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Principal Symposium on 'Lipid absorption and metabolism: physiological and molecular aspects'

Chairman's introduction

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After human ancestral lines diverged at least five million years ago, only minimal changes have occurred within the collective human genome. From that time until the Late Palaeolithic, 35 000–15 000 years ago, the human diet did not change a lot; man kept to the diet for which he was genetically programmed. As summarized from the work of Boyd Eaton (1992), the Stone Age diet was characterized by a balanced intake of wild animals and plant foods providing about 12·5 MJ/d, moderate amounts of animal fat (about 30 g/d) and vegetable fat (about 50 g/d). At this time fat represented slightly more than 20% of energy intake.

Tremendous changes in food habits have occurred in Western industrialized countries during the last century, and especially the last 40 years, leading to the modern dietary habits as observed at the end of this millenium. Compared with the Stone Age diet, the modern Western diet is characterized by a high fat intake (36–44% of energy intake), a very low intake of polyunsaturated and monounsaturated fatty acids (polyunsaturated: monounsaturated:saturated 0·3:0·5:1 *v.* 1·4:1·8:1), a very high *n*-6:*n*-3 polyunsaturated fatty acid (15 *v.* 2) and a low dietary fibre supply (15–20 *v.* above 40 g/d).

In fact, the modern human population has a limited capability to adapt efficiently to the recently adopted food pattern. Experimental and clinical, as well as epidemiological, evidence supports the concept that the major Western-world pathologies are associated with lipid intake and/or abnormalities in lipid handling. This is the case for cardiovascular diseases, several types of cancers and obesity-X syndrome. Given the important imbalance of the average present-day diet and the associated metabolic disturbances, modern nutritional recommendations ask for a reduced and more balanced fat intake (≤30% of energy intake, with saturated:monounsaturated:polyunsaturated (1:1:1, w/w) and *n*-6:*n*-3 polyunsaturated fatty acids about 5), and also a reduction in dietary cholesterol (≤300 mg/d).

Nowadays, the Western human population ingests daily about 80–150 g triacylglycerols, 2–5 g phospholipids, 0·3–0·8 g cholesterol, and 1–20 mg fat-soluble vitamins. This important amount of lipids can be assimilated through the overall process of fat digestion, which adapts efficiently to the level of fat intake, as illustrated by the doubling of the hydrolytic activities of gastric and pancreatic lipases (*EC* 3.1.1.3) under chronic

high-fat feeding as compared with low-fat feeding. In the stomach, dietary fats are coarsely emulsified and partially hydrolysed by gastric lipase. In the small intestine, extensive lipolysis goes on under the action of pancreatic lipase leading to very efficient absorption of free fatty acids, monoacylglycerols and lysophospholipids and to the partial absorption of cholesterol and fat-soluble vitamins. Given their key role, gastric lipase and pancreatic colipase-dependent lipase are being extensively studied in terms of enzyme structure, structure–function relationship and activities in the physiological conditions prevailing in the digestive tract.

Following intestinal uptake, the complex processing occurring in the enterocyte includes intracellular lipid transport, re-esterification and neo-synthesis, assembling of lipid and apoprotein moieties and secretion into the lymph as chylomicrons (long-chain fatty acids) or in the portal blood for short-chain and medium-chain fatty acids. Several lipid-binding proteins such as fatty acid translocase (FAT) and membrane or soluble fatty acid-binding proteins (FABP) are expected to be highly regulated and to play key roles in lipid assimilation and transport.

Inter-species comparisons frequently provide the source of basic metabolic mechanisms. In this regard, the understanding of lipid absorption and hepatic metabolism in ruminants is of great interest.

In the blood circulation, lipid absorption results in a postprandial phase characterized by a hypertriacylglycerolaemic state lasting for about 6 h after a usual 40 g fat meal in normal subjects. Thus, most of the day is spent in a postprandial hyperlipidaemic state. During this postprandial phase, a huge remodelling of lipoproteins occurs as a concomitant of the intravascular lipolysis of chylomicron triacylglycerols. This highly complex situation results from the competition between endogenous (hepatic VLDL-apoB100 and LDL) and exogenous (intestinal chylomicrons-apoB48) lipids for enzymic lipolysis, exchanges with HDL particles and cellular uptake. Most of these steps are regulated at the same time by the intensity of lipid fluxes and by hormone secretions (especially glucose-dependent insulinotrophic polypeptide and insulin) which are tremendously altered after a mixed meal. The effects of the amount and the nature of lipid ingested as well as the time and frequency of ingestion are under investigation. Finally, lipids are taken up by peripheral tissues and the liver. Whether this postprandial process is directly atherogenic is a crucial question.

The proper functioning of the liver involves the uptake of various lipoprotein species via receptor pathways for an important part. After intracellular processing, re-secretion of lipid moieties occurs in the form of HDL and VLDL particles in the circulation or as dispersed structures composed of phospholipids, free cholesterol, proteins and bile salts in bile.

In the adipose tissue, normal regulation of cell metabolism ensures a balance between free fatty acid esterification into triacylglycerols for storage and intracellular triacylglycerol lipolysis releasing free fatty acids. The key enzyme in this process is the hormone-sensitive lipase whose activity is regulated by insulin.

In other types of cells, such as immuno-competent cells, it is now recognized that the nature of fatty acids, especially polyunsaturated fatty acids, regulates the synthesis and secretion of cytokines (interleukins), prostaglandins and leukotrienes. How the immune system and the adipose tissue could interact deserves special attention.

Finally, recent work has shown that fatty acids possess the capacity to act directly on the cell nucleus by interacting with regulatory proteins thus acting as transcription factors

regulating gene expression. This is especially the case during cell growth and differentiation. Relevant work of this kind has been performed in the case of the maturation of adipoblast to pre-adipocyte and adipocyte during which long-chain fatty acids stimulate gene expression and promote cell proliferation.

As illustrated by the programme of the present symposium, the integration of the data obtained from regulation of gene expression and cell trafficking, enzyme structure–function relationships, physico-chemical organization of lipids, nutritional adaptations and hormonal regulations, metabolic conversions and comparative physiology is probably the way to further improve our understanding of lipid absorption and metabolism and, thus, to document the nutrient–health and disease relationship and provide a sound basis for nutritional recommendations.

REFERENCE

Boyd Eaton, S. (1992). Humans, lipids and evolution. *Lipids* **27**, 814–820.

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