerable importance. The ratio of (n-6) to (n-3) fatty acids in the diet should be approximate to 5:1. According to the Bavarian section of the German Nutrition Survey (1986) and the Bavarian Nutrition Survey (1996), the diet of this population is moving towards these nutritional recommendations, but the amounts of total fat and saturated fatty acids are still too high.

THE FRENCH POSITION

In France, the recommendations are called "Apports Nutritionnels Conseillés" (ANC) and the CNERNA (Centre National d'Études et de Recommandations sur la Nutrition et l'Alimentation) is responsible for this publication which is based on the work of committees of experts over a 2 year-period. The next publication will appear in May 1999. Figure 7 shows the changes in recommendations that have occurred over the two past decades and also the anticipated changes that will probably occur in the next decade. Note the significant changes occurring since the 1980s'.

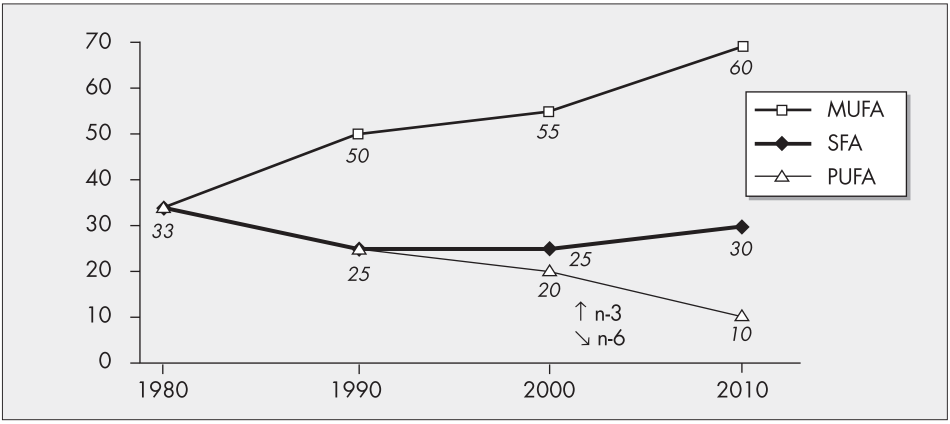

Figure 7. Evolution of recommendations (% fatty acids in the diet) (from D. Lanzmann).

Concerning lipids, defining a nutritional balance between the different fatty acids is a very important objective. Nevertheless, this balance is difficult to achieve because fatty acids are numerous and their physiological functions multiple and complex. For example, oleic acid, which has been shown not to share unfavorable effects on body weight, may also increase the triglyceride secretion by the liver, depending on the Δ9-desaturase activity.

The essential PUFAs and their derivatives have structural functions in the membrane phospholipids, and are also precursors of eicosanoids. These fatty acids include

2 families ((n-6) and (n-3)) and not less than 6 fatty acids per family, with interactions and competition. MUFAs are also involved in various cellular functions such as protection against CHD. Even saturated fatty acids, which are known to increase CHD risk, are of considerable interest as they activate certain proteins by acylation (myristoylation and palmitoylation) and thus are of great importance for cellular mechanisms. Finally, attempts to study the effects of some fatty acid are complicated by the fact that addition of these acids must be accomplished by removing some other fatty acid.

Moreover, such nutritional recommendations must include statements on the lipid percentage of the daily energy intake, as well as cholesterol intake, which are difficult to establish for experts and difficult to observe for consumers.

Recommendations are difficult to establish due to the complexity of fatty acids interactions, of the relative requirements of different fatty acids, and the physiological status of the consumer. In order to avoid dangerous simplifications, and aside from soberly saying: “You must eat a little bit of everything”, we must persuade physicians, dieticians, industries and consumers to acquire more knowledge in this field, and to develop nutritional education.

AN ATTEMPT TO A CONSENSUS

A general discussion followed the presentation of recommendations in an attempt to a consensus. The panel included the participants who have given recommendations for Italy, Germany, and France, and those who have given other data (from Belgium, the Czech Republic, France, Italy, Norway, the UK and the USA).

Table I. Consensual recommendations

Fat	Consensus	Remarks
Total fat, % of total E	≤ 30%	First step as 35%
Saturated FA + trans, % of total E	≤ 10%	Sum of trans and saturated FA to avoid unnecessary emphasis on trans
MUFA, % of total E	≈ 15%	More than 50% of total fat is recommended in France
PUFA, % of total E	< 7%	
(n-3) PUFA, % of total E	no	
Minor components of PUFA, % of total E	no	
Ratio (n-6)/(n-3)	≈ 5	
Vitamin E, mg/g PUFA	≥ 0.6	
Cholesterol, mg	< 300 mg	Not a major point

The general agreement resulting from this international discussion is shown in table I.

The main concern was to reinforce guidelines on lowering total fat (≤ 30% of total energy) and saturated fatty acids (≤ 10% of total energy) as a fundamental preventive measure. However, precise target levels have not been defined while this precision is desirable, since changing to a low-fat diet may alter mood (table II).

Table II. Alterations in mood after changing to a low-fat diet: results of change of diet from an average UK medium-fat diet (41% energy from fat) to a slightly lower-fat diet than recommended in British guidelines (25% energy from fat). From Wells et al., Br J Nutr 1998 (with permission)

	Intervention group		**Control group**		**p**
Measure*	**Before**	**After**	**Before**	**After**	**(ANOVA)**
Anger-hostility	1.3	3.4	0.6	0.3	0.021
Depression-dejection	0.2	1.4	0.2	0.0	NS
Tension-anxiety	3.6	3.8	4.2	1.8	0.025
Confusion-bewildement	3.3	2.5	2.7	2.2	NS
Vigour-activity	14.3	14.3	20.0	17.8	NS
Fatigue-inertia	4.6	3.1	1.4	1.1	NS

*: profile of mood states questionnaire (McNair et al., 1971).

CHAPTER V

REGULATORY ASPECTS OF NOVEL FOODS (EUROPEAN UNION REGULATION)

When new products enter the market, the consumer must be assured of their quality and safety. Consequently, the food industry requires toxicological and nutritional guidance in the evaluation of novel foods and food ingredients to identify potential risks that must be appropriately managed. A wide range of novel foods and ingredients is covered by EU regulations (Directive 97/25 8/EEC) applicable to the marketing of foods and food ingredients which have not hitherto been used for human consumption to a significant degree within the EU and which fall under the following categories:

- foods and food ingredients containing or consisting of genetically modified organisms within the definition of Directive 90/220/EEC,
- foods and food ingredients produced from, but not containing, genetically modified organisms,
- foods and food ingredients with a new or intentionally modified primary molecular structure,
- foods and food ingredients consisting of isolated from microorganisms, fungi or algae,
- foods and food ingredients consisting of or isolated from plants and food ingredients isolated from animals, except for foods and food ingredients obtained by traditional propagating or breeding practices with a history of safe use,
- foods and food ingredients to which have been applied a production process not currently used, where that process gives rise to significant changes in the composition or structure of the foods or food ingredients which affect their nutritional value, metabolism or level of undesirable substances.

The diversity of novel foods covered by the EU regulation is such that a check-list approach to safety evaluation is inappropriate. Rather, a case study approach that takes into account the composition of the NF, its intake, its role in the diet and the intended target group is required. The “safest concept” provides a means of targeting the safety evaluation on the nutritional or toxicological level. Novel foods may be classified as follow:

- substantially equivalent to a traditional counterpart with further information required to demonstrate their safety,
- sufficiently similar to a traditional counterpart or differing from it only in particular, well-defined, characteristics. The evaluation will focus on those differences,
- not substantially equivalent to a traditional counterpart. Extensive testing of the whole food is required. Testing should follow in this case a scientifically-based hierarchical approach involving literature reviews, chemical analysis, appropriate in vitro and in vivo tests, and, if necessary, confirmation of safety and nutritional value in humans. A survey of consumer health after the novel food has been introduced into the market may provide additional assurance of safety.

CHAPTER VI

ANALYTICAL ASPECTS

Exploring the health implications of fatty acids inevitably requires the examination of reliable analytical data covering a large range of subjects, from extraction, the sampling of raw material in food, analysis separation and identification of a specific component such as fatty acids and triglycerides, and the evaluation of degradation (hydrolytic or oxidative), to the determination of minor components and impurities such as quality control. However, the various analytical methods in use, their deficiencies in accuracy and precision, especially with relatively low amounts of minor components of fatty acids, as well as differences in their adaptability to the analysis of foods compared with biological samples, indicate the need for a thorough review of available analytic techniques with the aim of simplifying and standardizing routine analysis and improving fine analysis. Such an improvement may be provided by new techniques, but also by a combination of techniques currently available given the diversity of the parameters studied (length of the carbon chain, number, position and geometry of double bonds...).

DETERMINATION OF FAT CONTENT

The most suitable method for determining the trans isomers of fatty acids (TFAs) is high resolution capillary gas-chromatography with a polar column. The main components of TFAs in hardened fats are different isomers of octadecaenoic acid, predominantly elaidic and trans vaccenic acids (18:1t9 and t11, respectively) (table III). Other isomers are usually present in minor concentrations in both oils and trans configurations.

An example has been provided using one 50 M- and one 100 M-long capillary column (covered with CP-Sil 86, internal diameter 0.25 mm, df 0.2 µm) for the resolution of cis and trans isomers of octadecenoic acid. The 100 M-long column separated the major components well overlapping t12(13) with c6(7) isomers. Minor 18:1t15 was co-eluted with oleic acid. Different unresolved isomers were observed with the 50 M-long column: t11 - c6(7), t12 - c9. Trans vaccenic acid, the second predominating isomer, was coeluted with petroselinic and c7 acids, which are unusual in most foods and also in plasma. As a consequence, the short column may be used in clinical studies, where the determination of the minor t12 isomer is not essential.

Table III. Examples of isomers of octadecaenoic acid

Positional isomers	**Geometrical isomers**
cis 18:1t9 (n-9) Oleic acid	cis 18:1t9 (n-9) Oleic acid and
cis 18:1t11 (n-7) Vaccenic acid	trans 18:1t9 (n-9) Elaidic acid
cis 18:1t6 (n-12) Petroselinic acid	

A dramatically-simplified method for the routine determination of fat contents in foodstuffs was subsequently described: transesterification in the foodstuff, i.e. the formation of fatty acid methyl esters without previous isolation of the fat (figure 8). Transesterification is proposed as a method for determining fat content, in which fat is defined as the sum of the fatty acids calculated as triglycerides. In addition, appropriate for the determination of fat content this method is also suitable for the analysis of fatty acid composition. It offers three advantages: rapidity, globality, with the determination of all fatty acids, and a well-defined result. It disregards the often substantial amounts of material not consisting of fatty acids which reach the gravimetrically determined fat extract. On the other hand, fatty acids bonded to polar food constituents, which are not recovered in the fat extract, are also determined.

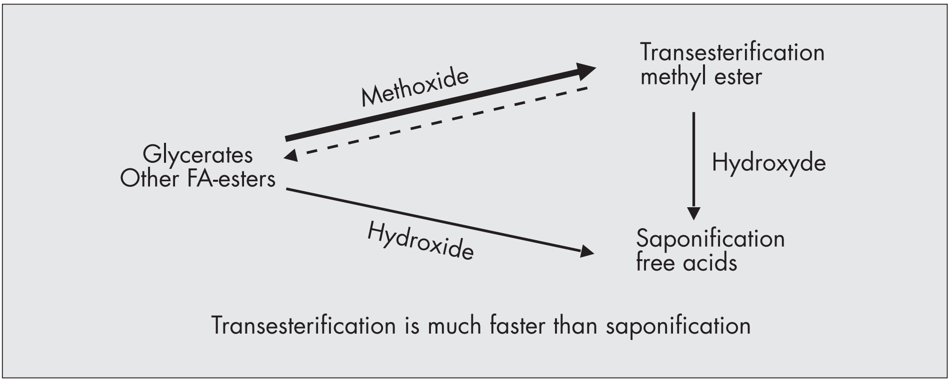

Figure 8. Base-catalyzed transesterification in water containing foods.

Transesterification in foodstuff must overcome the problem of water, which is often the predominating food component (as in an ice cream, for example). It is so much faster than saponification that the reaction can be stopped before the fatty acid methyl esters are hydrolyzed. Conditions have been optimized to achieve complete transesterification without noticeable saponification in 1 minute at ambient temperature. A short heating in dimethylformamide (e.g. of meat, cheese) or preparation of a slurry in water (e.g. milk powder) may be needed to render the fatty acids accessible during this 1 minute. The fat content is determined over an internal standard. Two to three further internal standards monitor completeness of transesterification, absence of saponification and discrimination by gas chromatography analysis.

Gas-chromatography is the method of choice to analyze fatty acids from vegetable or even marine oils. However, oils are very often submitted to different treatments before being consumed such as refining, frying, hydrogenation, during which a tremendous number of decomposition products is formed. Hydrogenation primarily leads to the formation of cis and trans C18:1 isomers while geometrical isomers of linoleic and linolenic acids may be formed during refining (deodorization step). Cyclic fatty acid monomers and other geometrical fatty acid isomers such as conjugated linoleic acid are also formed during frying. Since detailed analyses of such fatty acid isomers can only be carried out by gas-chromatography, a combination of different techniques may be proposed to circumvent the overlap between the different molecules. For example, $AgNO_3$-thin layer chromatography, reversed-phase-high performance liquid chromatography, and $AgNO_3$-HPLC may be combined with gas-chromatography.

Some examples of combination of methods have been given. The analysis of trans 18:1 isomers has been carried out using a 100 M polar column after a prefractionation by $AgNO_3$-thin layer chromatography in order to avoid the overlap between the cis and trans isomers. Analysis of cyclic fatty acid monomers from frying oils requires a combination of reversed phase and $AgNO_3$-HPLC prior to the analysis by gas-chromatography, providing a good separation of the C5 and C6 membered ring isomers. These different techniques may also be applied in the nutritional field, especially in studying the metabolism of unusual polyunsaturated fatty acids.

IDENTIFICATION OF FAT

Once separated, fatty acids should be identified. For this purpose, the technique of choice is mass spectrometry. Two derivatives are now widely used for determination of fatty acid structure by gas chromatography-mass spectrometry, i.e. 4,4-dimethyloxazoline (DMOX) and picolinyl esters. These are best considered as complementary to each other rather than simple alternatives. DMOX derivatives are much easier to separate by gas chromatography and may be preferred for separation and identification of closely related fatty acids, especially the common range of fatty acids found in animal and plant tissues. They are also useful for fatty acids with conjugated double bond systems. Picolinyl esters have somewhat different mass spectrometric properties, and are much more useful when functional groups are near either end of the aliphatic chain with iso and anteiso methyl branches (for example). It appears that DMOX derivatives can undergo rearrangements in which some of the carbons near the carboxyl end of the molecule are expelled, and this can obscure features of interest elsewhere in the alkyl chain. Hydrogenation and especially deuteration (with Wilkinson's catalyst) can often may resolve any doubts. The method of preparation of the derivatives is also important, as too vigorous conditions can cause isomerization or rearrangement of certain fatty acids.

Chemical changes occurring in lipids upon exposure to high-energy radiation have been extensively studied. Several classes of compounds including hydrocarbons, methyl and ethyl esters, cyclobutanones and other ring-containing structures, have been identified as radiolytic products of polyunsaturated fatty acids. These components were collected, fractionated and identified using vacuum distillation/Florisil column chromatography, gas chromatography and mass spectrometry. The combination of electron impact and chemical ionization mass spectral analysis was shown very valuable. On-line coupling of liquid chromatography-gas chromatography and mass spectrometry – which can be fully automated – has been successfully applied to the analysis of volatile radiolytic hydrocarbons and provides a powerful tool for routine analysis.

FUTURE ASPECTS

In food, the lipid substrates co-exist with various other non-lipid components (both major and minor). A multitude of interactions takes place, such as thermal interactions. The minor components may play a major role in a critical, delicate oxidative-antioxidative balance, whose mechanism is not fully understood.

The chemistry of oxidative changes occurring in lipids has been extensively studied. However, the oxidative reactions of food lipids cannot be solely considered as a chemical reaction, since they may be largely dictated by physical parameters to a large extent, such as the physical state of the lipid substrate and that of the medium, viscosity, porosity, surface area of interfaces, surface of active compounds, thermal conditions, relative humidity, etc.

The taking into consideration of these kinds of parameters may provide, in vitro, unexpected and contradictory findings. Because of the many parameters affecting numerous lipids, analysis of physical structure of food by magnetic nuclear resonance, mathematical models, multivariate statistics, and collection of data by bio-informatics should be helpful in increasing our understanding of these complex phenomena. However, whether these physical parameters may have significant implications in vivo, that is on food quality and health, remains to be determined.

CONCLUSION

Clearly, health and behaviour are major issues in the field of lipid research. The Workshop has put accurate scientific data into perspective and rather than simply banishing lipids seeks to promote them. It is hoped that this information will help to avoid sweeping assertions on major issues of health and behaviour, which have received considerable media attention, and that this knowledge about lipids will be used to fill the gaps in our understanding. In the final analysis, what could best inform or educate the consumer is the most important question.

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Lipids from Alpha to Omega

Lipids from alpha to omega... Indeed, it is the vast range of fatty acids, from alpha-linolenic acid to omega 3 and omega 6 fatty acids, that this book sets out to explore.

Not only does it offer a clear and concise summary of the latest known data on the physiology and physiopathologies of fatty acids, it also gives all the relevant facts about the implications that may arise from their consumption: from their acknowledged role, particularly in the prevention of cardiovascular and inflammatory diseases, to the public health strategies drawn up in Europe for providing nutritional information and recommendations.

The vital aspect of analytical expertise is also dealt with, as well as the new concept of «functional food».

In all, an accessible and practical book, bringing together the debates of international experts who met at the «Lipids from alpha to omega» workshop to discuss this essential topic.

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