Lipid metabolism in man

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Interest in lipid metabolism in man has been greatly stimulated by hypotheses concerning the role that dietary lipids might play in the aetiology of cardiovascular disease. Attention has been focused on the relations between dietary lipids and the metabolism of lipoproteins, bringing enormous advances in the understanding of human plasma lipoprotein metabolism during the last decade. Detailed knowledge of the metabolism of lipids in body tissues is, however, hampered by the lack of non-invasive methods and great reliance is placed on analogies with other species that can be more rigorously investigated. In this broad review, the following questions will be addressed. What is the state of our knowledge in man and to what extent must we rely on extrapolation from animal information? What is likely to happen if we change the diet significantly? What are the priorities for research?

Dietary lipids: amounts and types

Lipid metabolism begins in the fetus which in part builds its lipids from blood glucose. The long-chain polyunsaturated fatty acids essential for the fetal brain are accumulated by a series of metabolic steps, beginning with relatively simple precursors in maternal blood, continuing through cord blood, fetal liver and fetal brain (Crawford *et al.* 1976).

The newborn infant derives its lipid from human milk which supplies about 50–60% of dietary energy as lipid (Department of Health and Social Security, 1977). The lipid content changes during feeding and its composition is influenced by the mother's diet (e.g. Read *et al.* 1965*a*,*b*).

In cases where mothers are unable to breast feed, infant formulas supply lipid, the composition depending on whether the cow's milk fat has been retained or replaced by an alternative source. This subject has been reviewed in an earlier Nutrition Society symposium (Cockburn, 1983).

In the UK, our average daily intake of fat is about 97 g, made up of 41·9% saturated, 35·1% monounsaturated and 12·7% polyunsaturated fatty acids (Ministry of Agriculture, Fisheries and Food, 1984). *Trans*-isomers contribute about 7 g/d. Triacylglycerols account for about 90% of fat intake (about 90 g/d), but we should not forget the phospholipids (about 4–8 g/d), glycolipids (mainly from plant sources, about 1 g/d) and cholesterol (0·5–1 g/d) (Carey *et al.* 1983; Gurr, 1984).

Digestion

In most adults the process of fat digestion is very efficient and is mainly concerned with the hydrolysis of dietary triacylglycerols in the small intestine by a pancreatic lipase. At birth, the newborn has to adapt to the relatively high fat content of breast milk after relying mainly on glucose as an energy substrate in fetal life. The newborn baby can digest fat, albeit less efficiently than the older child or adult, because its pancreatic and biliary secretions are not fully developed (Hamosh, 1979*a*). Neonatal fat digestion is aided by the activity of a lipase secreted from the lingual serous glands and carried into the stomach where hydrolysis occurs, without the need for bile salts at a pH of around 4·5–5·5 (Hamosh, 1979*a*,*b*). The activity is probably stimulated both by the action of sucking and the presence of fat in the mouth, although the evidence for this is obtained

from animal experiments (Hamosh, 1979*a*). The products of hydrolysis are mainly 2-monoacylglycerols, diacylglycerols and non-esterified fatty acids, the latter being relatively richer in medium chain length acids than the original glycerides. There is also evidence that a lipase present in human breast milk also contributes to fat digestion in the newborn (Fredrikzon *et al.* 1978).

As the baby is weaned onto solid food, the major site of fat digestion shifts from the stomach to the upper small intestine. The stomach still has a role to play since its churning action helps to form a coarse emulsion of the fat which then enters the intestine and is modified by mixing with bile and pancreatic juice (Brindley, 1984; Carey *et al.* 1983). The main products of digestion are 2-monoacylglycerols and non-esterified fatty acids. Phospholipid digestion occurs by removal of the fatty acid from position 2 by pancreatic phospholipases. Much of the intestinal phospholipid in man is of biliary origin (7–22 g/d) whereas the dietary contribution is probably only of the order of 4–8 g/d (Carey *et al.* 1983). Biliary secretion is enhanced as the amount of dietary fat increases (Hill, 1974).

Cholesterol enters the small intestine both as free cholesterol and cholesterol esters, the latter being hydrolysed by pancreatic cholesterol esterase (*EC* 3.1.1.13) before absorption. As digestion progresses, the oil phase decreases in volume as the lipolytic products pass into 'mixed micelles': large molecular aggregates consisting of monoacylglycerols, long-chain fatty acids, bile salts and lysophospholipids. The mixed micelles are able to draw into the hydrophobic core the less water soluble molecules such as cholesterol, carotenoids, tocopherols and some undigested triacylglycerols.

The human large intestine contains large numbers of micro-organisms that are capable of modifying fats that are undigested and unabsorbed so that the composition of the faecal fat can be quite different from that of the diet (Carey *et al.* 1983).

Although it is possible to demonstrate differences in digestibility of different types of fats, long-chain unsaturated fatty acids being somewhat better digested than saturated ones, there is so much excess capacity in the human gut to digest fat and solubilize the digestion products that such compositional differences in triacylglycerols are probably rarely of physiological significance.

Absorption

Lipid absorption occurs predominantly in the jejunum. The digestion products pass from the mixed micelles (and possibly other intermediate dispersed phases) into the enterocyte membrane by passive diffusion (Carey *et al.* 1983). Surprisingly little is yet known about the molecular mechanisms involved in the traverse of lipolytic products into the enterocyte or their transport within the cell. A fatty acid binding protein has been described in rat intestinal mucosa but the presence or role of a similar protein in human gut is uncertain (Ockner & Manning, 1976).

The major site of resynthesis of triacylglycerols and phospholipids in the enterocyte is the endoplasmic reticulum and most of our knowledge of biosynthetic pathways is derived from experimental animals. The source of glycerol is primarily 2-monoacylglycerol during active fat absorption but the pathway starting from glycerol-1 (*sn*)-phosphate is present in gut mucosa as in many other tissues (Brindley, 1984). There are thought to be two enzymes involved in the re-esterification of cholesterol (a process that is necessary for efficient absorption): cholesterol esterase and acyl-CoA: cholesterol acyltransferase (*EC* 2.3.1.26). The latter enzyme is induced by high concentrations of dietary cholesterol (Tso, 1985). Most of these products of lipid resynthesis in the enterocyte are destined to be packaged into lipoproteins for transport to the tissues. Fatty acids with chain lengths of less than twelve carbon atoms, however, are absorbed as

non-esterified fatty acids, pass directly into the portal blood and are metabolized chiefly by β-oxidation in the liver (Brindley, 1984; Sickinger, 1975). We can calculate that about 4 g short- and medium-chain fatty acids/d enter the diet from dairy products. Further small amounts may be derived from food products that incorporate coconut and palm-kernel oils. Medium-chain triacylglycerols, refined from coconut oil and produced as cooking oils and spreads, are useful in diets for people who are unable to absorb long-chain fatty acids. Some very short-chain fatty acids derived by microbial fermentation of non-starch polysaccharides in the colon may be absorbed and contribute to lipid metabolism in man (Carey *et al.* 1983).

Lipid transport: the plasma lipoproteins

The problem of transporting water-insoluble lipids in the blood is solved by surrounding the lipid particles with a hydrophilic coat which includes phospholipids and proteins. Several surface apoproteins are synthesized in the enterocytes (apo-A, apo-B) whereas others (apo-C, apo-E) are acquired from other lipoproteins after entry into the circulation (Brindley, 1984; Sparks & Sparks, 1985). Fat feeding stimulates the intestinal synthesis of apo-A and B.

During active fat absorption, the predominant lipoprotein particles secreted from the enterocyte are the chylomicrons, large spherical particles 75–600 nm in diameter, consisting mainly of triacylglycerols (85–95%). These are secreted into the lymphatic vessels and pass via the thoracic duct to the jugular vein. The first organs they encounter are the lungs but they rapidly enter the capillaries of the muscle, heart, mammary gland, adipose tissue and other important tissues where they become entrapped by interaction with the enzyme lipoprotein lipase (*EC* 3.1.1.34). The apo-C component is necessary to activate this enzyme, which catalyses the hydrolysis of fatty acids before they are taken up by the tissues for use as a fuel (muscle), for storage (adipose tissue), synthesis of milk lipids (mammary gland) or incorporation into membrane lipids. About half the chylomicron triacylglycerol is hydrolysed in 2–3 min. Because the capacity of the tissue to remove fatty acids from the chylomicrons may not keep pace with such a rapid rate of hydrolysis, the affinity of the lipase for chylomicrons is weakened and a partly-degraded chylomicron ('remnant') is released back into the circulation. These particles, richer in cholesterol, are removed by the liver where they may be degraded and the cholesterol re-utilized, for example for bile salt synthesis.

A distinct group of lipoproteins, the very-low-density lipoproteins (VLDL) is also involved in triacylglycerol transport. These are smaller than chylomicrons and have proportionally less triacylglycerol and more cholesterol, phospholipid and protein. Although some are produced by the gut, the majority are formed in the liver to transport triacylglycerols that have been synthesized from carbohydrate. Therefore, when the human diet is rich in fat, chylomicrons represent the major means of lipid transport, but when carbohydrate predominates, triacylglycerol is transported mainly in VLDL. Their mode of uptake by tissues and degradation is similar to that of the chylomicrons.

In man, the low-density lipoproteins (LDL) represent the primary mode of transport of cholesterol in the blood for delivery to extrahepatic tissues. These are particles, 20–25 nm in diameter, comprising 75% lipid and 25% protein, which in man is almost entirely apo-B (Sparks & Sparks, 1985). Of the lipid, cholesterol comprises 60%, of which about 80% is in the form of cholesterol esters, mainly linoleate, oleate and palmitate. In a person with a plasma cholesterol concentration of about 2 g/l, about 70% is carried on LDL. The particles arise from partial degradation of VLDL in the capillaries of the adipose tissue. Triacylglycerols are removed by the action of lipoprotein lipase as well as peptides other than apo-B, leaving a lipoprotein (LDL) richer in cholesterol. At the

same time, much of the free cholesterol is converted into cholesterol ester by the action of a plasma enzyme, lecithin-cholesterol acyltransferase (*EC* 2.3.1.43; LCAT) which transfers a fatty acid from phospholipid to cholesterol (Marcel, 1982).

LDL can donate cholesterol to tissues for the vital function of membrane synthesis by two mechanisms: passive uptake by endocytosis or by a specific receptor-mediated uptake mechanism (Goldstein & Brown, 1977; Havel, 1986) in which the receptor 'recognizes' the apo-B component of the LDL and binds to it. The LDL–receptor complex is taken into the cell and the LDL is degraded by enzymes. The resulting free cholesterol interacts with intracellular membranes to inhibit cholesterol biosynthesis. Thereby, endogenous cholesterol biosynthesis is regulated by the amount available from the diet. Several defects in lipoprotein metabolism leading to abnormal blood lipid concentrations have been correlated with defects in the receptor-mediated uptake mechanism (Goldstein & Brown, 1977).

The so-called high-density lipoproteins (HDL) play a vital role as 'scavengers' for cholesterol. The cholesterol is present in plasma lipoproteins mainly as cholesterol esters. The enzyme LCAT converts the free cholesterol in HDL into cholesterol esters and the cholesterol-depleted lipoproteins thus formed interact with membranes, and pick up free cholesterol. It is then transported to the liver where it is degraded and the HDL are returned to the plasma to continue the cycle. This is a mechanism whereby the unwanted accumulation of excessive cholesterol in membranes is prevented (Marcel, 1982).

It will be clear from the foregoing that apoproteins have not only an important role in 'solubilizing' lipids in the plasma but also in providing specificity for lipoprotein interactions in cells. Several disorders in which lipid accumulates can be traced to disorders in apoproteins and recent work has shown that these may be genetically determined (Galton, 1985). Further advances in molecular genetics should make it possible to define genetic markers for coronary atheroma and other diseases involving lipid metabolism.

Fatty acid metabolism

Quantitatively the most significant components of lipids for human biochemistry and nutrition are the fatty acids, of which there are many hundreds of naturally-occurring structures. As far as we know, only two of these are absolutely essential in the human diet (linoleic acid, *cis*,*cis*-9,12-octadecadienoic, and α-linolenic acid, all-*cis*-9,12,15-octadecatrienoic); the remainder can be synthesized within the body de novo (Gurr & James, 1980).

In the normal healthy body, lipid biosynthesis is regulated in the face of changing needs and dietary intakes. Most body tissues contain enzymes for the biosynthesis of fatty acids and their esterification in triacylglycerols, phospholipids and other body fats. This is known from experiments with samples of biopsy tissue, limited tracer studies in vivo or by inference from studies in other species. When the fat content of the diet is very low, rates of fatty acid synthesis are high, particularly in the liver, to supply the needs of the body in respect of structural and storage fats. Almost all our knowledge of the details of fatty acid biosynthesis comes from animals which are normally fed on very-low-fat diets, the main products being palmitic (hexadecanoic) and oleic (*cis*-9-octadecenoic) acids. This hardly ever occurs, however, in Western man, whose diet generally contains a high proportion of energy as fat. At most times, the enzymes of fat synthesis are probably 'switched off' and the needs for both storage and structural fats are satisfied from dietary intake. 'Turnover' of lipids, however, proceeds continually in all tissues and a low level of enzymic activity may be present at all times. Fatty acid synthesis in human

adipose tissue (isolated cells or subcellular fractions) increased up to elevenfold when subjects were changed from a normal to a high-carbohydrate diet (Sjöström, 1973). Even so, fatty acid synthesis *de novo* was of little quantitative importance even under stimulated conditions. High rates of fatty acid synthesis can occur in the mammary gland during lactation. The medium-chain fatty acids, caprylic (octanoic) and capric (decanoic) acids, are produced specifically by the mammary gland and in no other tissue. They can therefore act as a 'marker' of endogenous fatty acid synthesis. When the amount of fat in the human diet is very low there is a marked elevation of the milk medium-chain fatty acids compared with the concentrations in the milk of women on a high-fat diet (Read *et al.* 1965*a*). The proportion is highest about 8 h after the main meal and falls to lower concentrations within a few hours (Read *et al.* 1965*b*).

Diet may control fatty acid synthesis in several ways: by influencing the synthesis of the enzymes of fatty acid biosynthesis or their activity, through the availability of cofactors, such as pantothenic acid and biotin, or by influencing concentrations of circulating hormones which induce or suppress the synthesis of some enzymes of lipid metabolism. The dominant role is undoubtedly played by insulin which suppresses glucose synthesis in the liver, encourages glycogen and fatty acid synthesis, stimulates the uptake of glucose into adipose tissue and inhibits the breakdown of the triacylglycerols in that tissue, but other hormones such as thyroxine, glucagon and the corticosteroids are also involved (Gurr & James, 1980).

To achieve the desired physical properties of lipids in cells, a high degree of unsaturation is required. Virtually all tissues contain enzymes (desaturases) that insert double bonds into saturated fatty acids, normally at position 9. Hence, palmitic and stearic acids, arising either from the diet or biosynthesis in the tissues, are desaturated to palmitoleic (9-hexadecenoic) and oleic (9-octadecenoic) acids respectively. Enzymes are also present that catalyse the introduction of further double bonds into unsaturated fatty acids to produce polyunsaturated fatty acids. These desaturations give rise to several families of polyunsaturated fatty acids (see Fig. 1). In the course of evolution, human beings and other animal species lost the ability to make the enzymes that catalyse the introduction of double bonds into positions 12 and 15 as present in linoleic and α-linolenic acids which are formed in plants. Yet these fatty acids and higher polyunsaturated fatty acids derived from them (Fig. 1) are essential to life; therefore they must be present in the diet.

The essentiality of linoleic acid is well documented (Söderhjelm *et al.* 1970). In an early experiment, 400 infants were given milk formulas containing different amounts of linoleic acid. When the formulas contained less than 0·1% of the dietary energy as linoleic acid, clinical and chemical signs of essential fatty acid deficiency ensued (see Fig. 1). The minimum requirements for linoleic acid were judged to be about 1% of dietary energy and this is still generally accepted as the average requirement for man, although it has been argued that additional amounts are required in pregnancy and lactation (Food and Agriculture Organization, 1978). No general consensus exists on whether there is an absolute requirement for α-linolenic acid (Zöllner, 1986). The most compelling evidence is the case of a girl who displayed neurological symptoms 4–5 months after being on total parenteral nutrition in which the fat component was a safflower oil emulsion containing mainly linoleic and only a minute amount of linolenic acid. When safflower oil was replaced by soya-bean oil containing much more linolenic acid, the neurological symptoms disappeared (Holman *et al.* 1982). More recently, Bjerve *et al.* (1987) provided evidence for α-linolenic acid deficiency in elderly patients fed by gastric tube. It seems quite certain that only very small amounts are needed in human diets (Zöllner, 1986).

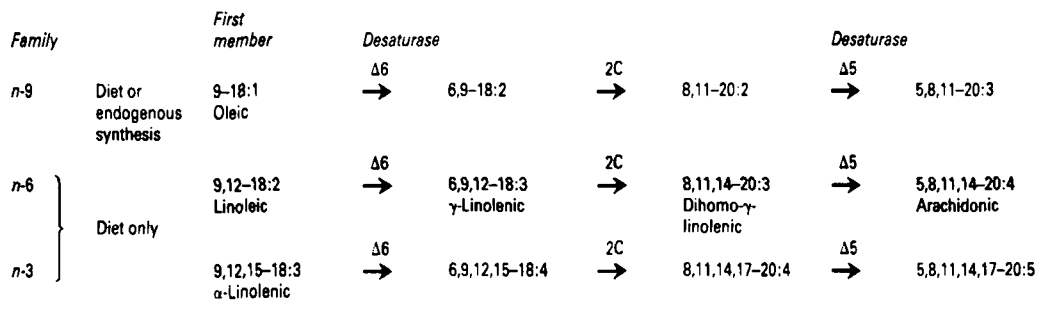

Fig. 1. Pathways for the elongation and desaturation of unsaturated fatty acids in man.

The shorthand nomenclature is as follows: the number before the colon indicates the number of carbon atoms in the fatty acid chain; the number after the colon shows the number of double bonds; the sequence of numbers before the hyphen indicates the positions of the double bonds from the carboxyl carbon which is numbered as carbon-1. All double bonds are in the *cis*-geometrical configuration. Note that desaturations and chain elongations proceed alternately and that the double bonds are always separated by a methylene (CH_2) group. Thus α-linolenic acid (all-*cis*-9, 12, 15–18:3) is:

$$\underset{15}{CH_3.CH_2.CH} = \underset{12}{CH.CH_2.CH} = \underset{9}{CH.CH_2.CH} = \underset{1}{CH(CH_2)_7COOH}$$

Fatty acids are also grouped in families named by numbering from the methyl end of the chain to the last double bond in the sequence. Thus α-linolenic acid in the above example belongs to the '*n*-3' family (sometimes written ω3) while linoleic and oleic acids belong to the *n*-6 and *n*-9 families respectively. Because human tissues do not possess the desaturases that insert double bonds in positions 12 or 15, the fatty acids of these different families cannot be interconverted and the parent acids of the *n*-3 and *n*-6 family must be obtained from the diet (essential fatty acids). Normally, sufficient linoleic acid is present in the diet for the *n*-6 pathway to be predominant. When there is little linoleic acid in the diet the *n*-9 pathway from oleic acid is the major pathway. The end-product, 5, 8, 11–20:3, accumulates. The ratio, 5, 8, 11–20:3/5, 8, 11, 14–20:4 (triene:tetraene ratio) is used as a biochemical index of essential fatty acid deficiency, values above 0·4 being taken arbitrarily as indicative of deficiency.

The essentiality of these fatty acids is thought to be due on the one hand to their specific role in the structure and function of cellular membranes and on the other to their conversion into a series of oxygenated metabolites: the eicosanoids (including prostaglandins, prostacyclins, thromboxanes and leukotrienes) so-called because their main precursors are the polyunsaturated fatty acids with chain lengths of C_{20}, the eicosenoic acids.

Although the quantitative significance of the eicosanoids in man is unknown, an enormous number of investigations has demonstrated their wide involvement in physiological and pathophysiological reactions like vascular resistance, platelet aggregation and thrombosis, wound healing, inflammation and allergy. Several studies have demonstrated that altering the amounts and types of *n*-6 and *n*-3 fatty acids (see Fig. 1) in the diet can influence the spectrum of eicosanoids produced (e.g. Horrobin *et al.* 1984). For example, substitution of fish oils in which *n*-3 polyunsaturated fatty acids predominate for diets in which linoleic acid (*n*-6) is the main polyunsaturated fatty acid (as typified by the UK diet) results in changes in plasma and platelet membrane fatty acid profiles from arachidonic to eicosapentaenoic acid as the predominant polyunsaturated fatty acid and the reduction in the formation of thromboxane A2 by platelets, an eicosanoid that stimulates their aggregation (Weber *et al.* 1986). The mechanisms by which the relative proportions of the different eicosanoids are regulated and particularly how dietary influences are mediated, the quantitative significance of the different pathways and sites

of synthesis and the quantitative relation between the requirements for essential fatty acids which are measured in g and the daily production of eicosanoids, which is measured in μg are subjects for further research.

Because the same desaturases are involved in the metabolism of the different polyunsaturated families (Fig. 1), it can be demonstrated that substrates on the different pathways compete with each other for desaturases, thus influencing the proportions between the end-products formed. This leads to a concept of 'balance' between the fatty acids in the diet. Thus if the ratios of, for example, saturated: *n*-6, *trans*-unsaturated: *n*-6, *n*-9: *n*-6 or *n*-3: *n*-6 become extreme, the balance between the end-products of essential fatty acid metabolism and by extension, the balance between different eicosanoids is upset and subtle pathophysiological processes may ensue. We are only just beginning to understand what we mean by an 'acceptable balance' or what is 'extreme'.

The conversion of polyunsaturated fatty acids into eicosanoids is an example of enzymically controlled oxidation. Uncontrolled oxidation of polyunsaturated fatty acids by free-radical chain reactions can occur in the presence of oxygen and a catalyst such as iron. The living body is protected against such uncontrolled peroxidation by two main mechanisms: (1) the organization of lipids in membrane bilayers in juxtaposition with lipid-soluble antioxidants such as vitamin E and (2) the presence of enzyme systems such as superoxide dismutase (*EC* 1.15.1.1) which destroys initiating radicals. There is growing evidence that diets deficient in natural antioxidants like vitamins C and E and environmental factors producing free radicals (e.g. smoking) can cause 'oxidative stress' which, if it overtaxes an individual's capacity to scavenge free radicals, can lead to degenerative changes over long periods (e.g. Gey, 1986).

To understand human fatty acid metabolism in more detail under practical living conditions, it is essential to develop better non-invasive methods in vivo. The most promising are those that employ stable isotopes since they involve little or no hazard and improved techniques in mass spectrometry now enable experiments to be performed more sensitively and more cheaply than a few years ago. As examples, the presence of an active Δ5-desaturase that converts dihomo-γ-linolenic acid into arachidonic acid (see (Fig. 1) in human plasma has been demonstrated using deuterium-labelled dihomo-γ-linolenic acid (El Boustani *et al.* 1986), while Emken *et al.* (1980) have compared the metabolism of *cis*- and *trans*-octadecenoic acids in human plasma using triple-labelled deuterated substrates.

Adipose tissue

Adipose tissue development begins in fetal life and the newborn baby weighing 3·5 kg has about 560 g adipose tissue. Fetal adipose tissue has to synthesize most of its fat from glucose; fat cells, therefore, possess all the pathways for lipid biosynthesis *de novo*. These enzymes are largely suppressed by the high fat intake later in life. Adipose tissue is, however, anything but an inert mass of fat and the lipids contained in it are undergoing continuous 'turnover' even when the total mass of stored fat is neither increasing or decreasing. The half-life of linoleic acid in adult adipose tissue has been estimated at between 350 and 750 d (Hirsch *et al.* 1960). The activity of lipoprotein lipase determines the rate of entry of circulating fatty acids into the fat cell and 'hormone-sensitive lipase' is responsible for hydrolysing the stored fat before export of the fatty acids into the bloodstream, where they are carried on albumin, before further metabolism in the liver or muscle. The major pathway for complete degradation of fatty acids is by mitochondrial β-oxidation in these tissues and overall rates of fatty acid degradation have been measured by the carbon dioxide expired after administering a dose of labelled fatty acid (e.g. Issekutz *et al.* 1968).

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In view of this turnover of fatty acids, it is not surprising that the composition of the fatty acids in adipose tissue triacylglycerols reflects that in the diet quite soon after a meal. This was graphically illustrated in human babies by Widdowson *et al.* (1975) as a result of a 'natural' experiment. It had become customary for Dutch mothers to feed their babies a formula in which the manufacturers had replaced cow's milk fat by vegetable oil rich in linoleic acid. The concentration of linoleic acid in the Dutch babies' adipose tissue rose steadily, reaching nearly 50% of total fatty acids in some children by 40 weeks of age, whereas in the British babies it remained at between 2 and 4%. There was even a slight difference at birth, suggesting that the Dutch mothers' diets also contained more linoleic acid than their British counterparts and that this had influenced the composition of fetal fat.

Recently there has been interest in the composition of adipose tissue in relation to mortality and morbidity from cardiovascular disease. A higher content of linoleic acid has been found in the adipose tissue of men living in Edinburgh (where cardiovascular disease incidence is relatively high) compared with those in Stockholm where it is lower, and in healthy Scottish men compared with patients prone to coronary heart disease (Wood *et al.* 1987). It is unlikely that metabolism of this fatty acid in adipose tissue is directly related to the disease but that compositional differences reflect at least one difference in habitual dietary intake between these two populations. Katan *et al.* (1986) have further developed the technique of fatty acid analysis of human adipose tissue biopsy samples as a tool in epidemiological studies to indicate fatty acid intakes of individuals since dietary estimates by dietary survey methods contain a large random error (Katan *et al.* 1986). The same authors have also used the method to assess the amount of stored *trans*-unsaturated fatty acids for which there is also a close relation between dietary intake and adipose tissue concentration (British Nutrition Foundation, 1987). This is not, however, true of all dietary fatty acids. For example, the adipose tissue concentrations of α-linolenic and arachidonic acids are always lower than would be predicted from the amounts present in the diet. This probably arises due to discrimination against certain fatty acid structures by the enzymes that incorporate fatty acids into triacylglycerols; these acids are preferentially esterified in membrane phospholipids.

Conclusion

Interest in lipid metabolism began with man but as attention turned to working out the details of biochemical pathways for lipid biosynthesis, which required subcellular fractions from internal organs, experimental animals became the predominant sources of information. Now, with the drive created by the need to understand the changes in lipid metabolism during degenerative diseases, attention has again returned to man. The development of more sensitive techniques to measure small enrichments of stable isotopes should further encourage human studies. The study of internal organs such as heart, kidney and muscle will remain a problem but in the longer term, techniques such as nuclear magnetic resonance spectroscopy may develop sufficiently to attack this problem. Adipose tissue biopsy can yield slices, isolated cells and subcellular fractions. The development of a perfused placenta preparation (Kuhn & Crawford, 1986) shows considerable promise for the study of this important and accessible tissue. Lipid metabolism is surely an exciting area to encourage bright young nutritional biochemists to enter.

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