BRIEFING PAPER

The health effects of dietary unsaturated fatty acids

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Summary

Fat provides energy; indeed it is the most energy dense of all the macronutrients, with 1 g providing 37 kJ (9 kcal). However, the constituent parts of fat, fatty acids, are required by the body for many other functions than simply as an energy source, and there is an increasing awareness of the potential health benefits of specific types of fatty acids. Fatty acids are long hydrocarbon chains, with a methyl group at one end (the omega or *n*-end) and an acid group at the other. Unsaturated fatty acids are hydrocarbon chains containing at least one carbon–carbon double bond; monounsaturated fatty acids contain one double bond, and polyunsaturated fatty acids (PUFAs) contain many double bonds. The position of the double bond relative to the omega end determines whether a PUFA is an *n*-3 (omega 3) or an *n*-6 (omega 6) fatty acid.

Most fatty acids can be synthesised in the body, but humans lack the enzymes required to produce two fatty acids. These are called the essential fatty acids and must be acquired from the diet. In humans, the essential fatty acids are the *n*-3 PUFA α-linolenic acid and the *n*-6 PUFA linoleic acid. Although humans can elongate dietary α-linolenic acid to the long chain *n*-3 PUFAs eicosapentaenoic acid and docosahexaenoic acid, the rate of synthesis may not be sufficient to meet requirements, and it is, therefore, recommended that good sources of these fatty acids, namely, oil-rich fish, are also included in the diet.

Fat is found in most food groups, and foods containing fat generally provide a range of different fatty acids, both saturated and unsaturated. In the UK, the major dietary sources of unsaturated fatty acids include meat & meat products, cereals & cereal products and potatoes & savoury snacks; primarily as a result of the vegetable oil used in processing. Recommended intakes of both total fat and the different types of fatty acids have been set for the UK population, and it is possible to monitor fat intake from the data collected in nationwide dietary surveys. As a population, we are not currently meeting these recommendations, so there is still scope for dietary change. In Western diets, *n*-6 fatty acids are the predominant PUFAs, and this is in line with current dietary advice to consume a minimum of 1% energy as *n*-6 PUFAs and 0.2% energy as *n*-3 PUFAs. The balance of *n*-3 and *n*-6 PUFAs in Western diets has changed substantially over the last 100 years or so, and as the two families of PUFAs share a common metabolic pathway, concerns have been raised that this might be detrimental to health; what is becoming increasingly clear is that both *n*-3 and *n*-6 PUFAs have independent health effects in the body, and as intakes of the *n*-6 PUFAs are within the guidelines for a healthy diet, concerns about the *n*-6 to *n*-3 ratio are driven by low intakes of *n*-3 rather than high intakes of *n*-6. Currently in adults *n*-6 PUFAs contribute to 5.3% energy.

Detecting associations between components of the diet and risk of various diseases is notoriously complex and in many cases, the evidence is still accumulating. Cardiovascular disease, characterised by hardening and narrowing of blood vessels and/or the development of blood clots, is one of the leading causes of mortality and morbidity worldwide. The type and total amount of dietary fat has a clear part to play in affecting an individual's disease risk, yet the precise mechanisms by which unsaturated fatty acids reduce cardiovascular disease risk are still unclear. A number of mechanisms whereby dietary fatty acids could influence the progression of

cardiovascular disease and its risk factors have been identified. These include effects on blood lipid concentrations, blood pressure, inflammatory response, arrhythmia and endothelial function, along with many other effects, both known and as yet undefined. A well-established risk factor for cardiovascular disease is an elevated plasma low density lipoprotein (LDL) cholesterol concentration. Replacing saturated fatty acids with either monounsaturated fatty acids or *n*-6 PUFAs reduces LDL (the 'bad') cholesterol, and so reduces the risk of developing the disease. Unsaturated fatty acids, such as linoleic acid or monounsaturated fatty acids, also slightly raise high density lipoprotein (HDL) (the 'good') cholesterol, which assists in the removal of triacylglycerols from the bloodstream. Interest in the health effects of the long chain *n*-3 PUFAs found in fish oils is also increasing. There is strong supportive, but not yet conclusive, evidence that these fatty acids protect against fatal heart disease. On the basis of this conclusion, in 2004 the Scientific Advisory Committee on Nutrition advised the UK government to adopt the population-wide dietary recommendation to eat at least two portions of fish per week, of which one should be oil-rich, equivalent to 0.45 g of the long chain *n*-3 PUFAs per day. In recent years, the potential health benefits of α-linolenic acid has attracted attention, and evidence is mounting on the role that this *n*-3 fatty acid may play in preventing the progression of cardiovascular disease, although it is currently unclear what, if any, association exists.

Brain cells are especially rich in certain long chain PUFAs. This has led to the suggestion that dietary status of these long chain fatty acids might influence cognitive function and behaviour. Research in this field is still in its early stages, but there is a small amount of evidence to suggest improvements in cognitive function following fatty acid supplementation. In contrast, it is well established that pregnant women must have an adequate supply of the long chain *n*-3 PUFAs before and throughout pregnancy and lactation to support normal growth, neurological development and cognitive function of the baby. As *n*-6 PUFAs are more abundant in the diet, achieving an adequate intake is less problematic. However, this is not the case for the *n*-3 PUFAs; increasing fish consumption beyond two servings of oil-rich fish per week or relying on fish oil supplementation is not appropriate during pregnancy due to the potential problems associated with heavy metal contamination of fish, or the high vitamin A level in some fish oil supplements.

Unsaturated fatty acids have also been associated with a number of other diseases and although the evidence is by no means conclusive, it is an area that is attracting a huge amount of interest. Dietary fat affects a number of different metabolic pathways, including those involved with glycaemic control, so the types and amounts of dietary fat may have a role to play in the management of type 2 diabetes. Unsaturated fatty acids may also be associated with a reduced risk of developing certain cancers, including cancers of the colon, breast and prostate, although currently the level of evidence is not deemed sufficient by authoritative bodies, such as the World Cancer Research Fund, World Health Organization and the Department of Health, to make any specific dietary recommendations. There are a number of inflammatory conditions, such as asthma, Crohn's disease and arthritis, which could potentially be alleviated by dietary modification. The fatty acid composition of cell membranes can be altered by consumption of both *n*-3 and *n*-6 PUFAs, and this can result in

reduced inflammatory activity. However, whether this effect brings about a significant reduction in clinical symptoms is still unclear. It is also important to note that there are concerns that the beneficial effects on certain disease outcomes are only observed with very high intakes of unsaturated fatty acids, which could realistically only be achievable by supplementation. Few nutritionists would be comfortable recommending supplement use as the only alternative to fish, as this can be expensive and goes against the idea that all the nutrients that our bodies require can be obtained from the food that we eat if the right choices are made.

Unsaturated fatty acids are now a nutritional hot topic, and their presence in foods has attracted both public and industrial interest. There is currently no specific legislation to control the use of health claims relating to the fatty acid content of foods. However, a European Union (EU) Directive is expected imminently which will formally set down the criteria that a product will have to meet in order to make any nutrition or health claim. With regards to the current recommendations, those for the UK are in line with those around the world. However, as a population, we need to increase our consumption of long chain *n*-3 PUFAs and decrease intake of saturated fatty acids. To facilitate this, food technologists are looking at ways in which the fatty acid profile of a food can be modified in order to bring dietary improvements without requiring a major change in dietary habits. However, public health messages surrounding the optimum intakes of fatty acids must be clear and consistent to ensure that a favourable change in the fatty acid profile of the UK diet occurs.

Keywords: cardiovascular disease, cognitive function, dietary recommendations, infant development, oil-rich fish, unsaturated fatty acids

1. Introduction

Fat is perceived to be the 'baddie' of all the nutrients, linked to obesity, cardiovascular disease (CVD) and cancer. However, being the most energy dense of the macronutrients, it does play an important part in ensuring that we meet our daily energy requirements and enables the absorption of fat-soluble vitamins and carotenoids. Additionally, there is mounting appreciation by health professionals, nutrition scientists and the general public of the ever-increasing number of health benefits that have been associated with different types of dietary fats.

This Briefing Paper was written to consolidate the wealth of new evidence surrounding the health effects of both mono- and polyunsaturated fatty acids into one resource. This paper complements the Task Force Report on CVD (Stanner 2005), and updates the unsaturated fatty acids Task Force Report (BNF 1992) and the *n*-3 fatty acid Briefing Paper (BNF 1999), all published by the British Nutrition Foundation (BNF).

In the early stages of compiling this Briefing Paper, it was decided not to focus on the *trans*-unsaturated fatty acids, instead basing the report on the *cis*-unsaturated fatty acids. *Trans*-fatty acids are treated very differently by the body, and their effects are more akin to the mainly atherogenic saturated fatty acids than the *cis*-forms of the unsaturated fatty acids. The consensus view of the UK Food Standards Agency is that they are harmful to health and display no known nutritional benefits. The BNF published a Task Force Report on *trans*-fatty acids in 1995, and many of the conclusions of this report are still relevant today (see BNF 1995). Indeed, over the past decade, population intakes of *trans*-fatty acids have fallen and are now well below the recommended 2% of total energy set by the Department of Health in 1991 (DH 1991). This is not to say that intakes of *trans*-fatty acids are not still a problem, and

dietary advice states that those individuals who are in the top end of the distribution of intake should still make efforts to reduce their intakes. In BNF's most recent Task Force report on CVD, the effects of *trans*-fatty acids were considered, and they were declared to be as bad, if not worse, for heart health as saturated fatty acids (Stanner 2005). Where appropriate, consideration of *trans*-fatty acid intakes and recommendations have been made in this report, but their specific health effects have not been included.

This Briefing Paper is in four parts; the first two sections briefly describes the chemistry, digestion, absorption and metabolism of fatty acids (*What are unsaturated fatty acids?*) before giving a detailed update on dietary sources and current levels of intake (*Unsaturated fatty acids in the UK diet*). This section has a UK focus. The Briefing Paper then describes new research on the role of unsaturated fatty acids, as part of a healthy balanced diet, in the context of CVD, diabetes, cancer, inflammatory conditions, fetal development and cognitive function (*Unsaturated fatty acids in health and disease*). The Paper concludes by discussing issues regarding labelling and opportunities to increase intake of unsaturated fatty acids in the diet (*Unsaturated fatty acids and public health*).

2. What are unsaturated fatty acids?

2.1 The chemistry of fatty acids

Fatty acids are the building blocks from which fats (lipids) are made. Fatty acids found in foods and fats stored in the body are mainly present in the form of triacylglycerols (TAGs), a glycerol molecule backbone to which three, often different, fatty acids are attached (Fig. 1). Fatty acids can be present at any of three positions on the glycerol molecule (termed *sn*-1; *sn*-2 and *sn*-3). The presence of different fatty acids at different positions on the glycerol molecule will also influence its characteristics (*i.e.* melting point and digestibility).

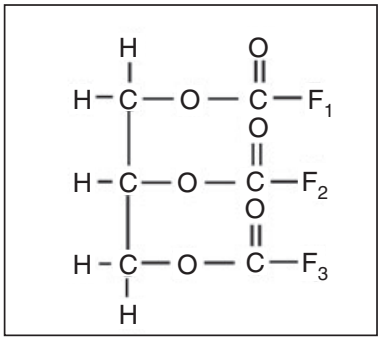


Figure 1 The structure of triacylglycerol. The fatty acids in the *sn*-1, *sn*-2 and *sn*-3 positions (F_1, F_2 and F_3) will, most likely, be different.

Fatty acids are made up of a backbone of carbon atoms, with a methyl group (CH_3) at one end [the omega (ω) or *n*-end] and a carboxyl group (COOH) at the other [the delta (Δ) end; see Fig. 2]. Hydrogen atoms are joined to the string of carbon atoms, forming a hydrocarbon chain.

Fatty acids vary in length from 2 to 80 carbons, but are typically present in food as 14, 16, 18, 20 and 22 carbon atom chains. Short chain fatty acids, such as butyric acid (4 carbon atoms) or propionic acid (3 carbon atoms) are formed in the gut when polysaccharides are fermented by the anaerobic bacteria present in the large intestine. Certain short chain fatty acids, namely, butyrate, are believed to be important for gut health (Bird *et al.* 2000). Technically, the long chain fatty acids contain 12 or more carbon atoms. However, this term is often used to describe the longer chain fatty acids that contain more than 20 carbon atoms, which may also be referred to as very long chain fatty acids. From this point on, this Briefing Paper will use the term 'long chain' to describe fatty acids with more than 20 carbon atoms.

Carbon chain length influences the characteristics of a fatty acid, as does the presence or absence of double bonds between carbon atoms.

- If all of the carbons in the fatty acid chain are linked by single bonds (*i.e.* the fatty acid contains all the hydrogen atoms that it can hold), the fatty acid is said to be a saturated fatty acid (SFA).
- If one or more double bonds are present in the fatty acid chain (*i.e.* the fatty acid does not hold its potential full complement of hydrogen atoms), the fatty acid is considered to be an unsaturated fatty acid.
  - If there is only one double bond present in an unsaturated fatty acid, it is said to be a monounsaturated fatty acid (MUFA).
  - If there is more than one double bond present, the fatty acid is said to be a polyunsaturated fatty acid (PUFA).

Double bonds in unsaturated fatty acids can be arranged in one of two ways; *cis*- or *trans*- configurations (see Fig. 3). Double bonds in foods are predominantly found in foods in the *cis*- form, where both hydrogen atoms are found on the same side of the fatty acid. The presence of a *cis*- bond in a fatty acid lowers the melting point of the fatty acid, making it more likely to be liquid at room temperature. *Trans*-fatty acids, where the hydrogen atoms are situated on opposite sides of the fatty acid, are less common in nature, but are typ-

ically found in small amounts in the fat of ruminant meats and in milk being formed in the rumen (part of the gastrointestinal tract) during digestion and subsequently absorbed as an energy source for the animal. These fatty acids can also be produced during the hydrogenation (hardening) of unsaturated oils as was traditionally used in margarine manufacture. The major unsaturated fatty acids present in the diet are shown in Table 1.

PUFAs can be further classified as either *n*-3 (omega 3) or *n*-6 (omega 6) PUFAs; to which family a PUFA belongs depends on the position of the first double bond in the fatty acid chain. All members of the *n*-6 family of fatty acids contain their first double bond between the sixth and seventh carbon atoms from the terminal methyl group, while all members of the *n*-3 family of fatty acids have their first double bond between the third and fourth carbon atoms (see Fig. 4).

2.2 Digestion, absorption and metabolism

Fat enhances the flavour and palatability of foods, and has been shown to slow the rate at which the stomach contents are emptied into the small intestine. As a result, fat leads to general feelings of satiety and satisfaction after a meal that are often difficult to mimic in reduced

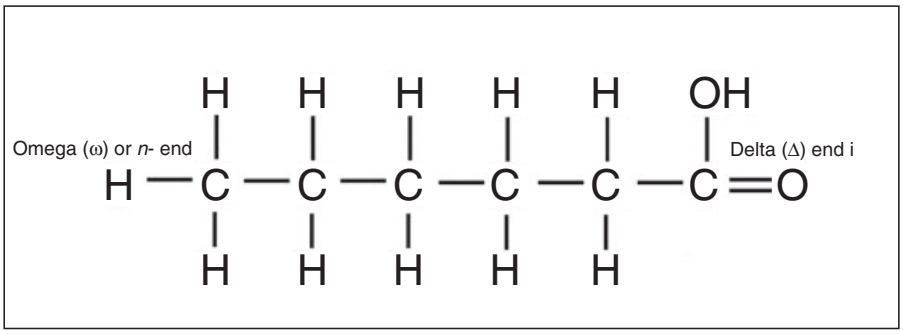


Figure 2 Structure of a fatty acid.

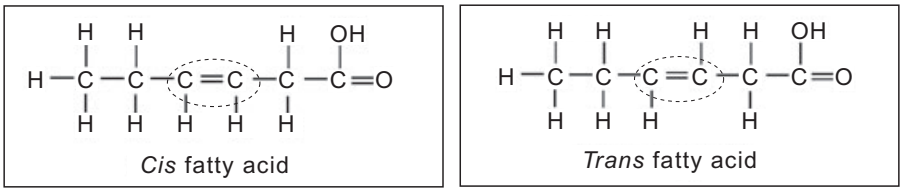


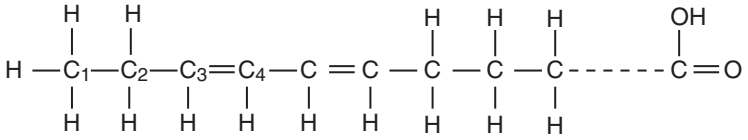
Figure 3 *cis*- and *trans*-configurations.

Table 1 Main unsaturated fatty acids present in food

Trivial name	Systematic name	Rich dietary sources
Monounsaturated fatty acids		
Palmitoleic (16:1*n*-7)	*cis*-9-hexadecenoic	Fish oil
Oleic (18:1*n*-9)	*cis*-9-octadecenoic	Olive oil, rapeseed oil, palm oil
Elaidic (18:1*n*-9 *trans*)	*trans*-9-octadecenoic	Partially hydrogenated fat
Trans-vaccenic (18:1*n*-7 *trans*)	*trans*-11-octadecenoic	Ruminant fats
Cis-vaccenic (18:1*n*-7)	*cis*-11-octadecenoic	Ruminant fats
Erucic (22:1*n*-9)	*cis*-13-docosenoic	Mustard seed oil
Polyunsaturated fatty acids		
Linoleic (18:2*n*-6)	9,12-octadecadienoic	Safflower oil, sunflower oil, corn oil
Gamma (γ)-linolenic (18:3*n*-6)	6,9,12-octadecatrienoic	Evening primrose oil
Arachidonic (20:4*n*-6)	5,9,11,14-eicosatrienoic	Ruminant meats (low levels)
Alpha (α)-linolenic (18:3*n*-3)	9,12,15-octadecatrienoic	Flaxseed oil, linseed oil, walnut oil
Eicosapentaenoic (20:5*n*-3)	5, 8,11,14,17-eicosapentaenoic	Fish oil, oil-rich fish
Docosahexaenoic (22:6*n*-3)	4,7,10,13,16,19-docosahexaenoic	Fish oil, oil-rich fish

Source: Sanders & Emery (2003).

1 *n*-3 PUFA



2 *n*-6 PUFA

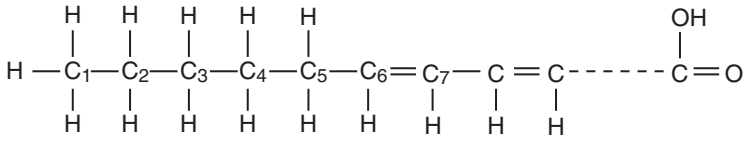


Figure 4 *n*-3 and *n*-6 fatty acids. PUFA, polyunsaturated fatty acid.

fat products. In order to be efficiently digested and absorbed, dietary fat must first be emulsified by bile secreted into the small intestine from the gallbladder. The fat droplets form small micelles that are dispersible in water and so can be acted on by pancreatic lipases cleaving the fatty acids at the *sn-1* and *sn-3* positions of the TAGs. The end-products from the digestion of fat: free fatty acids, a 2-monoacylglycerol, and very limited amounts of glycerol, are absorbed by diffusion across the gut wall into the cells of the intestine. Recently, work by Stremmel *et al*. (2001) has introduced the idea that fatty acids may be absorbed by carrier-mediated processes, involving transport proteins in the membranes of cells lining the small intestine. However, the importance of this route has been questioned, as the candidate transporter proteins are also found in other cells in the body where they have little to do with fatty acid transport (Tso *et al*. 2004). Regardless of this, the digestion of fat is very efficient, with typically more than 95% of dietary fat being broken down and absorbed (Sanders & Emery 2003).

The mode of transport away from the gut is dependent on chain length; the short to medium chain fatty acids (2–12 carbon atoms) are transported bound to the carrier protein albumin *via* the hepatic portal vein to the liver. However, dietary fat mainly consists of the longer chain fatty acids (>12 carbon atoms), which are reassembled in the intestinal cell into TAG. These are then packaged into lipoprotein particles known as chylomicrons and are transported *via* the lymph system into the peripheral circulation. The rate of lipolysis (breakdown of fat), absorption of fatty acids and transport might be influenced by the degree of unsaturation (see BNF 1992 for more details). However, the nutritional significance of this difference is unclear. The fatty acid at *sn*-2 may influence subsequent metabolism of chylomicrons and ultimately low density lipoprotein (LDL) cholesterol response. It has been suggested that dietary fats containing a predominance of *sn*-2 unsaturated triglycerides might be absorbed more slowly, and cleared more rapidly from the circulation compared with saturated fatty acids, resulting in reduced concentrations of TAGs in the blood after a meal (Yli-Jokipii *et al*. 2001). Conversely, SFAs in the *sn*-2 position are preferentially absorbed into the cells lining the intestines over SFAs at positions *sn*-1 and *sn*-2, which also has implications for the balance of TAGs in the blood after a meal (see Berry & Sanders 2005). It remains controversial as to the relevance of these findings to adults, as most of the work has been conducted in animals, and any work that has been carried out in humans has been conducted in infants (in the context of infant formula composition).

Once in the bloodstream, chylomicrons acquire apolipoprotein C (apoC) from high density lipoproteins (HDL). At the target cell (*e.g.* muscle), the apoC subunit activates the enzyme lipoprotein lipase, which is located within the endothelial cell membrane. This results in cleavage of the fatty acids, which are then transported into tissues for storage or metabolism.

Fatty acids undergo β-oxidation in mitochondria to release energy. The exact energy yield of the different fats is dependent on the chain length and the number of double bonds in the molecule, although 1 g of fat is assumed to release 37 kJ (9 kcal).

Most unsaturated fatty acids can be synthesised in the body following a series of fatty acid chain elongation and desaturation steps. This process is catalysed by the enzyme complex, fatty acid synthase. Plants contain desaturases capable of inserting double bonds at positions 3, 6 and 9 from the terminal methyl group. Animal and human desaturases are only capable of inserting double bonds at specific positions beyond carbon 6. Therefore, there are several fatty acids, termed essential fatty acids (EFA), which cannot be made in the body but are required for normal physiological function in humans. There are two specific EFAs: the *cis n*-6 PUFA linoleic acid (LA; 18:2*n*-6) and *cis n*-3 PUFA alpha (α)-linolenic

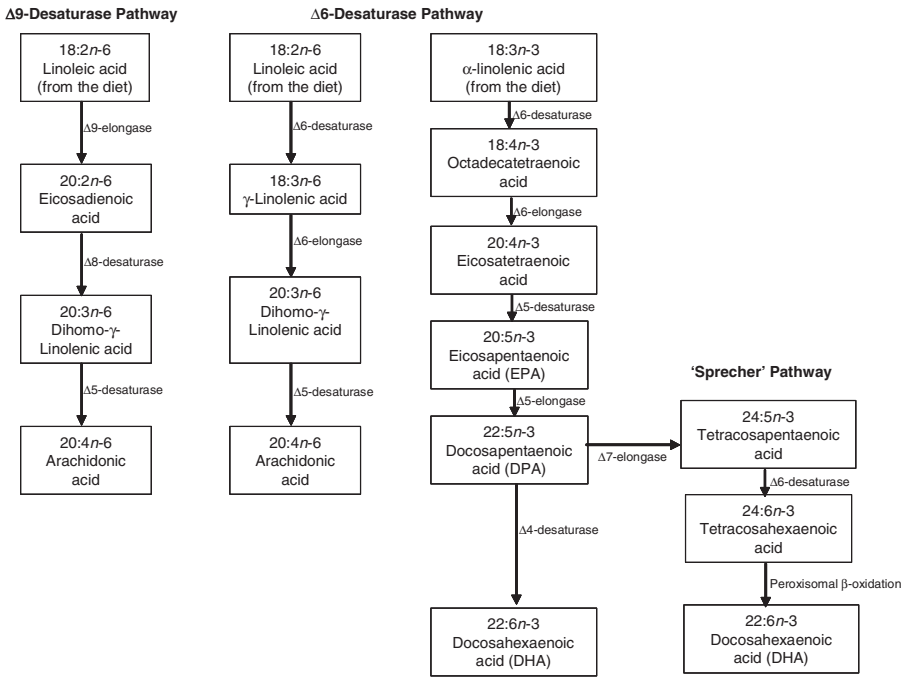


Figure 5 Metabolism of essential fatty acids (adapted from Napier & Sayanova 2005).

acid (ALNA; 18:3*n*-3). It is from these two 'parent' EFAs that the *n*-3 and *n*-6 fatty acid 'families' are derived through a series of enzyme catalysed desaturation and elongation reactions, that generally take place in the cell cytosol or in the mitochondria (see Fig. 5).

ALNA is metabolised to docosahexaenoic acid (DHA; 22:6*n*-3) *via* eicosapentaenoic acid (EPA; 20:5*n*-3) and docosapentaenoic acid (DPA; 22:5*n*-3), whereas LA is metabolised to arachidonic acid (AA; 20:4*n*-6) *via* gamma (γ)-linolenic acid (GLA; 18:3*n*-6) or eicosadienoic acid (20:2*n*-6) as two pathways are active. However, conversion is not 100% efficient. Desaturation of DPA at the Δ-4 position to produce DHA does not only occur by a single step catalysed by Δ-4 desaturase. There is an additional pathway, the 'Sprecher Pathway', which involves elongation and desaturation of DPA and tetracosahexenoic acid in microsomes followed by a chain-shortening step to DHA in peroxisomes (Sprecher 2000).

It has been estimated that less than 8% of ALNA is metabolised to EPA, and the capacity for the body to synthesise DHA appears to be particularly limited. It is estimated that only between 0.02% and 4% of ALNA is metabolised to DHA (Vermunt *et al*. 2000; Pawlosky *et al*. 2001; Burdge *et al*. 2002), with women having a greater capacity for DHA synthesis than men (Burdge & Wootton 2002). Feedback inhibition of enzymes involved in *n*-3 and *n*-6 fatty acid synthesis occurs; for example, if the amount of DHA in the diet increases, there is reduced metabolism of ALNA to EPA. Furthermore, *n*-3 and *n*-6 fatty acids compete for the enzymes involved in fatty acid elongation and desaturation, with certain enzymes having greater affinity for *n*-3 fatty acids and others having greater affinity for the *n*-6 series (see BNF 1999).

The metabolites of the EFAs have many different functions. DHA and AA are major constituents of membrane phospholipids, especially in the retina, brain (predominantly as DHA) and platelets (predominantly as AA). As the capacity to synthesise EPA and DHA from the EFA ALNA is very limited, dietary sources make a major contribution to the amount of both these *cis n*-3 PUFAs in the body (Burdge & Calder 2005a).

The 20 carbon metabolites of EFAs (EPA and AA) function as the basis for important regulatory signals known as eicosanoids. There are several different families of eicosanoids: the prostaglandins (which regulate muscle contraction, immune response and inflammation), prostacyclins (which inhibit platelet aggregation) and thromboxanes (which bring about platelet aggregation) are all formed by the action of cyclo-oxygenase enzymes; the leukotrienes (which affect microvascular and bronchial constriction or dilatation) and hydroxy-fatty acids (which regulate cell adhesion) are formed by the action of lipoxygenases. Eicosanoids are produced by cells to act in their immediate environment in response to extracellular stimuli, *e.g.* blood vessel dam-

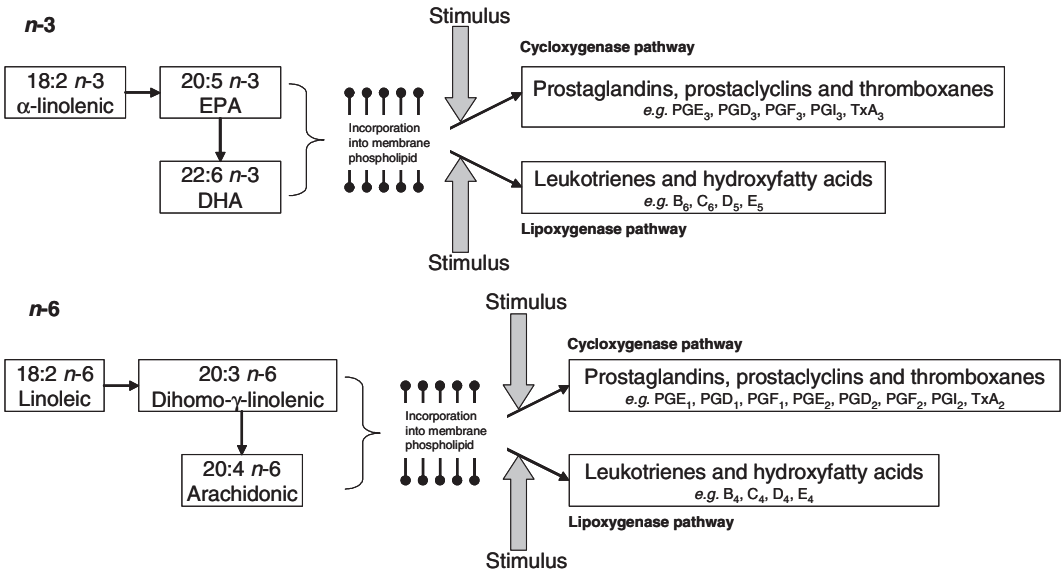


Figure 6 Mechanism of eicosanoid formation (adapted from Sanders & Emery 2003). DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PG, prostaglandin; Tx, thromboxane.

age. Eicosanoid formation from the two EFA families follows slightly different pathways (Fig. 6). However, they share a common set of enzymes, so the ratio of *n*-3 to *n*-6 PUFAs in the diet will affect which pathway is the most active. The activity of the different eicosanoids produced from EFAs varies; eicosanoids derived from the *cis n*-6 PUFAs typically exert stronger effects than those derived from *n*-3. Thus the diet has a role to play in determining the final mix and potency of eicosanoids.

2.3 Functions of unsaturated fatty acids

The major roles of lipids in the body are: to store energy, to provide energy, and to provide stable cellular membranes. Energy is stored in the body as TAGs in adipose tissue. Adipose tissue mainly consists of SFAs and MUFAs, although to some extent this is dependent on an individual's diet (see BNF 1992 for further details). The hormone insulin ensures that fatty acids in circulating lipoproteins are liberated and transported into adipose tissue by activating the enzyme lipoprotein lipase. Insulin is produced in response to glucose entering the blood from the gut, so concentrations are high after a meal. When the concentration of insulin in the blood drops (*i.e.* during fasting), hormone-sensitive lipase is activated and fatty acids are mobilised to meet energy demands. The free fatty acids are carried in the bloodstream bound to albumin to where they are needed in the tissue cells and are broken down in mitochondria by β-oxidation.

Unsaturated fatty acids are found in membranes as esterified phosphoglycerides (also known as phospholipids). The degree of unsaturation introduces 'kinks'

Key points:

What are unsaturated fatty acids?

- Fatty acids are the building blocks from which lipids are made. Fatty acids are found in foods and are stored in the body mainly in the form of triacylglycerols (a molecule of glycerol combined with three fatty acid chains).
- Unsaturated fatty acids are hydrocarbon chains containing at least one carbon–carbon double bond.
- Most fatty acids can be synthesised in the body. Those that cannot are termed EFAs and must be acquired from the diet. In humans, the EFAs are the *n*-3 (omega 3) PUFA α-linolenic acid (ALNA) and the *n*-6 (omega 6) PUFA linoleic acid (LA).
- Oxidised metabolites of fatty acids are called eicosanoids. These compounds act as regulatory signals in the body and can bring about inflammatory effects.
- Fatty acids are used in the body as a means of energy storage, to provide energy, and to provide stable cellular membranes.

into the hydrocarbon chain and affects the ability of the phosphoglycerides to pack together. However, chains containing multiple double bonds pack together better than chains containing few double bonds, as the chains adopt a helical configuration. Thus, membranes containing high proportions of the long chain PUFAs are the most stable, *i.e.* they are the most permeable to water, ensuring efficient intracellular metabolism. (For further details on the structural role of unsaturated fatty acids, see BNF 1992.)

3. Unsaturated fatty acids in the UK diet

3.1 Sources of fat in the diet

Fat is found in most food groups, and foods containing fat generally provide a range of different fatty acids, both saturated and unsaturated. Table 2 outlines the unsaturated fatty acid content of a range of different foodstuffs that are commonly consumed in the British diet. Further details about the contribution that these, and other, foods make to total fat intake are included in a following section (*Major contributors to unsaturated fatty acid intake*).

Table 2 Fat in the diet (g fat/100 g food)

	Total fat g/100 g	MUFA g/100 g	*cis*-PUFA g/100 g	
			n-3	*n*-6
Cod liver oil	99.9	44.60	24.40	3.50
Olive oil	99.9	73.00	0.70	7.50
Vegetable oil (blended)	99.9	53.20	6.50	23.26
Margarine	84.4	19.92	1.29	8.33
Butter	82.2	18.48	1.41	2.27
Polyunsaturated spread	68.5	15.12	0.16	33.40
Peanuts	46.0	22.03	0.35	12.75
Cheese (cheddar)	32.7	7.14	0.99	0.77
Chocolate (milk)	30.7	9.45	0.09	1.02
Biscuits (digestives)	20.3	7.37	0.09	1.86
Avocados	19.3	14.50	0.07	1.16
Cream (single)	19.1	4.54	0.11	0.49
Cakes (sponge)	16.7	5.51	0.31	0.81
Eggs	11.2	4.31	0.08	1.61
Chips	11.0	2.69	0.01	0.16
Lamb (raw, lean)	8.0	2.58	0.16	0.28
Oil-rich fish, *e.g.* salmon	7.8	3.23	1.85	0.27
Beef (raw, lean)	4.3	1.76	0.07	0.17
Pork (raw, lean)	4.0	1.50	0.09	0.61
Whole milk	4.0	0.93	0.02	0.10
Chicken (white meat)	3.7	1.58	0.13	0.60
Yogurt (whole milk)	3.0	0.71	0.05	0.07
White bread	1.9	0.25	0.04	0.62
Semi-skimmed milk	1.7	0.39	0.01	0.05
White fish, *e.g.* cod	0.7	0.08	0.26	0.02

Source: FSA (2002).
MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.

Unsaturated fatty acids in meat: The fatty acid composition of meat is dependent on whether or not the species is a ruminant. In ruminant animals (*e.g.* cows), the majority (>90%) of the dietary unsaturated fatty acids are hydrogenated to SFAs in the rumen during digestion. Hence, beef traditionally contains a higher proportion of SFAs compared with some other meats. Non-ruminant meat, *e.g.* pork, contains proportionally more unsaturated fatty acids, but its composition is still dependent on the fatty acid profile of the animal feed (Table 3). MUFAs also contribute a considerable proportion of the fat content of meat (approximately 25%).

In recent years, animal husbandry techniques have been modified to produce meat with a more favourable fatty acid profile. Initially, the aim was to reduce the SFA content, but now scientists are developing feeds that will increase the concentrations of the long chain *n*-3 PUFAs in meat and ultimately enhance human health (see Nugent 2005 and *Unsaturated fatty acids and public health*).

Unsaturated fatty acids in milk: The lipids in milk and other dairy products are mostly short and medium chain SFAs and MUFAs (Table 4). Milk contains relatively low concentrations of PUFAs. As with meat, work is ongoing to improve the fatty acid profile of milk, and there is particular interest in enhancing the concentration of the long chain *n*-3 PUFAs (see *Unsaturated fatty acids and public health*).

Unsaturated fatty acids in fish: The flesh of white fish and seafood typically contain very low amounts of fat (1–2%; Table 5). The fat that is present tends to be long chain *n*-3 PUFAs. The flesh of oil-rich or fatty fish is a richer source of fatty acids than white fish (5–20% depending on the breeding cycle). Oil-rich fish include sardines, salmon, pilchards, mackerel, herring and trout, whether canned, fresh or frozen. However, although fresh tuna is considered to be an oil-rich fish, during the canning process the fat content of the fish is substantially reduced, so canned tuna is not included in the oil-rich fish group. Examples of white fish are cod, haddock, turbot, bream and sea bass.

Like humans, fish are not capable of synthesising long chain *n*-3 PUFAs. However, fish either feed on micro-organisms (such as algae) or on smaller fish that have eaten these PUFA-synthesising micro-organisms themselves, thereby acquiring long chain *n*-3 PUFAs *via* the diet. The fish that store their fat in their flesh thus pro-

Table 3 The unsaturated fatty acid composition of lean, raw meat (g fatty acids/100 g meat)

		MUFA (g/100 g)			PUFA (g/100 g)				
	Total fat (g/100 g)	14:1	16:1	18:1 Oleic	18:2 LA	18:3 ALNA	20:4 AA	20:5 EPA	22:6 DHA
Beef	4.3	0.02	0.15	1.54	0.11	0.03	0.02	0.01	0
Lamb	8.0	0.01	0.13	2.37	0.13	0.09	0.02	0.02	0.01
Pork	4.0	0	0.09	1.36	0.54	0.05	0.04	0.01	0.01
Chicken	3.7	0	0.04	0.42	0.16	0.02	0.01	tr	0.01

Source: MAFF (1998).
AA, arachidonic acid; ALNA, α-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; LA, linoleic acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; tr, trace.

Table 4 The unsaturated fatty acid composition of cow's milk (g fatty acids/100 g milk)

		MUFA (g/100 g)			PUFA (g/100 g)				
	Total fat (g/100 g)	14:1	16:1	18:1 Oleic	18:2 LA	18:3 ALNA	20:4 AA	20:5 EPA	22:6 DHA
Whole milk	4.0	0.04	0.07	0.80	0.07	0.02	0	0	0
Semi-skimmed	1.7	0.02	0	0.34	0.03	0.01	0	0	0
Skimmed	0.3	0	tr	0.06	0.01	tr	0	0	0

Source: MAFF (1998).
AA, arachidonic acid; ALNA, α-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; LA, linoleic acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.

Table 5 The unsaturated fatty acid composition of raw, fresh fish (g fatty acids/100 g fish)

		MUFA (g/100 g)			PUFA (g/100 g)				
	Total fat (g/100 g)	14:1	16:1	18:1 Oleic	18:2 LA	18:3 ALNA	20:4 AA	20:5 EPA	22:6 DHA
Cod	0.7	0	0.01	0.05	tr	tr	0.02	0.08	0.06
Herring	13.2	0.01	1.06	1.50	0.29	0.18	0.04	0.51	0.69
Salmon	6.3	n/a	0.25	1.35	0.17	0.30	0.27	0.32	1.12
Mackerel	16.1	0	0.59	1.91	0.30	0.22	0.07	0.71	1.10

Source: MAFF (1998).
AA, arachidonic acid; ALNA, α-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; LA, linoleic acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.

vide a source of long chain *n*-3 PUFAs when they are eaten. Salmon is the most popular oil-rich fish in the UK. To provide salmon in sufficient quantities to meet public demand, increasing amounts of the salmon available in supermarkets are obtained from fish farms rather than caught from wild fish stocks. Farmed fish do not have the same direct access to a ready supply of the *n*-3 PUFA-synthesising algae and smaller fish as wild fish do. Therefore, they must be provided with fish oils rich in long chain *n*-3 PUFAs as part of their diet. In the opinion of the European Food Safety Authority (EFSA), there are no consistent differences between wild and farmed fish in terms of either safety or nutritional value (Question N° EFSA-Q-2004-22; Opinion adopted on 22 June 2005). Species, season, location, diet, lifestage and age of the fish all have a major impact on both the

nutrient and contaminant levels. However, these levels vary broadly within species and between species in both wild and farmed fish.

Unsaturated fatty acids in eggs: Egg yolk is approximately 30% fat. The fatty acids present are predominantly SFAs and MUFAs (including oleic acid – 4 g/100 g). There are few PUFAs in conventionally produced eggs.

Unsaturated fatty acids in plants: Plant cell membranes contain some fat, mainly as palmitic, palmitoleic, oleic, linoleic and α-linolenic acids, although the exact amounts are very small (typically less than 1 g per 100 g). Green vegetables account for much of the intake of ALNA in the human diet.

Unsaturated fatty acids in fats and oils: Fats and oils are differentiated by their physical characteristics; fats being solid at room temperature and oils liquid. Fatty acids are mainly present as TAGs (see *What are unsaturated fatty acids?*) although, over time, some hydrolysis does occur and small amounts of free fatty acids are present. This is undesirable as even low concentrations of free fatty acids result in unacceptable flavours and eventually lead to rancidity. Animal fats, such as lard, suet and butter, typically contain a greater proportion of the SFAs. The fish oils, including cod liver oil, are rich sources of the long chain *n*-3 PUFAs; whereas oil-rich fish store fat in their flesh, the white fish store fat in their liver.

Plants store much of their own energy as oil in their seeds. The fatty acid composition of the seed oils varies widely (Table 6). Typically, one fatty acid will dominate. Margarine was traditionally produced by the hydrogenation of vegetable oils, often the mainly unsaturated sunflower and rapeseed oils. However, different methods of production are now used, and the fatty acid composition of margarines and fat spreads can vary considerably. Spreads have a similar composition to margarine but are usually lower in fat, there being a spectrum of fat contents across the product range. In this case, water is used to bulk out these spreads, making some of these products, especially those with lower fat contents, unsuitable for frying. Reduced fat spreads can be used for baking. *Trans*-PUFAs may be produced during incomplete hydrogenation. However, in Europe efforts have been made to reduce or remove *trans*-PUFAs from margarine and spreads through product reformulation and the use of new techniques (Upritchard *et al*. 2005). Furthermore, some manufacturers have increased the amount of *n*-3 fatty acids present (as ALNA) in margarines and fat spreads, and endeavour to incorporate long chain *n*-3 fatty acids (see *Unsaturated fatty acids and public health*).

Unsaturated fatty acids from supplements: From a recent nationwide dietary survey, 40% of women and 29% of men reported taking a nutritional supplement (Henderson *et al*. 2002). Of them, 39% took cod liver oil, or other fish-based supplements, which will make a

Table 6 The typical unsaturated fatty acid composition of selected fats and oils (g fatty acids/100 g oil)

		MUFA (g/100 g)			PUFA (g/100 g)				
	Total fat (g/100 g)	14:1	16:1	18:1 Oleic	18:2 LA	18:3 ALNA	20:4 AA	20:5 EPA	22:6 DHA
Butter	82.5	0.69	1.24	15.80	0.95	0.46	0.09	0.08	0
Margarine	81.7	0	0.23	29.21	12.42	3.36	0	0	0
PUFA spread	68.5	0	0.09	14.96	33.26	0.09	0	0	0
MUFA spread	62.7	0	0.18	30.51	9.65	1.98	0	0	0
Cod liver oil	99.9	0	0	18.30	2.60	1.10	0.90	1.40	8.30
Linseed oil*	99.9	0	0	20.20	12.70	53.30	0	0	0
Olive oil	99.9	0	0.70	71.90	7.50	0	0	0	0
Palm oil	99.9	0	tr	37.10	10.10	0	0	0	0
Peanut oil	99.9	0	tr	43.30	31.00	0	0	0	0
Rape oil	99.9	0	0.20	57.60	19.70	9.60	0	0	0
Soybean oil	99.9	0	0.10	20.80	51.50	7.30	0	0	0
Sunflower oil	99.9	0	0.10	20.20	63.20	0.10	0	0	0

Source: MAFF (1998) (*Data obtained from USDA 2005).

AA, arachidonic acid; ALNA, α-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; LA, linoleic acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.

significant contribution to the unsaturated fatty acid content of their diets. Supplements available typically contain DHA and EPA in doses approximating 100–200 mg.

3.2 Dietary recommendations for fat

Fat is the most energy-dense macronutrient, so it is therefore important that guidelines are set to ensure that the population consumes adequate amounts of the individual fatty acids without encouraging people to consume more energy than they require. Opportunities also exist to take the potential health benefits of the unsaturated fatty acids into consideration and aim to achieve a more optimal ratio of the *n*-3 to *n*-6 PUFAs. Current UK recommendations (Table 7), which were derived in 1991 by the Committee on Medical Aspects of Nutrition Policy (COMA), state that the population average for total fat consumption should not exceed 35% of daily food energy intake (or 33% of daily total energy intake, *i.e.* including energy consumed as alcohol). Population averages for the different types of fatty acids are: SFAs should not exceed 11% of daily food energy; MUFAs should make up approximately 13% of daily food energy and *cis*-PUFAs approximately 6.5%. In order to avoid the atherogenic effects of the *trans*-fatty acids, the population average should not exceed 2% of daily food energy. In 1991, recommendations for specific fatty acids were only made for the EFAs LA (*n*-6 PUFA) and ALNA (*n*-3 PUFA) on the basis of prevention of deficiency. These fatty acids should contribute at least 1% and at least 0.2% of daily food energy respectively (*i.e.* 2.78 g of *n*-6 and 0.56 g of *n*-3 based on a 2500 kcal diet; DH 1991). At the time these guidelines were set, fat contributed approximately 40% of daily food energy, so in order to achieve these targets, dietary modification was required (Gregory *et al.* 1990).

Table 7 Adult UK dietary reference values for fat expressed as a percentage of daily total energy intake (food energy in brackets)

	Individual minimum	Population average	Individual maximum
SFA		10 (11)	
cis-PUFA		6 (6.5)	10
n-3	0.2		
n-6	1.0		
MUFA		12 (13)	
trans-fatty acids		2 (2)	
Total fat		33 (35)	

Source: DH (1991).
MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

In 1994, the guidelines for intakes of PUFAs were revised to take into account the cardio-protective effects afforded by the long chain *n*-3 PUFAs (see *Unsaturated fatty acids in health and disease*). The COMA report on CVD advised that there should be no further increase in intakes of *n*-6 PUFA as the population target had been achieved, and that the intake of long chain *n*-3 PUFA should increase from 0.1 to 0.2 g per day (DH 1994).

Recommendations for adults over the age of 65 years are the same as those for the general population. The adult recommendations are also appropriate for children over the age of 5 years. Up to the age of 5 years, the proportion of dietary energy derived from fat and fatty acids should fall from about 50%, as supplied by breastfeeding, to that recommended for adults (*i.e.* 35% of total energy). Any modifications of dietary fat intake should not begin until after a child's second birthday.

The most recent government recommendations relating to the consumption of unsaturated fatty acids were issued in 2004 (SACN/COT 2004). A committee consisting of representatives from both the Scientific Advisory Committee on Nutrition (SACN) and the Committee on Toxicology (COT) assessed the health impacts of increasing intakes of the long chain *n*-3 PUFAs, taking into account the potential toxicological hazards of consuming the recommended levels from oil-rich fish, known to be the richest source of these fatty acids. They endorsed the population recommendation to eat at least two portions of fish per week, of which one should be oil-rich, and agreed that this recommendation should also apply to pregnant women. Two portions of fish per week, one white and the other oil-rich, equate to approximately 0.45 g/day long chain *n*-3 PUFAs (3.15 g/week). The report added that: 'An increase in population oily fish consumption to one portion a week, from the current levels of about a third of a portion a week, would confer significant public health benefits in terms of reduced risk of cardiovascular disease. There is also evidence that increased fish consumption might have beneficial effects on fetal development'. It was also acknowledged that some groups, especially men and boys, could benefit from greater intakes. However, there was a concern about increasing total intakes of oil-rich fish more than 1 portion per week in girls and women of child-bearing age because of the potential risk of contaminants present in fish having an adverse effect on subsequent pregnancies, although the safe upper limit from a toxicological point of view was deemed to be 2 portions (Table 8).

Table 8 FSA guidelines on fish intake for the UK population (adapted from SACN/COT 2004)

Up to 2 portions of oil-rich fish per week	Up to 4 portions of oil-rich fish per week
Girls and women who might have a baby one day	Other women
Women who are pregnant or breastfeeding	Men and boys

Source: SACN/COT (2004).

Table 9 Total daily amount of fat in the diets of adult men and women (amount as percentage of food energy in brackets)

	Men	Women
Total fat	86.5 g (35.8%)	61.4 g (34.9%)
SFA	32.5 g (13.4%)	23.3 g (13.2%)
trans-fatty acids	2.9 g (1.2%)	2.0 g (1.2%)
MUFA	29.1 g (12.1%)	20.2 g (11.5%)
n-3 PUFA	2.3 g (1%)	1.7 g (1%)
n-6 PUFA	12.9 g (5.4%)	9.4 g (5.3%)

Source: Henderson *et al*. (2003).
MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

3.3 Intakes of unsaturated fatty acids

The average daily intake of fatty acids as reported in the most recent National Diet and Nutrition Survey (NDNS) of adults is shown in Table 9. The NDNS contains data collected from a national sample of adults aged 19–64 years, and is one of a programme of national surveys designed to gather information about the dietary habits and nutritional status of the British population (Henderson *et al*. 2003).

The average intake of total fat in the UK population is around the population target intake of 35% of food energy. The average intake of SFAs in both men and women is higher than the recommended target of 11% of food energy, and a further reduction is required. The recommendations for the MUFAs and total *n*-3 and *n*-6 PUFAs, listed in Table 7, are being met, on average.

The intakes of individual fatty acids are not available, but intakes of the *n*-3 and *n*-6 PUFAs as a percentage of food energy were well above the minimum levels set for total *n*-3 and *n*-6 PUFAs, even at the lowest 2.5 percentile of the distribution, suggesting that the percentage of respondents who failed to meet the minimum intakes recommended by the Department of Health in 1991 is likely to be low. Nevertheless, the lack of data of the individual fatty acids is a limitation of the NDNS, and currently there is no way of monitoring the consumption of the long chain *n*-3 PUFAs in the UK population other than estimation from figures relating to the consumption of oil-rich fish. Thus, currently, it is not known whether targets for long chain *n*-3 PUFAs EPA and DHA intakes are being met.

Table 10 Total daily amount of fat in the diets of boys and girls aged 4–18 years (amount as percentage food energy in brackets)

	Boys	Girls
Total fat	74.4 g (35.4%)	63.1 g (35.9%)
SFA	29.8 g (14.2%)	25.2 g (14.3%)
trans-fatty acids	2.9 g (1.4%)	2.4 g (1.3%)
MUFA	24.6 g (11.7%)	20.6 g (11.8%)
n-3 PUFA	1.5 g (0.8%)	1.5 g (0.8%)
n-6 PUFA	10.7 g (5.1%)	9.3 g (5.3%)

Source: Gregory & Lowe (2000).
MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

It is possible to estimate the average intake of the long chain *n*-3 PUFA provided that we have knowledge of their approximate concentrations in foods and the amounts of the foods consumed. Using this methodology, the average intake of the UK adult population has been estimated to be approximately 244 mg of long chain *n*-3 PUFA per day (Givens & Gibbs 2006). However, as oil-rich fish contribute about 131 mg per day of this total, and as only about 27% of the UK population consume any oil-rich fish, the average intake for the vast majority of the population will be only about 113 mg per day. For those who consume little or no fish, the intake will be as low as 46 mg per day, with poultry meat being a key supplier. All of the above intake figures are still considerably short of the recommended 450 mg of long chain *n*-3 PUFA per day, and thus there is much scope for dietary change.

Intakes of fatty acids in children aged 4–18 years

Intake data taken from the NDNS published in 2000 show that, although average intakes of total fat were close to the 35% of food energy target (Table 10), intakes of saturates were too high; only 8% were achieving the target of 11% energy from SFAs.

3.4 Major contributors to unsaturated fatty acid intake

Adults

Table 11 shows the major contributors to the intake of different types of fat in the UK. Men acquire a

Table 11 Percentage contribution of the main sources of fat intake in the UK adult diet

	Total fat		SFA		*trans*-PUFA		MUFA		*n*-3 PUFA		*n*-6 PUFA	
	M	F	M	F	M	F	M	F	M	F	M	F
Cereals & cereal products	19	20	17	19	25	26	17	18	17	16	20	20
Milk & milk products	14	15	23	25	15	16	9	11	4	4	2	3
Fat spreads	12	11	12	11	19	17	12	11	7	6	15	12
Meat & meat products	25	20	25	19	23	18	30	24	19	14	20	16
Fish & fish dishes	3	4	2	2	3	3	3	4	13	16	4	5
Potatoes & savoury snacks	10	10	7	7	7	6	11	12	17	16	13	13

Source: Henderson *et al.* (2002).

M, male; F, female; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

Table 12 Percentage contribution of the main sources of fat intake in the diet of UK children

	Total fat		SFA		*trans*-PUFA		MUFA		*n*-3 PUFA		*n*-6 PUFA	
	B	G	B	G	B	G	B	G	B	G	B	G
Children aged 4–10 years												
Cereals & cereal products	23	22	23	22	33	32	19	20	17	16	23	22
Milk & milk products	18	18	27	27	18	20	13	16	5	6	3	3
Fat spreads	9	10	8	8	12	13	8	8	7	7	18	18
Meat & meat products	17	17	15	15	14	14	22	20	15	15	16	16
Fish & fish dishes	2	2	1	1	2	2	2	2	5	7	3	3
Potatoes & savoury snacks	18	18	13	13	9	8	21	21	33	35	26	27
Children aged 11–18 years												
Cereals & cereal products	22	21	21	21	27	38	19	22	18	16	22	21
Milk & milk products	13	13	21	20	14	15	10	11	4	4	2	2
Fat spreads	9	9	7	8	12	13	8	7	6	6	15	15
Meat & meat products	22	19	21	18	19	16	26	20	17	15	18	16
Fish & fish dishes	2	2	1	1	1	1	2	1	5	5	2	2
Potatoes & savoury snacks	18	21	13	16	11	12	21	23	35	40	27	31

Source: Gregory & Lowe (2000).

B, boys; G, girls; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

higher proportion of their saturates from meat & meat products (25%) compared with women (19%). The main dietary sources of total *n*-3 PUFA are cereals & cereal products, meat & meat products, potatoes & savoury snacks, fish & fish dishes and vegetables (see Appendix 1 for a description of these groups). There are no significant differences between men and women. For both men and women, the contribution from fish & fish dishes increases with age (mainly due to increasing oil-rich fish consumption). The survey does not provide specific data for the long chain *n*-3 PUFAs. Cereals & cereal products, meat & meat products, and potatoes & savoury snacks are the main contributors towards *n*-6 PUFA intakes.

Children

Similar patterns of consumption are observed in children aged 4–18 years. Proportionally, slightly less fat is derived from meat & meat products and fat spreads, and more fat is derived from potatoes & savoury snacks, and cereal & cereal products when compared with a typical adult diet (Table 12).

3.5 Trends in intake

Trends in intake of, and expenditure on food items are best monitored by the Expenditure and Food Survey (EFS). The most recent data, pertaining to expenditure in 2003/4, were published in 2005. A variation of this

survey (National Food Survey) has been conducted since 1940, so consumption trends over time can be monitored. The 2005 report stated that over the past 30 years there has been:

- a steady decrease in consumption of carcass meat;
- a slight increase in consumption of fish;
- a huge decrease in consumption of whole milk, although the rate of this decline has lessened over the past 3 years (Defra 2005).

Intake of total fat and the unsaturated fatty acids appears to have been particularly affected by public health messages and technologies to reduce total fat and SFA and increase the proportion of unsaturated fat in the diet. Intake of *n*-6 PUFAs has almost doubled as a result of the popularity of vegetable oils and spreads rich in these fatty acids. Semi-skimmed milk was introduced in the 1980s, and now makes up 60% of the market (Defra 2006). Demand for lower-fat products has encouraged food producers to look at the systems they use. The meat industry has modified its production systems to favour a lower-fat end-product. As a result, over the past 20 years the fat content of carcass meat has reduced by more than 30% for pork, 15% for beef and 10% for lamb (Higgs 2000).

It is possible to estimate trends from the NDNS. When data from successive surveys are compared, it is apparent that there has been a slight decrease in *n*-6 PUFA consumption, which is especially apparent at the higher end of the distribution of intakes. Looking over a much longer period of time, there have been some quite substantial changes to the balance of the fatty acids in our diets. Over the last century, it has been suggested that despite total fat intake increasing up until around 1980, our intakes of *n*-3 PUFAs have decreased. In the same period of time, intakes of *n*-6 PUFAs have increased. As the metabolic pathways of these two families of fatty acids share some of the same enzymes, it is thought that consuming what some people consider to be higher amounts of *n*-6 may adversely affect the metabolism of the *n*-3 PUFAs.

There are questions as to whether this may have had an unfavourable effect on our health, which have triggered research into the *n*-6 to *n*-3 ratio. Currently the British diet provides these fatty acids in the ratio of 7:1. This has increased from the 1950s when the average diet provided *n*-6 and *n*-3 PUFAs in a ratio more like 4:1, and is substantially different from the 1.5:1 suggested to be consumed by Stone Age man. After considering the health effects of these, along with other, families of unsaturated fatty acids, the implications of this ratio will be discussed further (see *Unsaturated fatty acids and public health*).

4. Unsaturated fatty acids in health and disease

Detecting associations between nutrition and chronic diseases such as CVD and cancer is not an easy task. Consequently, a number of different approaches have been taken by researchers, attempting to link dietary factors with disease states. Figure 7 outlines the four main types of research: mechanistic; epidemiological; biomarker trials; and clinical trials. Each approach has its own strengths and weaknesses, and individuals tackling research in this area often have to make compromises when selecting which method to use (Figure 7).

The published studies have used various approaches, so it is very important to take into account the relative

Key points:

Unsaturated fatty acids in the UK diet

- Fat is found in most food groups, and foods containing fat generally provide a range of different fatty acids, both saturated and unsaturated.
- Recommended intakes of both total fat and the different types of fatty acids have been set for the UK population. We are not currently meeting these recommendations, so there is still scope for dietary changes.
- Major dietary sources of unsaturated fatty acids include meat & meat products, cereals & cereal products and potatoes & savoury snacks.
- In Western diets, *n*-6 fatty acids are the predominant PUFAs, although this is in line with current dietary advice to consume a minimum of 1% energy as *n*-6 PUFA and 0.2% energy as *n*-3 PUFA.
- The balance of *n*-3 and *n*-6 PUFAs in Western diets has changed substantially over the past 100 years or so. As the two families of PUFAs share a common metabolic pathway, concerns that this might be detrimental to health have been raised.

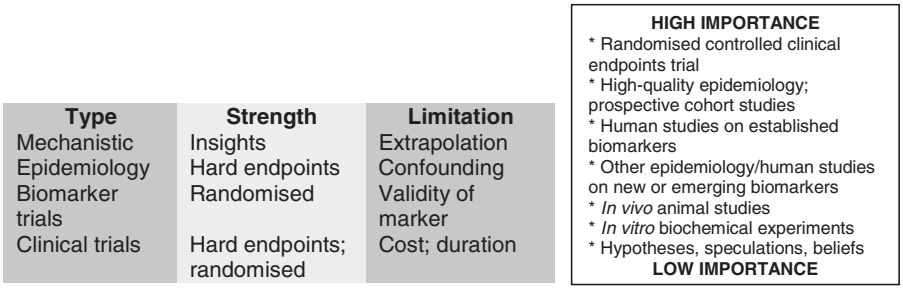


Figure 7 The various approaches available to researchers investigating diet–disease interactions.

importance of each of the different types of evidence when generating a consensus opinion on the health effects of diet. In general, randomised controlled trials with well-defined, clinical endpoints are considered to be the 'gold standard', but in reality, these trials are very difficult to conduct. Nutrition research does not especially lend itself to this form of study, because diet as an exposure is difficult to randomise in an effective way, particularly throughout the long periods of time required to investigate effects on disease. (Supplement trials are more easily randomised, but their effects are not always equivalent to those observed when a whole diet is consumed.) Instead, high-quality epidemiological studies, involving large cohorts of healthy individuals followed over a long period of time, provide some of the strongest evidence of any interaction. This is not to say that the other forms of study do not offer valuable evidence, it is just that their findings must be interpreted with caution, especially when extrapolating from mechanistic studies in the laboratory or in animal models to humans.

The World Health Organisation (WHO) reviewed the evidence relating dietary fat to the risk of developing a number of chronic diseases in 2003. Their findings are summarised in Table 13. As yet, there are no definitive answers, and it is clear that more research is required in order to fully understand the complex relationship that fat and the individual fatty acids have in influencing the risk of developing various diseases.

This following section will take a brief look at some of the major studies that have been published and outline some of the potential mechanisms whereby dietary unsaturated fatty acids might affect disease risk. We will begin by considering CVD as it is in this area that diet–disease associations are thought to be the most convincing.

Table 13 Strength of the evidence linking dietary fat and risk of chronic disease

	Decreased risk	No relationship	Increased risk
CVD			
Convincing	EPA/DHA; LA		C14,16 SFA
Probable	ALNA; Oleic acid	Stearic acid	
Possible			C12 SFA
Type 2 diabetes			
Probable			SFA
Possible	*n*-3 PUFAs		Total fat
Cancer			
Possible	*n*-3 PUFAs		Animal fats

Source: WHO/FAO (2003).
ALNA, α-linolenic acid; CVD, cardiovascular disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; LA, linoleic acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

4.1 Unsaturated fatty acids and cardiovascular disease

CVD, encompassing coronary heart disease (CHD), stroke and other diseases of the cardiovascular system, is one of the leading causes of mortality and morbidity worldwide. Death rates have been falling in most developed countries. However, in the UK, morbidity associated with CVD appears to be increasing, at least in the oldest age groups (see Frayn & Stanner 2005). More people today survive heart attacks than ever before, but many go on to develop chronic heart failure or angina, which is associated with a reduced quality of life. For this reason, it is important to reduce the incidence of CVD and the occurrence of heart attacks or stroke and at the same time, reduce morbidity in those who experience CVD.

CVD is a consequence of two interrelated pathological processes: atherosclerosis (hardening and narrowing of blood vessels) and thrombosis (blood clotting) (see Fig. 8). Atherosclerosis is characterised by the accumulation of lipids in the blood vessel walls over a long period of time. This can lead to impaired flow of blood (and therefore oxygen) to the heart, and angina pectoris (chest pain). A heart attack (myocardial infarction: MI) is usually precipitated by a blockage in the coronary artery following the rupture of an atherosclerotic

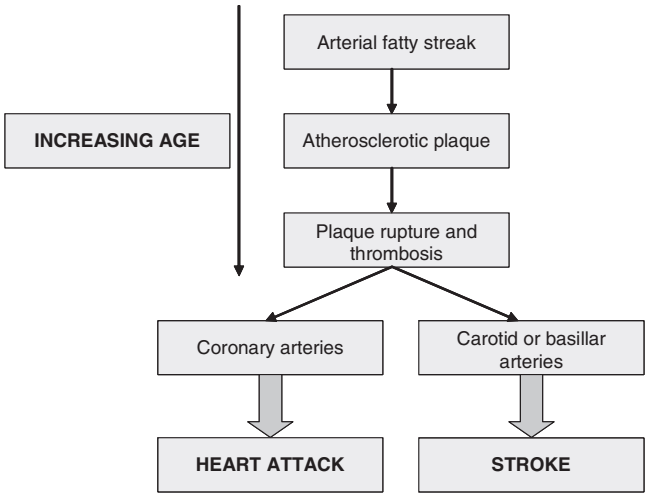


Figure 8 The interrelated pathologies of coronary heart disease and stroke (adapted from Sanders & Emery 2003).

plaque in the arterial lumen. A stroke occurs when a blockage disrupts the blood flow to the brain. (For an extensive review of the aetiology, see Frayn & Stanner 2005.)

Established risk factors for CVD include age, sex, ethnicity, hypertension, abnormal blood lipids (dyslipidaemia), diabetes, obesity, physical inactivity and smoking. While these established risk factors can explain a high proportion of risk, there still remains some variability unexplained, and a number of emerging risk factors for CVD have been identified, *e.g.* endothelial dysfunction (see Sattar & Ferns 2005), metabolic syndrome (see Coppack *et al.* 2005), and fetal and maternal nutrition (Fall 2005). Diet is recognised as an important modifiable risk factor for CVD; for example, diets rich in fruit and vegetables are associated with a reduced risk of CVD (see Buttriss 2005a). The amount of fat in the diet and type of fatty acids consumed can influence the risk of CVD and its risk factors.

Dietary fatty acids and risk of CVD

Evidence for the association between unsaturated fatty acid consumption and CVD comes from a wide-range of sources: cross-cultural comparisons; prospective (cohort) studies; case–control studies and intervention trials.

Unsaturated fatty acids and CHD

MUFA: Studies comparing disease rates in different countries have suggested an inverse association between MUFA intake and death from CHD. Indeed, the mortality rate from CHD is very low in Mediterranean countries where the 'typical' traditional diet is low in SFAs and high in MUFAs (as a result of high intakes of olive oil). Although the diets of Mediterranean countries can vary, MUFAs typically account for 16–29% of energy intake (Kris-Etherton 1999). Further evidence for an inverse association between MUFA intake and CVD comes from the Nurses' Health Study, a prospective study with a follow-up period of 14 years conducted in more than 80 000 women aged 34–59 years at entry. It reported that a 5% increase in energy derived from MUFA is associated with a significant 19% reduction in risk of developing CHD in women with no history of CHD (Hu *et al.* 1997). In the Lyon Diet Heart Study, patients randomised to receive a Mediterranean-type diet, including high MUFA, had significant reductions in the risk of death from cardiovascular causes or non-fatal acute myocardial infarction (73%), as well as in cardiac mortality (76%) and total mortality (70%) (de Lorgeril *et al.* 1994).

While there are a number of other epidemiological studies that confirm a protective effect of MUFAs on CHD (*e.g.* Artaud-Wild *et al.* 1993; Pietinen *et al.* 1997), there are also a number of studies that refute an association, including the Framingham Heart Study (Posner *et al.* 1991).

***n*-6 PUFA:** Little research has been conducted on the influence of *n*-6 PUFAs and overall risk of CHD in recent years; rather, most research has concentrated on the influence of *n*-6 PUFAs on risk factors for CHD. The randomised clinical trials testing long-term effects of high-LA diets on CHD incidence were conducted in the 1960s and early 1970s, and are thus often overlooked when conducting literature searches. A statistically significant 20% decrease in the incidence of CHD was observed in the Los Angeles Veterans' Study. In this instance, men were randomised to a diet containing roughly 40% of energy from fat, of which over a third (38%) was LA in the intervention group compared with only 10% in the control group (Dayton *et al.* 1969). However, the findings over this period are inconsistent, with four randomised controlled trials showing an independent, protective effect of *n*-6 PUFA (MRC 1968; Dayton *et al.* 1969; Leren 1970; Turpeinen *et al.* 1979) and nine epidemiological studies showing no significant relation (Hu *et al.* 2001). It should be noted that no trial to date has shown an adverse effect of a high *n*-6 PUFA diet on CHD risk. A more recent analysis of the data has suggested that the ratio of PUFA to SFA in the diet might be an important risk factor for CHD, and that it is diets that are rich in *n*-6 PUFAs, but low in SFAs that are cardio-protective (Garcia-Palmieri *et al.* 1980; Gordon *et al.* 1981; McGee *et al.* 1984).

A number of case–control studies suggest that lower dietary intakes, and lower plasma or adipose concentrations, of LA are associated with a reduced risk of CHD (Simpson *et al*. 1982; Wood *et al*. 1987); others do not find this association (Fehily *et al*. 1987; Thomas *et al*. 1987). However, case–control studies cannot establish cause or effect as they investigate differences after the onset of disease. Prospective studies reporting the influence of *n*-6 PUFAs on CHD risk are relatively few as the majority tend to report on overall intake of PUFAs. Miettinen *et al*. (1982) reported an inverse association between the proportion of LA in serum phospholipids at baseline and CHD incidence at 5-year follow-up. Recently, the Kuopio Ischaemic Heart Study reported that LA was strongly inversely associated with CHD mortality (Laaksonen *et al*. 2005).

***n*-3 PUFA:** A large number of epidemiological studies report an inverse association between intakes of long chain *n*-3 PUFAs from fish and risk of CHD; several ecological studies have reported a lower incidence of CHD in fish-eating populations, but such studies do not control for other lifestyle factors that may influence the CHD risk (Hirai *et al*. 1980; Bjerregaard & Dyerberg 1988). The Zutphen Study, a cohort of the Seven Countries Study, was the first prospective study to report a lower risk of CHD in men who consumed fish (Kromhout *et al*. 1995), but this relationship was not confirmed in the East Finland cohort of the Seven Countries Study, where intakes were positively associated with risk (Oomen *et al*. 2000). The Nurses' Health Study and the Physicians' Health Study have both reported a beneficial effect of fish consumption on sudden cardiac death. In the Nurses' Health Study, consumption of fish was associated with a decreased risk of CHD events and death from CHD (Hu *et al*. 2002). This protective effect has been attributed to the long chain *n*-3 PUFAs in fish, *i.e.* EPA and DHA and confirmed in a nested case–control study where blood concentrations were measured (Albert *et al*. 2002). When comparing cases with controls, mean blood EPA and DHA concentrations were significantly lower, as were total long chain *n*-3 PUFA concentrations. Men in the group consuming the highest levels of *n*-3 PUFAs were 90% less likely to die from a sudden cardiac event (>17 years of follow-up) than the lowest *n*-3 PUFA consumers. Fish consumption in the same study was also associated with a reduced risk of sudden cardiac death.

Supplementation interventions with long chain *n*-3 PUFAs appear to have a beneficial effect on cardiac health. A well-respected, large, randomised controlled trial found that a fish oil concentrate providing 0.56 g of DHA and 0.28 g of EPA per day decreased the incidence of sudden cardiac death by 45% and all-cause mortality by 20% (GISSI 1999). Additionally, in the Diet and Reinfarction Trial (DART), dietary advice to eat two portions of oil-rich fish per week, which provided 1 g of long chain *n*-PUFA per day, decreased the incidence of fatal CHD by 29% over a period of 2 years (Burr *et al*. 1989). A recent meta-analysis to establish whether the individual effects found in a number of different studies were consistent, reported that long chain *n*-3 PUFAs reduced risk of sudden cardiac death by 30%, but not risk of non-fatal MI (Bucher *et al*. 2002). In the 11 studies analysed, intakes of DHA ranged 0.6–3.7 g/day and EPA 0.3–6.0 g/day. A further randomised controlled trial investigating the influence of long chain *n*-3 PUFA supplementation and CHD incidence in patients with suspected mycocardial infarction, reported a protective effect of fish oil supplementation on cardiac death (Singh *et al*. 1997). However, there are misgivings with regards to the way that this study was conducted; there has been considerable debate in the scientific community about the reliability of the findings (White 2005).

The follow-up of the DART study (DART 2) reported an unexpected 29% increase in CVD mortality in the group advised to eat oil-rich fish (Burr *et al*. 2003). This is not consistent with other studies, and the authors suggested that other aspects of individuals' lifestyles may have changed when the dietary advice was given. Additionally, the trial was halted for a short period of time because of funding problems, which may have adversely affected the outcome. However, this illustrates the importance of considering all studies when evaluating the effect of a dietary constituent on disease risk. A recent meta-analysis reviewed 48 randomised controlled trials and 41 cohort studies, investigating the effect of *n*-3 PUFA (EPA, DHA and ALNA) for at least 6 months in adults (both healthy and those with some form of CVD risk factor) on CVD outcomes (Hooper *et al*. 2006). Pooled estimate showed no strong evidence of a reduced risk of: total mortality; CVD events; or cancer. However, the findings of this meta-analysis appear to have been influenced by the inclusion of the DART 2 study involving more than 3000 men with angina. As mentioned previously, this study reported an unexpected 26% increase in cardiac deaths in the men taking the long chain *n*-3 PUFA supplements (Burr *et al*. 2003).

However, as not all individuals consume oil-rich fish, there is also much interest in the *n*-3 PUFA ALNA that is obtained from predominantly plant-based sources. ALNA is also associated with a reduced risk of fatal CHD, possibly as it appears to reduce blood LDL cholesterol concentrations in a similar manner to LA or

oleic acid (Layne *et al*. 1996; Freese & Mutanen 1997). A meta-analysis of five prospective cohort studies assessing ALNA intake and CHD risk reported that intakes of 1.2 g/day are associated with a statistically non-significant reduction in risk of fatal CHD of 21% (Brouwer *et al*. 2004). There have been several clinical trials that have investigated the influence of increased intakes of ALNA on CHD risk (Natvig *et al*. 1968; de Lorgeril *et al*. 1994; Singh *et al*. 1997). These trials comprise the Lyon Diet Heart Study, in which individuals who had experienced a first MI were randomised to receive dietary advice to consume a Mediterranean-type diet, including ALNA or no dietary advice, and followed up for a period of 5 years. The authors reported a lower incidence of cardiac death and non-fatal myocardial infarction after consumption of 1.1 g ALNA/day, relative to control treatment (de Lorgeril *et al*. 1994). However, the findings from individual clinical trials have not been consistent, and thus their findings must be interpreted with caution. Some also consider four classic PUFA trials as supportive of the ALNA hypothesis, as they included soybean oil, which is rich in ALNA as well as the *n*-6 PUFA LA (MRC 1968; Dayton *et al*. 1969; Leren 1970; Turpeinen *et al*. 1979).

Unsaturated fatty acids and stroke Despite the wealth of scientific literature on the influence of unsaturated fatty acids on CHD, relatively few studies have investigated the influence of unsaturated fatty acids on stroke risk. Even fewer studies have investigated the influence of unsaturated fatty acids on the different types of stroke: ischaemic and haemorrhagic stroke.

MUFA: The measurement of different classes of unsaturated fatty acids in serum, plasma or red blood cells of ischaemic stroke cases and of controls suggests that higher proportions of MUFAs are associated with a reduced risk. However, the numbers of cases identified in some of these studies have been small (Ricci *et al*. 1997).

***n*-6 PUFA:** A recent prospective study reported that a higher intake of LA, as determined by the measurement of serum fatty acids, was associated with a reduced risk of ischaemic stroke in Japanese men (Iso *et al*. 2001).

***n*-3 PUFA:** Epidemiological evidence points towards an inverse association between fish/long chain *n*-3 PUFA consumption and total stroke (Keli *et al*. 1994; Zhang *et al*. 1999) and ischaemic stroke (He *et al*. 2002, 2004; Iso *et al*. 2002), but also a positive association with haemorrhagic stroke (Bjerregaard & Dyerberg 1988). It has been hypothesised that differences in the incidence of ischaemic and haemorrhagic stroke can be explained by the level of fish/*n*-3 PUFA consumption, although few intervention studies have investigated their influence and data that exist are inconsistent. However, it has been reported that serum concentrations of ALNA are inversely related with risk of total stroke (Simon *et al*. 1995), and that increased serum, plasma or red blood cell concentrations of EPA and DHA are associated with a reduced risk of stroke (Ricci *et al*. 1987). A meta-analysis of eight randomised controlled trials, conducted in individuals with no history of stroke, failed to show any statistically significant association between intake of *n*-3 PUFAs and risk of fatal or non-fatal stroke (Briel *et al*. 2004).

Clearly, further clinical trials are required to confirm or refute an association between unsaturated fatty acids and risk of ischaemic and haemorrhagic stroke. In particular, further studies are required to investigate the influence of individual *n*-3 PUFAs on stroke risk and on the different types of stroke.

Dietary fatty acids and the development of CVD risk factors

Some of the beneficial effects of unsaturated fatty acids on cardiovascular health can be explained by their influence on established risk factors for CVD, *e.g.* blood lipids and blood pressure.

Unsaturated fatty acids and blood lipoproteins Raised blood cholesterol, particularly LDL cholesterol, is a well-established risk factor for CHD; HDL cholesterol concentrations are inversely associated with risk. Elevated TAG concentrations are also associated with an increased risk of CHD (Austin 1989; Assman *et al*. 1998).

Meta-analyses report that both MUFAs and, to a greater extent, total PUFAs (*i.e. n*-3 and *n*-6 fatty acids together), when substituted for SFAs in the diet, reduce both total cholesterol and LDL cholesterol, and increase HDL cholesterol (Mensink & Katan 1992; Clarke *et al*. 1997; Howell *et al*. 1997). An isocaloric substitution of MUFA and total PUFAs for carbohydrate does not have any influence on fasting TAG concentrations (Mensink & Katan 1992).

***n*-6 PUFA:** LA acts to lower total and LDL cholesterol without influencing HDL cholesterol or TAG concentrations (Mensink & Katan 1989). On occasion, MUFAs have been preferentially recommended over *n*-6 PUFAs as substitutes for SFAs in the diet. The rationale behind these guidelines has been a belief that *n*-6 PUFAs effect an undesirable reduction in HDL cholesterol. However, a meta-analysis has concluded that a 1% energy substitution of *n*-6 PUFAs, MUFAs and SFAs for carbohy-

drate, resulted in an increase in HDL cholesterol of 0.005, 0.006 and 0.013 mM and a change in LDL cholesterol of –0.020, –0.008 and +0.013 mM respectively (Fig. 9; Clarke *et al.* 1997). Similar effects were also calculated in the meta-analysis of Mensink *et al.* (2003). These data suggest that it is prudent to replace SFAs with a mix of *n*-6 PUFAs and MUFAs in order to ensure that an appropriate balance of fatty acids is consumed.

***n*-3 PUFA:** A critical review of 65 trials indicated that short-term supplementation of very high doses (7 g) of long chain *n*-3 PUFAs does not influence total cholesterol (Harris 1997). Although not significant, there was a tendency for LDL and HDL cholesterol to rise, while long chain *n*-3 PUFAs were shown to lower blood TAG concentrations. Similar effects have been observed in a population of Inuits in Greenland, who despite high dietary fat intakes (especially high in *n*-3 PUFAs), had lower TAG concentrations compared with the Danish population (Dyerberg & Bang 1982; Bjerregaard *et al.* 1997). The *n*-3 PUFA, ALNA, acts in a similar way to LA (*i.e.* lowers total and LDL cholesterol without influencing HDL cholesterol). There is much interest in the effect of the long chain *n*-3 PUFAs DHA and EPA on blood lipoprotein concentrations, although the nature of the effect is unclear and further studies are required. There is more consensus in reported effects of EPA and DHA on TAG concentrations; most published studies reporting significant reductions at doses in the region on 4 g/day (Hamazaki *et al.* 1996; Grimsgaard *et al.* 1998; Mori *et al.* 2000; Woodman *et al.* 2002; Buckley *et al.* 2004). Meta-analyses are clearly required once sufficient randomised controlled trials have been conducted, to determine the precise dose–response relationships between intakes of long chain *n*-3 PUFAs and lipoprotein concentrations.

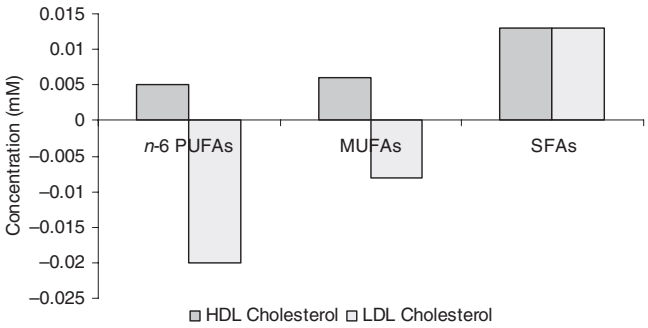


Figure 9 Change in the concentration of HDL- and LDL cholesterol when 1% energy as carbohydrate is replaced by that of *n*-6 PUFAs, MUFAs or SFAs (Clarke *et al.* 1997). HDL, high density lipoprotein; LDL, low density lipoprotein; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

Unsaturated fatty acids and blood pressure Elevated blood pressure (hypertension) is another established risk factor for CVD, although it predicts risk of stroke more strongly than CHD. As blood pressure increases, so does the CVD risk; in the Seven Countries Study for every 10 mmHg rise in systolic blood pressure and every 5 mmHg rise in diastolic blood pressure, the risk of all-cause mortality rose by 28% in both normotensive and hypertensive individuals (van den Hoogen *et al.* 2000).

MUFA: Several studies have investigated the influence of MUFAs on blood pressure. Epidemiological studies report an inverse association between MUFA intake and blood pressure (*e.g.* Williams *et al.* 1987; Panagiotakos *et al.* 2003; Psaltopoulou *et al.* 2004). Intervention studies that have investigated the substitution of dietary SFA with MUFA report a reduction in blood pressure (Mensink *et al.* 1988). However, the extent of reduction was not significantly different from that observed in individuals fed a high-carbohydrate, low-fat diet. The current view is that in healthy normotensive individuals, increasing the proportion of MUFAs in the diet will have only minor effects, if indeed any, on blood pressure.

***n*-6 PUFA:** Few studies have investigated the influence of *n*-6 PUFAs on blood pressure. Some studies report an inverse association between intake and blood pressure (Iacono *et al.* 1983; Folsom *et al.* 1996), while others do not (Sacks *et al.* 1987). More recently, Iso *et al.* (2002) reported an inverse association between serum LA concentrations and blood pressure. However, there is very little evidence from intervention studies. As with MUFAs, it is unclear what effect *n*-6 PUFAs have on blood pressure, and more research is needed in this area.

***n*-3 PUFA:** Far more studies have investigated the effect of the *n*-3 PUFAs on blood pressure, in an attempt to identify how these fatty acids influence CVD risk in light of their neutral effect on blood cholesterol. Such studies suggest a blood-pressure-lowering effect of 2–3 g/day long chain *n*-3 PUFAs in individuals with hypertension (Appel *et al.* 1993; Morris *et al.* 1993; Geleijnse *et al.* 2002). The effect of long chain *n*-3 PUFAs on blood pressure in individuals with normal blood pressure is less clear. Those studies that have looked at the influence of DHA or EPA alone have tended to use doses in the region of 4 g/day, or have reported conflicting findings (Conquer & Holub 1998; Mori *et al.* 1999; Theobald *et al.* 2003). Clearly, further research is required to determine the influence of low doses of individual long chain *n*-3 PUFAs on blood pressure.

Unsaturated fatty acids and endothelial function

There has been much interest in the role of the endothelium (the layer of cells lining the blood vessels) in

CVD over recent years (see Frayn & Stanner 2005). The endothelium is a selective barrier between the blood and the underlying tissue, which nutrients, solutes, hormones, macromolecules and leukocytes (white blood cells) can cross. The endothelium has many functions, including: control of vascular homeostasis; maintenance of blood flow through vessels in response to blood-borne and locally produced chemical and physical stimuli; regulation of vessel tone and haemostasis; and regulation of coagulation and fibrinolysis and thrombosis.

It is thought that the loss of normal endothelial function (endothelial dysfunction) is one of the earliest stages of atherosclerosis. Endothelial dysfunction describes impaired endothelium vasodilator responses following exposure to an endogenous stimulus (vasodilatation can also occur following the administration of exogenous compounds, such as salbutamol or glyceryl trinitrate, used to relieve the symptoms of angina pectoris). It also describes altered endothelial permeability, increased adhesion molecule expression and leukocyte adhesion to the endothelium, increased thrombosis and impaired fibrinolysis (see Sattar & Ferns 2005). Endothelial dysfunction can occur following injury to the endothelium; injury can be caused by raised blood cholesterol, cigarette smoking, infection, hypertension, inflammation, insulin resistance and diabetes mellitus. Endothelial dysfunction has been observed in children with hypercholesterolaemia and adults with risk factors for CVD (see below) in the absence of atherosclerosis (Celermajer *et al*. 1992). Furthermore, coronary endothelial function has been shown to be a predictor of atherosclerosis progression and coronary events (Schächinger *et al*. 2000; Halcox *et al*. 2002). Diet is known to modulate endothelial function (see Brown & Hu 2001). Consumption of a high-fat meal has been shown to impair endothelial function (Plotnick *et al*. 1997; Vogel *et al*. 1997), possibly through the increased presence of TAG-rich particles, which have been suggested to exert pro-oxidant effects.

MUFA: It has been suggested that MUFAs have beneficial effects on endothelium-dependent dilatation as determined by the measurement of markers of endothelial function (see Sattar & Ferns 2005). Few studies have investigated their influence *in vivo*. A MUFA-rich meal has been shown to impair short-term endothelial function in healthy subjects (Ong *et al*. 1999). However, in the longer-term, beneficial effects of a MUFA-rich diet have been reported. Fuentes *et al*. (2001) reported an improvement in endothelial function in individuals with hypercholesterolaemia receiving a MUFA-rich Mediterranean diet compared with a diet high in SFAs. Similarly, Esposito *et al*. (2004) reported beneficial effects of a MUFA-rich Mediterranean diet in individuals with metabolic syndrome.

***n*-6 PUFA:** Correlations between concentrations of individual PUFAs in plasma and endothelial function suggest that higher concentrations of AA and dihomo-γ-linolenic acid are associated with endothelial dysfunction (Pegge *et al*. 2001a). However, there are currently no data available from intervention studies that support this association.

***n*-3 PUFA:** There is evidence to suggest that high doses of *n*-3 PUFAs may have beneficial effects on endothelial function, although this seems to be more apparent in individuals already displaying CVD risk factors. Both *in vitro* and *in vivo* studies looking at markers of endothelial function support such an association (Seljeflot *et al*. 1998; Johansen *et al*. 1999; Hjerkinn *et al*. 2005). Nestel *et al*. (2002) reported a beneficial effect of both EPA and DHA on arterial compliance in dyslipidaemic subjects at a dose of 3 g/day over a period of 7 weeks; greater benefit was seen with EPA.

Beneficial effects of long chain *n*-3 PUFAs have also been observed on vessel wall resistance, implying an improvement in endothelial function (Chin *et al*. 1993). It has been reported that supplementation with 4 g/day of *n*-3 PUFAs over a period of 4 months improved endothelial function in hypercholesterolaemic individuals (Goodfellow *et al*. 2000). A long-term intervention study conducted in healthy male subjects reported that 2 g/day of ALNA over a period of 6 months, relative to placebo, impaired endothelial function (Pegge *et al*. 2001b). On the other hand, Mori *et al*. (2000) noted a benefit of both EPA and DHA at a dose of 4 g/day on endothelial function in overweight, mildly hyperlipidaemic men over a period of 6 weeks, with greater benefit being observed with DHA. However, a recent study conducted in healthy middle-aged subjects suggested that moderate intakes of DHA did not result in any improvement in endothelial function (H. Theobald et al., British Nutrition Foundation, manuscript in preparation). Thus again, further research is required to determine the association between *n*-3 PUFAs and endothelial function in the general population.

Unsaturated fatty acid and atherogenesis

Atherosclerosis, one of the key processes in the development of CHD, is characterised by the accumulation of lipid in the blood vessel walls. It is also a consequence of persistent inflammation as atherosclerotic lesions contain both inflammatory and smooth muscle cells. Diet can influence the progression of atherosclerosis, *i.e.* atherogenesis (Ross 1999).

Animal studies suggest that both MUFAs and PUFAs reduce atherogenesis, with two recent studies suggesting that hamsters fed a MUFA-rich diet developed less early atherosclerosis than hamsters fed a PUFA-rich diet (Nicolosi *et al.* 2002, 2004). That said, further animal studies point towards a reduction in the progression of atherosclerosis with increased intakes of long chain *n*-3 PUFAs (Weiner *et al.* 1986; Davis *et al.* 1987; Mortensen *et al.* 1998). Few human studies have investigated the influence of unsaturated fatty acids on the progression of atherosclerosis, although it has been suggested that *n*-3 PUFAs may be incorporated into atherosclerotic plaques and thereby influence their stability, thus influencing risk of thrombus formation (Rapp *et al.* 1991).

However, a recent systematic review of randomised controlled trials investigating the impact of ALNA on CVD risk markers reported that although supplementation may cause a small decrease in fibrinogen and plasma fasting glucose concentrations, most CVD risk markers were not significantly affected. Indeed, the authors concluded that there was insufficient evidence to recommend dietary supplementation with ALNA to reduce CVD risk (Wendland *et al.* 2006).

Unsaturated fatty acids and arrhythmia

An arrhythmia is a disturbance of the normal rhythm of the heart. The heart normally beats 60–80 times a minute. During arrhythmia, the heart rate becomes abnormally rapid or slow, and/or irregular. Diseased heart muscle is especially prone to periods of irregular electrical activity; the subsequent arrhythmias are potentially lethal and are often the cause of sudden cardiac death. Arrhythmias can also be triggered when the blood supply to the heart tissue is restricted. A restricted blood supply can also result in the release of fatty acids from cell membranes and thus, like the generation of prostaglandins, the ratio of *n*-3 to *n*-6 fatty acids in the membrane is important. In the case of arrhythmia, this is even more pronounced as it seems that there is a preferential release of *n*-3 PUFAs when they are present in the membrane. This is of benefit as *n*-3 PUFAs appear to protect against arrhythmias (O'Neill 2003). *n*-3 PUFAs alter the electrical properties of the surface membrane of the cell, raising the threshold for the generation of an action potential. Therefore, any stimulus that could lead to arrhythmia would have to be larger in order to exceed the increased threshold (McLennan *et al.* 1992).

Evidence that demonstrates an anti-arrhythmic effect in humans is mounting, although the picture is not yet completely clear. Data published from a recent randomised controlled trial suggest that daily supplementation with fish oil does not reduce the risk of further arrhythmia among patients with a recent episode of sustained ventricular arrhythmia. Indeed, fish oil may even be pro-arrhythmic in some patients (Raitt *et al.* 2005). However, Geelen *et al.* (2005) have demonstrated that daily supplementation with 1.5 g of *n*-3 PUFAs from fish significantly decreases heart rate. Additionally, another recent trial has reported that there is increasing evidence that, for individuals at a high risk of fatal ventricular arrhythmias, regular daily ingestion of fish oil fatty acids may significantly reduce the risk of death (Leaf *et al.* 2005). In fact, the conclusions drawn from a recent meta-analysis state that data from randomised controlled trials are suggestive of a reduction in heart rate following fish oil supplementation, which is especially apparent in those individuals with higher baseline heart rates (Mozaffarian *et al.* 2005a).

Unsaturated fatty acids and thrombogenesis and fibrinolysis

Thrombogenesis is the process by which blood forms a clot within intact blood vessels. Generation of a clot can cause a heart attack or a stroke in an artery that is already narrowed by atherosclerosis. Conversely, fibrinolysis is the process whereby the fibrin clot is broken down. The enzyme, plasmin, breaks up the fibrin mesh, leading to the production of circulating fragments that are cleared by other proteinases. The fibrinolytic system is activated in parallel with the clotting system when a blood vessel is damaged. Any factor that disturbs this natural balance can produce a blood clot. Following an external 'trigger' to promote clot formation, fatty acids are released from the platelet membrane and are converted into eicosanoids (see *What are unsaturated fatty acids?*).

Diets rich in fish or fish oil have been associated with decreased platelet aggregation and increased bleeding time (see BNF 1999). This is believed to be due to higher proportions of the weaker-acting eicosanoids (thromboxane A_2 and prostacyclin I_3) formed from the *n*-3 PUFAs (Fig. 10). It is not certain whether unsaturated fatty acids have any effect on components in the coagulation cascade; a diet containing higher proportions of MUFAs or PUFAs to SFAs may attenuate the acute procoagulant effects of fatty meals (Roche *et al.* 1998; Kelly *et al.* 2001). Similarly, there is little evidence confirming the role of dietary fatty acids in fibrinolysis (see Frayn & Stanner 2005). LA, EPA and the MUFA oleic acid increase the transcription of a fibrinolytic inhibitor, plasminogen activator inhibitor 1 (PAI-1) *in vitro* (Nilsson *et al.* 1998). However, this effect has not consistently

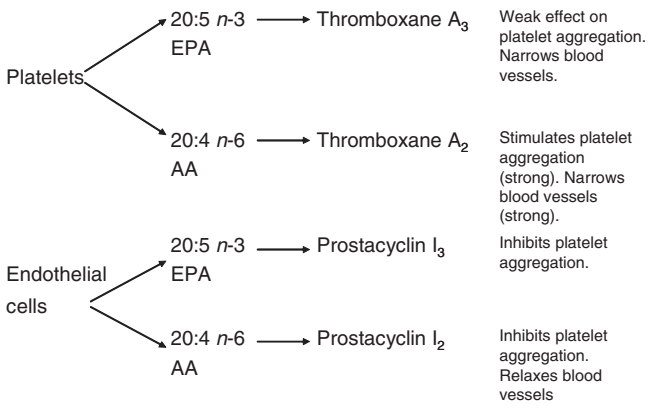


Figure 10 Formation of eicosanoids from *n*-6 and *n*-3 PUFA; their effects on platelet aggregation and the diameter of blood vessels (adapted from BNF 1999). AA, arachidonic acid; EPA, eicosapentaenoic acid; PUFA, polyunsaturated fatty acid.

been observed in supplementation studies conducted *in vivo* (Emeis *et al*. 1989; Hansen *et al*. 2000).

Concluding remarks

Associations between types of fat in the diet and CVD are among the most convincing in all of nutritional epidemiology, and it is universally accepted that a diet high in saturated fatty acids will increase a person's risk of suffering from some form of heart disease or stroke. However, the influence that separate families of, or even individual unsaturated fatty acids have both on the risk of CVD and on development of its risk factors is beginning to be appreciated. Increasing amounts of evidence are now available for consideration for anyone attempting to generate a consensus view on this issue, and the relative importance that each type of study should be given has been discussed.

Although not without critics, many studies seem to support the idea that the long chain *n*-3 fatty acids found in fish oils protect against fatal heart disease. This has been suggested in cohort studies (*e.g.* the Nurses' Health study), intervention trials with fish (*e.g.* DART study) or interventions with fish oil supplements (*e.g.* GISSI prevention trial). Manufacturers of products containing pre-defined amounts of the long chain *n*-3 PUFAs are now able to make scientifically substantiated claims related to a healthy heart (see *Unsaturated fatty acids and public health*), and there is an increasing consumer awareness of the cardiac benefits of including these fatty acids in the diet. Questions are now being raised as to the amount of these long chain *n*-3 PUFAs that is required in the diet to gain the most benefit. Currently, SACN has recommended intakes of 0.45 g per day from oil-rich fish for the general population (SACN/COT 2004). However, beneficial effects observed in secondary prevention trials, *i.e.* those assessing the efficacy of long chain *n*-3 PUFA supplementation to reduce the risk of a secondary cardiac event in individuals diagnosed with a heart condition, are at levels in the order of 1 g per day.

Alternative sources of *n*-3 PUFAs are plant oils, such as linseed, rapeseed and nut oils, which are rich in the 'parent' *n*-3 PUFA ALNA. ALNA can theoretically be elongated to DHA and EPA, although there are suggestions that this pathway is not efficient enough to produce EPA and DHA in sufficient quantities (Burdge & Calder 2005a, 2005b; see *What are unsaturated fatty acids?*). Vegetarians, who refrain from consuming fish, will clearly be obtaining all their dietary long chain *n*-3 PUFA from this route. As a group, vegetarians experience lower CVD rates than the general population, similar to those seen in populations consuming large amounts of oil-rich fish. Although there are other lifestyle factors associated with being a vegetarian that protects against CVD, there is increasing interest in the health benefits of ALNA. As mentioned earlier, there is conflicting evidence of the effect of ALNA supplementation on CVD incidence from cohort studies (Wendland *et al*. 2006), although this is clearly an interesting hypothesis, and more studies are required to determine what, if any, association exists.

Meanwhile, evidence of an effect of the *n*-6 PUFAs, including LA, on CVD risk is strong and consistent. Although many of the data are derived from trials conducted decades ago, there has been little argument that *n*-6 PUFAs favourably alter the concentrations of LDL- and HDL cholesterol, thus reducing CVD risk.

Finally, returning to the initial assertion that a diet high in saturated fatty acids will increase a person's risk of suffering from some form of heart disease or stroke, we now appreciate that certain SFAs may not be as atherogenic as was previously thought. Contrary to expectation, blood cholesterol concentrations appear to decrease when stearic acid is fed compared with other SFAs. This may be a result of stearic acid's direct effects on cholesterol absorption and excretion, or may come about by some unknown mechanism (Berry & Sanders 2005). This is a clear illustration of the advances that are possible in tailoring specific diets as our understanding of disease mechanisms and the individual nutrient components of food increases.

4.2 Unsaturated fatty acids and diabetes

There are two major types of diabetes mellitus: type 1 and type 2 diabetes. Both are characterised by raised

Key points:

Unsaturated fatty acids and cardiovascular disease

- CVD, characterised by hardening and narrowing of blood vessels and/or the development of blood clots, is one of the leading causes of mortality and morbidity worldwide.
- The precise mechanisms by which unsaturated fatty acids reduce CVD risk are as yet unclear. Numerous mechanisms whereby dietary fatty acids could influence the progression of CVD and its risk factors have been identified. These include effects on blood lipid levels, blood pressure, inflammatory response, arrhythmia and endothelial function, along with many other effects, both known and as yet undefined.
- An elevated plasma LDL cholesterol concentration is a well-established risk factor for CVD. Replacing SFAs by either MUFAs or *n*-6 PUFAs reduces LDL cholesterol, thus reducing the risk of CVD. Unsaturated fatty acids, such as LA or MUFAs, also raise HDL cholesterol, which assists in the removal of TAGs from the bloodstream. So it is prudent to replace SFAs with a mix of *n*-6 PUFAs and MUFAs in order to ensure that an appropriate balance of fatty acids is consumed.
- There is strong supportive, but not yet conclusive evidence that long chain *n*-3 PUFAs found in fish oils protect against fatal heart disease, and population-wide dietary recommendations have been made to support this.
- Evidence is mounting on the role that the *n*-3 PUFA ALNA may play in preventing the progression of CVD, although it is currently unclear what, if any, association exists between ALNA intake and CVD risk.

blood glucose concentrations due to either a lack (type 1) or reduced action, or a lack (type 2) of the hormone insulin. As unsaturated fatty acids are capable of affecting a number of different metabolic pathways, it is not surprising that much work has been conducted investigating the effect of unsaturated fatty acids on the body's response to glucose.

Individuals with diabetes are at a two- to fourfold increased risk of CVD. Consequently, dietary management of diabetes involves maintaining both blood glucose and blood lipid concentrations at as near normal levels as possible to reduce the possibility of associated complications developing. As with individuals without diabetes, elevated LDL cholesterol increases risk of the formation of fatty deposits in the blood vessels, and this affects CVD risk. MUFAs and *n*-6 PUFAs have similar qualitative effects on the concentrations of circulating TAGs and LDL- or HDL cholesterol in individuals with diabetes as in individuals without diabetes, resulting in reduced CVD risk (Berry 1997; Ros 2003). Conversely, the *n*-3 PUFAs have a favourable effect on TAG concentrations but no effect on total, LDL- or HDL cholesterol in individuals with diabetes, so do not modulate CVD risk by this mechanism (MacLean *et al*. 2004). However, as in individuals without diabetes, *n*-3 PUFAs result in an improvement in other risk factors for CVD, such as the blood is less likely to clot, blood pressure is reduced and protects against ventricular arrhythmias (see *Unsaturated fatty acids and cardiovascular disease*).

To prevent other complications of diabetes, *e.g.* diabetic neuropathy and retinopathy, it is necessary to regulate blood glucose concentrations (Diabetes UK 2006).

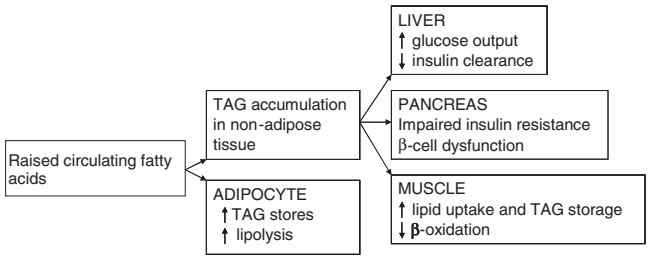


Figure 11 The metabolic effects of circulating fatty acids on glycaemic control. TAG, triacylglycerol.

Excessive intake of fats leads to an accumulation of TAGs in many tissues. This can bring about a number of metabolic disturbances, ultimately resulting in hyperglycaemia (Fig. 11). Dietary management of diabetes includes the recommendation to adopt a 'low fat' diet, although the levels of intake of fat are not essentially very different from those recommended for the general population (Table 14). SFAs should provide less than 10% of total daily energy. SFAs impair insulin sensitivity, possibly because the presence of TAGs containing SFAs in muscle cell membranes reduces the amount of glucose that is taken up from the bloodstream when the concentration of insulin is raised (Montell *et al*. 2001).

However, there is now much interest in the fatty acid profile of the diet and the effect that this can have on insulin sensitivity. A low-fat diet (21% energy from fat) and a high-MUFA diet (35% energy from fat) appear to afford similar glycaemic control (*e.g.* Luscombe *et al*. 1999). This was assessed by fasting glucose concentrations and glycosylated haemoglobin (a marker of longer-

Key points:

Unsaturated fatty acids and diabetes

- Fatty acids have an effect on a number of different metabolic pathways, including those involved with glycaemic control.
- Dietary recommendations for individuals with diabetes are to consume a low saturated fat diet because of the increased risk of developing CVD on diets high in SFAs.
- High-MUFA diets have been associated with improvements in glycaemic control. However, currently there is insufficient evidence to make dietary recommendations.

Table 14 European Recommendations of the Diabetes Nutrition Study Group related to dietary fat

Saturated and *trans*-unsaturated fatty acids should provide under 10% total daily energy. A lower intake (<8% energy) may be beneficial if LDL cholesterol is elevated.
Oils rich in MUFAs are useful fat sources and depending on individual preferences, MUFA may provide 10–20% of total energy, provided that total fat intake does not contribute more than 35% of total energy.
PUFAs should not exceed 10% of total daily energy.
Total fat intake should not exceed 35% of total energy.
For those who are overweight, fat intake below 30% may facilitate weight loss.
Consumption of two to three servings of fish (preferably oil-rich fish) each week and plant sources of *n*-3 PUFAs (*e.g.* rapeseed oil, soybean oil, nuts and some green leafy vegetables) will help ensure an adequate intake of *n*-3 PUFAs.
Cholesterol intake should not exceed 300 mg/day and be further reduced if LDL cholesterol is raised.

Source: Mann *et al.* (2004).

LDL, low density lipoprotein; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.

term glycaemic control). In light of similar findings reported by other researchers, it has been suggested that provided the amount of SFAs in the diet is low, a high-MUFA diet has a similar effect on glycaemic control as a high-carbohydrate/low-fat diet, and may confer some additional improvement in CHD risk factors (see Ros 2003). However, it has been demonstrated that a low-fat, high-complex carbohydrate diet caused weight loss in individuals with type 2 diabetes, which was not observed in individuals fed a high-MUFA diet (Gerhard *et al*. 2004). The low-fat diet did not cause the plasma TAG concentrations to increase and did not worsen glycaemic control. Thus, the researchers concluded that such diets may be very useful in the dietary management of type 2 diabetes due to the improvement in metabolic control known to occur when excess weight is lost (Gerhard *et al*. 2004). Again, it is clear that more research is needed in this area to determine whether the ratio of unsaturated fatty acids is an important consideration when recommending low-fat diets to individuals with diabetes.

4.3 Unsaturated fatty acids and cancer

Approximately 30% of all human cancers may be influenced by diet, lifestyle and physical activity, although the estimate lies somewhere between 10% and 80% (Doll & Peto 1981). Diet is considered to be a major determinant of risk for certain cancers, such as colorectal cancer, where the aetiology is well understood and it is evident that along with physical activity, diet plays a key role. However, for cancers at other sites, such as lung cancer, diet plays a relatively small part in determining the likelihood that an individual will develop the disease, and other factors, including smoking, are better predictors of risk. To date, very few definite relationships between dietary factors and cancer risk have been established; however, this has not stopped numerous foods and food components being branded the new 'superfood' against cancer. In most cases, the strength of the message portrayed by the media and some health professionals is greater than the strength of the evidence associating diet with cancer risk.

Historically, dietary fat has been considered to be one of the main dietary risk factors, and has been reported to influence the risk of developing breast, colon and prostate cancers (WHO 1990). Evidence for this association has mainly arisen from comparisons of cancer incidence rates between populations with different dietary habits (ecological studies); rates being higher in the Western world where intakes of fat, often estimated from food balance sheets, are greater (Shike *et al*. 1990). This is a very imprecise method of detecting diet–disease interactions as there are many confounding factors and their effects are often not taken into account. Thus, the observed association between high fat intakes and increased cancer risk may not be causal. Following publication of more sensitive epidemiological studies, as well as laboratory-based experimental studies, the con-

Table 15 Summary of the evidence linking dietary factors with cancer at all sites

Evidence	Decreased risk	Increased risk
Convincing	Physical activity (colorectum)	Overweight and obesity (oesophagus, breast, endometrium, kidney); alcohol (oral cavity, pharynx, larynx, oesophagus, liver, breast); aflatoxin (liver); Chinese-style salted fish (nasopharynx)
Probable	Fruit and vegetables (oral cavity, stomach, colorectum); physical activity (breast)	Preserved meat (colorectum, oesophagus); salt-preserved foods and salt (stomach); very hot drinks and food (oral cavity, pharynx, oesophagus)
Possible/insufficient	Fibre; soya; **fish**; ***n*-3 fatty acids**; carotenoids; vitamins B_2, B_6, folate, B_{12}, C, D, E; calcium; zinc, selenium, non-nutrient plant constituents (*e.g.* allium, lignans, flavonoids, isoflavones)	**Animal fats**; heterocyclic amines; polycyclic aromatic hydrocarbons; nitrosamines.

Source: WHO/FAO (2003).
Bold, unsaturated fatty acids.

sensus view has drifted towards the possibility of there being an association rather than judging the evidence to be convincing (see Table 15; WHO/FAO 2003).

Cancer is a complex disease requiring multiple gene mutations to occur, usually over many decades (carcinogenesis). Certain fatty acids have the ability to prevent the formation of, inhibit the progression of, or directly kill cancer cells *in vitro* when they are taken from a number of organs (lung, breast, colon, and UV-induced cancer). However, other fatty acids can also promote carcinogenesis, making the mechanism behind any possible association between total dietary fat and cancer more ambiguous.

MUFAs: The work of Keys *et al*. (1986) established that the major explanatory factor for the differences in cancer rates seen in the regions bordering the Mediterranean Sea was the plant-based Mediterranean diet. Trichopoulou *et al*. (2000) estimated that up to 25% of new colorectal cancer cases, 15% of new breast cancer cases and 10% of new prostate cancer cases could be prevented if 'Western' countries adopted a Mediterranean-style diet, *i.e*. a diet rich in fruit, vegetables, fish, legumes, whole grains and, most notably, oleic acid-rich olive oil. Because of this, it was thought that MUFAs might have a protective effect against the development of cancers. *In vitro* studies have suggested that MUFAs reduce the occurrence of molecular biomarkers typically associated with carcinogenesis, *e.g*. lipid peroxidation damage or oxidative stress. However, the Mediterranean diet is different from a traditional Western diet for more reasons than solely its MUFA content. Intakes of fruit, vegetables and whole grains are significantly higher in the countries bordering the Mediterranean, and thus there might be other components of the diet or even the lifestyle that are bringing about the observed health benefits. This discrepancy is evident in the lack of any distinct evidence associating MUFA intakes or serum concentrations with a significant reduction in cancer incidence rates.

The 1997 report of the World Cancer Research Fund (WCRF 1997), entitled *Food, Nutrition and the Prevention of Cancer: A Global Perspective*, concluded that there was a small amount of evidence that MUFAs might influence cancer risk based on the strength of the evidence from epidemiological, intervention and experimental studies.

PUFAs: The role of PUFAs in affecting cancer risk is even less clear. Experimental, laboratory-based studies suggest that PUFAs can act as tumour promoters. PUFAs are susceptible to oxidation, which also generates free radicals that can then go on to damage DNA. In contrast with these lab-based and animal studies, studies in humans have found little evidence of any association between intake of polyunsaturated or vegetable fat and risk of cancer, especially at recommended intake levels (*e.g*. Hunter & Willett 1993; Giovannucci & Willett 1994). However, this is not always the case (Pearce & Dayton 1971), and so in spite of this generally reassuring evidence and the 'no effect' conclusion of a review and meta-analysis on this issue (Zock & Katan 1998), many within the scientific community are still concerned that high intakes of PUFAs may increase the risk of cancers.

With recent interest in specific families of, or even individual fatty acids, associations between cancer incidence and estimated intakes or plasma concentrations of these fatty acids are being investigated. Without doubt, this adds confusion as studies are often not large enough or designed well enough to detect such specific associations and as a result, a number of contradictory findings have been published. It would be prudent to mention that currently, in the opinion of the WCRF (1997), the UK's Department of Health (DH 1998) and the World Health Organization/Food and Agriculture Organisa-

Key points:

Unsaturated fatty acids and cancer

- Unsaturated fatty acids, namely, *n*-3 PUFAs and MUFAs, may be associated with a reduced risk of developing certain cancers, including cancers of the colon, breast and prostate.
- However, the level of evidence is not deemed sufficient by authoritative bodies, such as the WCRF, WHO and the Department of Health, to make any specific dietary recommendations on individual fatty acids and cancer risk.
- Instead, it is prudent to eat a healthy balanced diet that contains plenty of fruit, vegetables and high-fibre, starchy foods, and to try to keep to a healthy weight.

tion (WHO/FAO 2003), there is not enough evidence to make recommendations on the intake of specific fatty acids as a means of preventing cancer.

When cancer incidence rates are compared between countries with very different intakes of particular fatty acids, there is a clear suggestion that fish consumption, providing a source of the long chain *n*-3 PUFAs, decreases cancer risk (Fernandez *et al*. 1999). However, this is one of the least sensitive types of studies that can be conducted as there are so many differences inherent in the populations that cannot be properly accounted for. Over time, increasing numbers of case–control or cohort studies that are assessing differences in breast (*e.g*. Gago-Dominguez *et al*. 2003), prostate (*e.g*. Sonoda *et al*. 2004) and colorectal cancer incidence (*e.g*. Tokudome *et al*. 2006) in subsets of the population exposed to varying amounts of *n*-3 PUFAs are being published. Nevertheless, there is still no consistent consensus on the effect of *n*-3 PUFA, and no dietary recommendations have been made in the context of cancer prevention.

There is very little or no evidence associating intakes of *n*-6 PUFAs (AA or LA) with prostate cancer (Astorg 2004), colorectal cancer (Nkondjock *et al*. 2003) or breast cancer (Kohlmeier 1997) when actual intakes in whole populations are considered. There is certainly laboratory-based experimental evidence showing effects on cancer cell growth (*e.g*. Bartsch *et al*. 1999; Guthrie & Carroll 1999), or tumour formation in animals, but this cannot be extrapolated to the general population and certainly is insufficient to make dietary recommendations.

4.4 Unsaturated fatty acids and inflammatory conditions

Inflammation is a non-specific response to tissue damage. It occurs to protect the tissue from further damage and so, under normal circumstances, is a desirable event. However, if the response is exaggerated, misdirected or long-term, inflammatory conditions can lead to further tissue damage. As mentioned previously, eicosanoids are produced from EPA or AA, which are released from the cell membrane phospholipids. The eicosanoids derived from AA, including prostaglandin E_3 and leukotriene B_5, are more inflammatory than those produced from EPA. Thus a shift in the balance of EPA and AA in the membrane phospholipids might affect the inflammatory response, leading to either a more pro- (AA) or anti-inflammatory (EPA) environment (Calder 1998). There are, however, other mechanisms that have been suggested that exert their effects either downstream of altered eicosanoid production or are independent of this. Such mechanisms include a suppression of the production of pro-inflammatory cytokines or modulation of adhesion molecule expression. In many instances, these effects occur as a result of altered gene expression (see Calder 2005).

There are a number of inflammatory conditions, such as asthma, Crohn's disease or arthritis, which could potentially be alleviated by dietary modification. This is of great interest to individuals living with these chronic conditions as many are unhappy with the prospect of a lifetime of drug treatment. Observational epidemiological studies have highlighted a low incidence of chronic inflammatory or autoimmune disorders in populations of native Greenland Inuits and in Japan, both of which have a high dietary intake of long chain *n*-3 PUFA from seafood (*e.g*. Takemura *et al*. 2002; Backer *et al*. 2004). Researchers have been assessing the efficacy of long chain *n*-3 PUFAs in fish oil and *n*-6 PUFAs found in sunflower oil and evening primrose oil. Very little research has been conducted using MUFAs. In general, the fatty acid composition of cell membranes can be altered by both the *n*-3 and the *n*-6 PUFAs tested, and this results in reduced inflammatory activity. However, whether this effect brings about a significant reduction in clinical symptoms is still unclear.

Asthma

Asthma is a disease in which the circular smooth muscles lining the air tubes of the lung are liable to go into

a state of spasm. When this occurs, the airway is narrowed and breathing becomes difficult. Breathing may be worsened by the excess mucus secretions from the cells lining the lungs. Bronchospasm may be induced by numerous stimuli, including allergic reaction, infection or exertion. The leukotrienes and prostaglandins are implicated in the inflammatory cascade that occurs in asthmatic airways and therefore, as the nature of these eicosanoids are known to be influenced by diet, there may be the potential for dietary management. However, intervention trials to date have been shown little improvement in the clinical manifestation of this disorder. Because of the formation of pro-inflammatory eicosanoids from the *n*-6 PUFAs, it has been hypothesised that the ratio of *n*-6 to *n*-3 PUFAs in the diet will be important. Broughton *et al*. (1997) studied the ability of dietary PUFAs at various ratios of *n*-6 to *n*-3 in an asthmatic population to ameliorate respiratory distress. Low *n*-3 ingestion is reported to increase respiratory distress during an asthma attack. However, beneficial effects of *n*-3 PUFAs were not observed in all individuals who received the supplement. Instead, respiratory improvements were only observed in people with a measurable altered leukotriene excretion.

Clinical intervention studies have provided conflicting results, most likely due to lack of an adequate number of subjects in some and not taking into consideration the background diet or genetic variation. There is a clear need for more carefully designed and controlled clinical trials in the therapeutic application of high doses of *n*-3 fatty acids for the management of asthma (Simopoulos 2002).

Inflammatory bowel disease

Crohn's disease and ulcerative colitis, collectively known as inflammatory bowel disease (IBD), are related but distinct complex disorders with immunologic, environmental and genetic components. Crohn's disease is a long-term illness that causes inflammation in the gut. It can affect any part of the digestive system from the mouth to the anus. The parts most often affected are the ileum and the colon. Symptoms of Crohn's disease include: diarrhoea; abdominal pain; fever; weight loss; and a general feeling of being unwell. It is unknown which factors might trigger the inflammatory response. Ulcerative colitis affects the colon and rectum. Like Crohn's disease, it is unknown exactly what triggers ulcerative colitis, but it is most common in young and middle-aged adults. It is characterised by chronic inflammation and ulceration of the gastrointestinal lining that can lead to anaemia, toxic megacolon (a life-threatening complication of intestinal conditions characterised by a very inflated colon), or colorectal cancer. Many studies have reported the effect of *n*-3 PUFA supplementation on certain clinical outcomes, including sigmoidoscopic score, histologic score, induced remission, and relapse in IBD patients (Endres *et al*. 1999).

When the combined effect from a number of intervention studies was assessed by meta-analysis, it was determined that *n*-3 PUFAs had no effect on the relative risk of relapse in ulcerative colitis patients. There was, however, a statistically non-significant reduction in requirement for corticosteroids for individuals receiving *n*-3 PUFAs relative to placebo. No studies assessed in this meta-analysis evaluated the effect of *n*-3 fatty acids on requirement for other immunosuppressive agents (MacLean *et al*. 2005). Relapse rates in patients with Crohn's disease reduced substantially over a 12-month period, during which patients received a fish oil supplementation (Belluzzi *et al*. 1996).

Although these findings are promising, there have not been sufficient studies to warrant a dietary recommendation regarding the use of *n*-3 PUFAs in the management of IBD and indeed, management of this condition would require supplementation at doses far exceeding those that could be obtained by increasing oil-rich fish in the diet. It is clear that further, larger-scale intervention trials are required before such advice can be given to IBD patients.

Arthritis

Arthritis describes a condition involving the inflammation of the joints. There are more than 200 different types of arthritis, including rheumatoid arthritis, gout and ankylosing spondylitis. The most common form is osteoarthritis (degenerative arthritis). This is caused by general wear and tear of the joints and is unaffected by diet. Rheumatoid arthritis is an inflammatory condition and occurs when the body's immune system starts to destroy the joint lining. Due to the involvement of inflammatory eicosanoids in the aetiology of the disorder, diet may be a potential therapeutic agent.

Ecological studies suggest that there are lower rates of incidence of rheumatoid arthritis in populations consuming large amounts of fish, *e.g.* the Japanese population (Pattison *et al*. 2004). The protective effect of a dietary factor is made even more likely when it is considered that the Japanese population harbours a particular genetic polymorphism that confers susceptibility to rheumatoid arthritis (James & Cleland. 1997). Similar protective effects were reported by a case–control study investigating the occurrence of the disorder in a group of

Key points:

Unsaturated fatty acids and inflammatory conditions

- There are a number of inflammatory conditions, such as asthma, Crohn's disease and arthritis, that could potentially be alleviated by dietary modification.
- The fatty acid composition of cell membranes can be altered by both *n*-3 and *n*-6 PUFAs, and this results in reduced inflammatory activity. However, whether this effect brings about a significant reduction in clinical symptoms is still unclear.
- There is a clear need for more carefully designed and controlled clinical trials in the therapeutic application of unsaturated fatty acids for the potential management of inflammatory conditions.
- To date, beneficial effects are only observed with very high intakes of unsaturated fatty acids, which would realistically only be achievable by supplementation.

Japanese women (Kremer *et al*. 1985). There have been no studies examining the effect of fish or *n*-3 PUFA intakes on the incidence of rheumatoid arthritis. However, several studies have reported on the effect of dietary *n*-3 PUFAs as a treatment for established rheumatoid arthritis.

A recent review of nine intervention trials has reported various clinical outcomes in patients with rheumatoid arthritis (MacLean *et al*. 2004). Supplementation with 1–7 g of *n*-3 PUFAs a day had no significant effect on patient report of pain or swollen join count, *i.e*. there was very little clinical improvement in the symptoms. However, some studies have reported a reduced requirement for corticosteroid or anti-inflammatory drugs, although this did not reach the level required for statistical significance (Kremer *et al*. 1995). Overall, the available data are insufficient to draw conclusions about the effectiveness of *n*-3 PUFAs in the treatment of arthritis (MacLean *et al*. 2004). An interesting new approach to the dietary management of rheumatoid arthritis is to consider a combination of fatty acids. A small-scale randomised controlled trial in only 43 patients reported by Berbert *et al*. (2005) suggested that long chain *n*-3 PUFA supplementation, in conjunction with MUFAs, may be an alternative dietary treatment for rheumatoid arthritis. Clearly, more trials are needed to determine whether this is in fact a significant, reproducible effect, but is an intriguing example of how it may be a combination rather than individual fatty acids that are involved in the pathologies of these inflammatory diseases.

4.5 Unsaturated fatty acids in fetal and infant development

The developing brain grows most rapidly during the third trimester of pregnancy and during infancy. Although different types of brain cell, such as glial cells, astrocytes and cerebral endothelium, can elongate and desaturate precursor EFAs, the mother is the main source of AA and DHA that accumulates in the developing brain. It is therefore important that there is an adequate supply of the long chain *n*-3 PUFAs to the mother during this time to support normal growth, neurological development and cognitive function of the growing fetus (Al *et al*. 1995).

If dietary intake is low, maternal body stores can be mobilised. AA requirements are likely to be met as there is plenty of LA, its precursor, in adipose tissue. However, there is less ALNA, and thus there is a reduced capacity for synthesis of the long chain *n*-3 PUFAs DHA and EPA. The PUFA status of the infant is highly correlated with that of the mother (Smita *et al*. 2000). During pregnancy, EFA concentrations in the mother's blood have been shown to fall by approximately 40%, with a concurrent increase in concentrations of the non-EFAs, as body stores are mobilised and depleted (Al *et al*. 1995). When more than one fetus is developing in the womb, the DHA status of each child is low when measured after birth. This is thought to be because the additional demands on the mother's EFA supply cannot be met adequately. Furthermore, the DHA concentration in the mother's plasma decreases after closely spaced pregnancies. Thus, pregnancy is a time when additional supplies of long chain *n*-3 PUFAs may be of benefit to some women to ensure an adequate supply of long chain *n*-3 PUFAs to the mother and the baby. Ideally women should enter pregnancy well nourished in this respect, having consumed moderate amounts of these fatty acids on a regular basis as part of a healthy balanced diet. This is because there is a possible risk of heavy metal or dioxin contamination of both oil-rich fish and fish oil supplements, which at this especially vulnerable period may affect the development of the unborn child (Hornstra *et al*. 1995). Thus, recommendations exist about the need to restrict intakes of oil-rich fish in women of

child-bearing age to up to 2 servings a week, which is considerably in excess of current average intakes (see *Unsaturated fatty acids in the UK diet*). Also fish oil supplements often contain added vitamin A, which is contraindicated for pregnant women, based on teratogenic risks associated with retinol.

The long chain *n*-3 PUFA status of the mother is of interest as low intakes are believed to be associated with premature delivery and low birthweight. This has been observed in a number of different populations assessed for fish intake, seafood intake and supplement use in mothers (Allen & Harris 2001; Olsen & Secher 2002; Oken *et al*. 2004). A possible mechanism by which long chain *n*-3 PUFAs might affect these factors is by altering the concentrations and types of the different prostaglandins that are involved in parturition. Alternatively, long chain *n*-3 PUFAs may bring about an improvement in blood flow to the placenta, resulting in more efficient transfer of nutrients from the mother to the fetus (Allen & Harris 2001).

After birth, the unsaturated fatty acid status of the infant also seems to be important. DHA and AA are present in human milk at fairly consistent concentrations (0.02 g/100 g), although women from populations that consume diets rich in the long chain *n*-3 PUFAs produce milk containing higher amounts of DHA (see BNF 1992). It is unlikely that the endogenous synthesis of DHA and AA from ALNA and LA respectively, is able to meet the requirements of the growing infant, thus most of these long chain *n*-3 PUFAs must, at this stage, be provided by the diet.

Infant formulas with fat derived from vegetable oil do not contain appreciable amounts of the long chain PUFAs (DHA and AA), and infants fed these conventional formulas have lower plasma AA and DHA concentrations than breastfed babies (Makrides *et al*. 1995). Supplementing formulas with long chain PUFAs increases plasma concentrations and also the proportion of DHA localised in the brain cortex (Makrides *et al*. 1994). Some studies using these supplemented formulas have reported adverse effects, such as reduced post-natal growth, when only DHA was added to the feed (Jensen *et al*. 1997) but, as long as the formula provides an adequate and balanced supply of both AA and DHA or ALNA, there should be no adverse effects on growth (Koletzko *et al*. 2001).

DHA is present in high concentrations in the phospholipids of retinal cell membranes; hence it is believed that the DHA intake is associated with visual function. This is borne out by the observation of Jorgensen *et al*. (2001) that there is a positive association between DHA in human milk and sharpness of sight (visual acuity) during infancy. As mentioned earlier, DHA and AA are also required for healthy neural cell development, and it has been suggested that DHA and AA intakes during infancy may affect cognitive function. Research in this area is still highly speculative, and some small-scale studies have found a positive association (McCann & Ames 2005; also see *Unsaturated fatty acids and cognitive function and behaviour*). However, two fairly recent cohort studies have found no association between DHA or AA concentrations measured in plasma from the umbilical vein and cognitive function at ages 4 or 7 years (Ghys *et al*. 2002; Bakker *et al*. 2003).

In summary, there is moderate evidence that PUFAs, and long chain *n*-3 PUFAs in particular, from either breastmilk or supplemented infant formula, are beneficial in the development of visual acuity and possibly cognitive performance in infants (Bryan *et al*. 2004). Adequate provision of the long chain PUFAs is required throughout pregnancy and early infancy, in order to

Key points:

Unsaturated fatty acids in fetal and infant development

- It is important that pregnant women have an adequate supply of the long chain *n*-3 PUFAs before and throughout pregnancy to support normal growth, neurological development and cognitive function of the growing fetus. As *n*-6 PUFAs are more abundant in the diet, achieving an adequate intake is less problematic.
- The PUFA status of the infant is highly correlated with that of the mother.
- Increasing fish consumption beyond two servings of oil-rich fish per week or relying on fish oil supplementation is not appropriate during pregnancy due to the potential problems associated with heavy metal contamination of fish, or the high vitamin A levels in some fish oil supplements.
- The increased requirements for DHA and AA during pregnancy and lactation will not be met solely by endogenous synthesis from ALNA and LA; dietary supply is also important.
- Breastmilk is a source of DHA and AA, and PUFA-supplemented infant formulas are now available.
- It is possible that the EFA status of the baby may affect visual acuity and cognitive performance during infancy.

provide sufficient DHA and AA for both the growing baby and the mother.

4.6 Unsaturated fatty acids and cognitive function and behaviour

Cognitive function

The brain is not fully developed until late adolescence when children can start reasoning like adults. However, the high DHA and AA concentrations in the brain must be maintained throughout life to ensure proper development and functioning of the central nervous system. Most research on the effect of DHA and AA in the development of cognitive function has focused on preterm infants, with some studies demonstrating beneficial effects on mental development and problem-solving ability (Willatts *et al*. 1998; Birch *et al*. 2000). Controlled intervention trials assessing improvements in older children have been limited to a single study of children with well-defined behavioural disorders. In this case, preliminary associations have been made between low fatty acid intakes and poor reading ability (Richardson & Montgomery 2005).

Epidemiological evidence suggests that dietary consumption of EPA and DHA, commonly found in fish or fish oil, may modify the risk for certain degenerative or neuropsychiatric disorders. As evidence, decreased blood concentrations of *n*-3 fatty acids have been associated with several neuropsychiatric conditions, including Alzheimer's disease, schizophrenia and depression (see Rogers 2001). Supplementation studies, using individual or combinations of *n*-3 PUFAs, suggest the possibility of decreased symptoms associated with some of these conditions. Thus far, however, the benefits of supplementation, in terms of decreasing disease risk and/or aiding in symptom management, are not clear, and more research is needed (Young & Conquer 2005).

Any possible effect on brain function and cognitive development is not limited to PUFAs. The Mediterranean dietary pattern, based on complex carbohydrates, fibre and non-animal fat, appears to be associated with some degree of protection against age-related cognitive decline. A clear reduction in risk of decline in cognitive function has been found only in population samples with very high intakes of MUFA from olive oil (>100 g of olive oil per day). However, whether this effect of olive oil is attributable exclusively to the high MUFA intake or to the concomitant presence of other bioactive food components, such as the antioxidant vitamins or polyphenols, or indeed other aspects of the diet or lifestyle of such individuals, remains to be clarified (Panza *et al*. 2004).

Behaviour

Research in this area is still highly speculative, not least because of the difficulties faced when assessing improvements in behaviour. However, behavioural disorders with well-defined aetiologies, such as attention deficit hyperactive disorder (ADHD), dyslexia, autism and dyspraxia, are possibly associated with errors of fatty acid metabolism. It is proposed that such errors may include: inefficient conversion of simple EFAs into longer chain EPA and DHA; unusually rapid breakdown or loss of these fatty acids; and problems in recycling, transporting and incorporating these long chain *n*-3 PUFAs into cell membranes (Richardson & Ross 2000).

There is very limited published empirical evidence for the beneficial effects of PUFAs on cognitive performance in children or adults. The research in this field, especially that concerning younger children, looks promising, but to date there have been very few published studies, and those that have been published, have tended to be small-scale studies, all with very different study methodologies. For example, plasma concentrations of long chain *n*-3 PUFAs were reported to be significantly lower in a study of hyperactive children compared with controls (Stevens *et al*. 1995). Supplementation studies in small groups of children with ADHD using both long chain *n*-3 PUFAs DHA and EPA at concentrations of approximately 500 mg per day, have shown an improvement in ADHD symptoms after 3 months of treatment (Richardson & Puri 2002). This is longer than observed when conventional pharmacological treatments are used. Childhood developmental and psychiatric disorders are complex multifactorial disorders. However, the study of long chain *n*-3 PUFAs and their metabolism could offer important new approaches to their early identification and management.

EFAs have been shown to benefit adult patients with depression, schizophrenia and dementia. Individuals whose character traits include deliberate self-harm and violence have also seen their symptoms ameliorated by the supplementation of EFAs from fish oil in a number of recent clinical trials (Hallahan & Garland 2004).

In summary, emerging evidence suggests that *n*-3 PUFAs may have a role in the control of the symptoms of neurological disorders such as ADHD and dyslexia (Bryan *et al*. 2004). What is required now are larger-scale, well-designed, well-controlled studies to confirm whether there really is a significant improvement in behaviour when the diet is modified, and at what levels

Key points:

Unsaturated fatty acids and cognitive function and behaviour

- Brain cells are especially rich in the long chain PUFAs DHA (*n*-3) and AA (*n*-6). This has led to the suggestion that dietary status of these long chain fatty acids might influence cognitive function and behaviour.
- Research in this field is still in its early stages, but there is a small amount of evidence to show improvements in cognitive function following fatty acid supplementation.
- It has been suggested that plasma concentrations of individual or combinations of fatty acids may reflect the incidence of certain mental disorders. The relevance of this still needs to be confirmed.
- Larger-scale, well-designed studies are required to confirm whether there really is a significant improvement in behaviour when the diet is modified.

of supplementation these effects are observed (Richardson 2004).

4.7 Emerging aspects of unsaturated fatty acids and health

Natural genetic variation (polymorphisms)

The study of interactions between nutritional and genetic factors is a new and important area of research. Indeed, one of the explanations of the inconsistencies between the findings of epidemiological studies may be slight genetic differences in populations that affect how individuals respond to changes in the fatty acid profile of their diets. Increased knowledge in this area and new techniques for measuring gene expression, gene polymorphisms, protein expression and metabolic profile will eventually allow a more refined approach to reducing risk for many different diseases, with diet interventions targeted towards individuals and subgroups that are genetically susceptible and responsive to the effects of nutritional factors. However, the search for candidate genes has proved to be more complex and their identification more elusive than originally thought, largely because much of the variation in risk results form interactions between environmental factors and the genome.

Nevertheless, there are several candidate genes that have been identified in the context of interactions with dietary fat that appear to determine an individual's risk of developing disease when exposed to different dietary fatty acids. One of the best understood is the interaction of the apoE gene. Apolipoprotein E is a component part of chylomicrons, which facilitates binding to specific receptors on peripheral liver cells. ApoE is essential for the normal metabolism of TAG-rich lipoprotein constituents. There are at least three slightly different versions of the apoE protein; the major versions are called E2, E3 and E4. These lipoproteins are encoded by slightly different versions of the apoE gene (alleles); the major versions are called ε2, ε3 and ε4. The most common allele is ε3, which is found in more than half of the population. However, in the UK population, approximately 25–30% of the population carry at least one copy of the apoE ε4 allele. These individuals have a higher total and LDL cholesterol concentration than individuals carrying two copies of the apoE ε3 allele, and are thus at an increased risk of developing atherosclerosis. People who carry two copies of the apoE ε2 allele are at risk for a condition known as hyperlipoproteinemia type III. This condition is characterised by increased levels of cholesterol, TAGs, and molecules called very low density lipoproteins (VLDL), which carry cholesterol and lipoproteins in the bloodstream. The influence of habitual SFA intakes on blood lipoprotein concentrations varies according to an individual's genetic makeup. SFAs increase LDL cholesterol in virtually all individuals. However, the higher SFA intake was associated with higher VLDL cholesterol and lower HDL cholesterol in carriers of the apoE ε2 gene compared with other subgroups. By contrast, carriers of the apoE ε4 gene had lower VLDL cholesterol and higher HDL cholesterol concentrations (*i.e.* a more favourable blood lipid profile) for the same intake of SFAs. These data demonstrate how the effect of a high saturated fat diet could be modulated by the apoE allele that an individual carries (Campos *et al.* 2001). It has been suggested that the apoE gene variant determines how individuals respond to fish oil supplementation. Despite a marked reduction in blood triglycerides, intakes of 3 g long chain *n*-3 PUFAs caused a 15% increase in LDL cholesterol concentrations in subjects carrying the apoE ε4 allele compare to those homozygous for ε3 (Minihane *et al.* 2000). However, despite a 7% increase in LDL cholesterol following supplementation with 0.7 g DHA, no effect of apoE genotype was observed on LDL concentration

(Theobald *et al.* 2004). Therefore, further research is warranted in this area to determine the true effect of *n*-3 PUFAs on LDL cholesterol, as there may be pertinent implications for population recommendations regarding increased long chain *n*-3 intakes.

Currently, personalised dietary advice to reduce risk of disease based on an individual's genetic profile is the focus of much debate. However, before bringing individuality to public health recommendations, numerous research questions on the role of specific fatty acids in the population's diet need to be addressed. Indeed, in the short-term it may be more appropriate to better personalise nutrition advice to the profile of CVD risk markers, such as high blood pressure, abnormal blood lipids or insulin resistance, instead of relying on large advances in nutrigenomic research.

Conjugated linoleic acid (CLA)

CLA describes a group of isomers of linoleic acid (an *n*-6 PUFA) in which the double bonds are located adjacent to each other at carbons 10 and 12, or 9 and 11. CLA is found naturally in the meat and milk of ruminant animals. CLA has received considerable attention following the publication of data from animal experiments that report anti-carcinogenic, anti-atherogenic and anti-diabetic properties (see Tricon *et al.* 2005). There have also been reports of CLA's ability to reduce body fat and immune function. Several studies of CLA supplementation in human subjects have now been published, but in contrast with animal studies, there has been much variation between reports on the health-related outcomes. Indeed, it has even been suggested that the *trans* isomers of CLA may well have adverse effects on health, especially with respect to insulin sensitivity and blood lipids. Before recommendations for CLA supplementation can be made, more controlled studies in specific populations with purified isomers of CLA are required.

Gamma linolenic acid (GLA)

GLA is an *n*-6 PUFA found naturally in human milk, evening primrose oil (7–10 g GLA/100 g), blackcurrant oil (15–20 g GLA/100 g) and borage oil (18–26 g GLA/100 g). Interest in GLA has grown since the discovery that some individuals have a limited capacity for conversion of LA to GLA (see Fig. 5). It has been suggested that reduced GLA formation may be associated with a diversity of conditions, including: ageing; diabetes; calcium, zinc or vitamin B_6 deficiencies; high cholesterol; rheumatoid arthritis; cancer; CVD and pre-menstrual syndrome (Bolton-Smith *et al.* 1997). GLA supplementation may be advantageous in these individuals as it is believed that it is the elongation product of GLA, dihomo-γ-linolenic acid, that accumulates after supplementation rather than AA. Thus the production of the pro-inflammatory eicosanoids from AA is attenuated. This may have the effect of alleviating some of the symptoms of these various conditions. However, not all researchers agree with this hypothesis, and it is clear that there are large gaps in our understanding of the effect of GLA. Thus, further research in this area is required before dietary recommendations can be made (Fan & Chapkin 1998).

5. Unsaturated fatty acids and public health

5.1 Labelling of unsaturated fatty acids

Currently, it is not mandatory to include information about the nutrient content on a food item unless the manufacturer wishes to make a nutrition claim. Although labelling is voluntary, the format of nutrition labelling on pre-packed foods is dictated by law (see BNF 2002) and must take one of two formats. The minimum amount of information that can be declared on a label is termed a group 1 declaration (which lists the energy, protein, carbohydrate and fat content of a food per 100 g or 100 mL; nutrition information may also be provided on a per-serving basis). Further information can be included in the form of a group 2 declaration (which lists group 1 nutrients plus sugars, saturates, fibre and sodium; see Fig. 12). MUFAs and PUFAs may also be declared within a food label, but only if the SFA

NUTRITION INFORMATION		
	Per 47 g	Per 100 g
Energy	689 kJ	1466 kJ
	163 kcal	347 kcal
Protein	4.7 g	10 g
Carbohydrate	26.9 g	57.2 g
(of which sugars)	3.1 g	6.6 g
Fat	4.1 g	8.7 g
(of which saturates)	0.6 g	1.3 g
Sodium	0.2 g	0.4 g
Fibre	7.8 g	16.6 g

Figure 12 An example of the layout of a typical nutrition information panel on a UK food item.

content of a food is also declared (this would therefore require a group 2 declaration). Information on any other nutrients must be provided if a claim has been made about it and if labelling regulations permit its inclusion in the nutrition panel.

Currently, there are no regulations in the UK regarding whether food manufacturers may claim that a food is a source of, or rich in, unsaturated fatty acids. Recently, however, the Joint Health Claims Initiative (JHCI), having assessed the scientific data relating to long chain *n*-3 PUFAs and CHD, approved the use of a generic health claim, relating to the long chain *n*-3 PUFAs (EPA, DPA and DHA) on pre-packed foods and associated advertising material. The following statement is permitted as long as the food provides at least 0.2 g of long chain *n*-3 PUFAs per serving and as long as certain other conditions are met: '*eating 3 g weekly, or 0.45 g daily, long chain omega-3 PUFAs, as part of a healthy lifestyle, helps maintain heart health*' (JHCI 2005). The JHCI is a joint venture between consumer organisations, enforcement authorities and industry trade associations in the UK to establish a Code of Practice for health claims on food. The Code is not seeking to replace food legislation; instead, it was established in the absence of legislation in an attempt to provide effective consumer protection and consistency in the use of health claims in the UK.

However, legislation in this area is imminent, and in preparation for this, The European Commission has requested the EFSA to issue an opinion on the scientific substantiation of nutrition claims relating to 'omega-3 fatty acids', MUFAs, PUFAs and unsaturated fatty acids, thereby quantifying the criteria that products would have to meet to be labelled as a 'source of omega-3' or 'high in polyunsaturated fat'. The health claims directive was presented to the European Parliament for its second reading in January 2006.

5.2 Are current UK recommendations adequate?

Back in 1992, when the BNF established a Task Force to evaluate the existing UK recommendations for intakes of unsaturated fatty acids, the situation was somewhat different from that found today. At that time, the main driver for setting dietary fat guidelines was to achieve a reduction in plasma LDL cholesterol, and the SFA intake was a major focus. Little or no account had been taken of other factors, such as plasma TAG concentrations, HDL cholesterol, fibrinogen, platelet aggregation and endothelial function, which are all now accepted to influence CVD risk. Thus, many of the recommendations made by the Task Force were: to better define intakes of the *n*-3 PUFAs, to look more carefully at the intakes of the individual *n*-6 PUFAs, and to consider the implications of the *n*-6 to *n*-3 ratio.

Today, following the SACN/COT report in 2004, we have dietary guidelines that take into account the role of the long chain *n*-3 PUFAs in maintaining a healthy heart. However, the subject of dietary fat has become even more complex. Fat is the most energy-dense nutrient, and some would see it as being rather irresponsible to encourage an increase in the consumption of any type of fat owing to the rising levels of obesity that we are currently experiencing around the world. Unless there is a clear message to simultaneously reduce the total amount of fat in our diets, while also substituting PUFAs and MUFAs for some of the remaining SFAs, some people may inadvertently increase their intake of total fat as well as the 'good fats', resulting in an increase in total energy intake and consequently exacerbating the obesity problem. Also nutritionists and dietitians recognise that consumption of oil-rich fish is not currently acceptable to a large proportion of the population (see *Unsaturated fatty acids in the UK diet*). The SACN/COT recommendations largely assume that the long chain *n*-3 PUFAs will be achieved by eating oil-rich fish. Although the Committees acknowledged that certain groups of the population do not eat fish, no specific recommendations were made for these individuals. Thus, it is pertinent to consider how the guidelines could be translated for those individuals who choose not to eat fish. Few health professionals would be comfortable recommending supplement use as the only alternative to fish, as this can be expensive and goes against the idea that all the nutrients that our bodies require can be obtained from the food that we eat. Alternative options are discussed in more detail in the subsection below.

Another point worth bearing in mind is that if supplements or fortified foods are a solution for achieving adequate *n*-3 PUFA intakes, what then is the correct level of intake that non-fish eaters should be aiming for? Are non-fish sources as efficient in delivering the health benefit, or is there some other dietary factor in oil-rich fish as well as long chain *n*-3 PUFA, which is bringing about the benefit? This query has arisen because although benefits of long chain *n*-3 PUFAs can be achieved by dietary means (*i.e.* by eating the recommended amounts of oil-rich fish to achieve an intake of 0.45 g/day), relying on supplements appears to require much higher intakes according to the results of supplementation trials (see Buttriss 2005a). The SACN/COT report considered this and noted that intakes of approximately 1 g/day were sufficient for a beneficial effect in

Table 16 Dietary guidelines relating to daily fat consumption (% of energy)

	USA and Canada	Europe (EURODIET)	FAO/WHO	UK
Fat	20–35	<30	35	<35
n-3 PUFA	0.6–1.2	200 mg DHA/EPA; 2 g ALNA	LA : ALNA = 5:1–10:1	>0.2 (450 mg DHA/EPA)
n-6 PUFA	5–10	4–8	4–10	>1

Source: DH (1991); FAO (1994); FNB (2005); Kafatos & Codrington (1999); SACN/COT (2004).
ALNA, α-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; LA, linoleic acid; PUFA, polyunsaturated fatty acid.

secondary prevention trials. However, higher levels of intake (approximately 3 g/day) were required to see improvements in some cardiovascular risk factors (SACN/COT 2004).

The most recent guidelines relating to fatty acid intakes are those published by the National Academy of Science (USA) in 2005. Here, as well as stating intakes to prevent deficiency, they also recommended acceptable micronutrient distribution ranges (AMDR), which take into account the possible health benefits while keeping in mind the high energy content of fat (Table 16). No dietary reference intakes have been set for MUFAs as it was considered that they are '*synthesized by the body and have no known independent beneficial role in human health and are not required in the diet*' (FNB 2005). However, recommended dietary amounts were set for the PUFAs LA and ALNA. The terminology used by the National Academy of Sciences is different from that which we use in the UK. In the USA, the acceptable intake (AI) for the *n*-6 PUFA LA is 5% of energy (17 g/day for men and 12 g/day for women). Additionally, an acceptable range of intakes has been defined; intakes above or below the boundaries of this range may potentially increase the risk of chronic diseases and affect long-term health. The upper boundary was set at 10% of energy as: this is much higher than most individual intakes; there is little epidemiological evidence investigating the safety of diets containing more than 10% of energy as *n*-6 PUFAs; and very high intakes of *n*-6 PUFA may create a pro-oxidant state that might increase the risk of chronic disease.

Meanwhile, for the *n*-3 PUFA ALNA, the AI is 0.6% of energy (1.6 g/day for men and 1.1 g/day for women), and they specifically state that 10% of this figure for ALNA can be consumed as EPA and DHA (*i.e.* 0.16 g using the value for men). The upper boundary of the AMDR is 1.2% of energy, and this is defined the highest individual intakes. The publication acknowledges the '*growing body of evidence [that] suggests that diets higher in ALNA, EPA and DHA may afford some degree of protection against CHD*'. Based on the suggestion that DHA and EPA should make up 10% of the ALNA intake, recommendations for intakes of DHA and EPA (0.16–0.32 g/day) are, therefore, lower than the 0.45 g per day recommended in the UK.

Looking at dietary recommendations elsewhere around the world, in Europe an expert committee brought together for the EURODIET project, recommended that dietary fat should contribute no more than 30% of energy intake, that *n*-6 PUFA should contribute 4–8% of energy, and that diets should contain 2 g of ALNA each day and 200 mg of the long chain *n*-3 PUFAs. Also, the FAO advises similar levels of intake, although they recommend an optimal ratio of LA to ALNA rather than a value for *n*-3 PUFAs alone (Table 16).

It is apparent from Table 16 that a variety of different approaches are currently being taken to define appropriate intakes of unsaturated fatty acids (see Buttriss 2005b).

5.3 Opportunities to increase intakes of long chain *n*-3 PUFAs

Increasing consumption of oil-rich fish (*e.g.* salmon and mackerel) is the most obvious way of increasing intakes of EPA and DHA. However, this presents a number of barriers: many people do not like the taste of oil-rich fish or avoid it because of lingering cooking smells; there are concerns about the sustainability of global fish stocks; there are concerns over the presence of persistent environmental pollutants in oil-rich fish; and also some people perceive oil-rich fish to be expensive although this is not necessarily the case. Furthermore, vegans and some vegetarians do not consume fish because of personal or religious beliefs.

There are a number of other ways in which intake can be increased:

- dietary supplements providing long chain *n*-3 PUFAs;
- foods enriched with long chain *n*-3 PUFAs;
- foods originating from animals fed on diets enriched with long chain *n*-3 PUFAs;
- novel sources of unsaturated fatty acids.

Supplements

Fish oil supplements are an effective way of increasing intakes of EPA and DHA. However, supplements should not take the place of a healthy balanced diet, and a dietary change to increase intakes of oil-rich fish is the preferred option. There are also concerns regarding the potential presence of persistent environmental contaminants in some fish oil supplements. Also, fish oil supplements are not acceptable to some groups of the population, such as vegans and some vegetarians. Supplements containing DHA derived from microalgae, which are suitable for vegetarians and vegans, are available in the UK, but not widely, and tend to be expensive.

Enriched foods and other functional foods

The addition of long chain *n*-3 PUFAs to commonly consumed foods is one way of increasing their consumption in the diet. Foods that have been successfully enriched with long chain *n*-3 PUFAs (through the addition of either fish oil or algal oil) include breads, mayonnaise, margarines and fat spreads, pasta, milk, infant formula, juice and soft drinks (Jacobsen 2004). However, some of these foods have suffered poor sales and are no longer available on the global market.

There are problems associated with the addition of long chain *n*-3 PUFAs to foods, as they are prone to oxidation. This can result in fishy, metallic flavours and the production of free radicals and reactive aldehydes, both of which have adverse effects on human health. A number of factors, including the presence of oxygen, antioxidants, salt, trace metals and moisture, pH, the viscosity of the food and temperature, all influence a food's susceptibility to oxidation. Such factors need to be considered when developing foods enriched with long chain *n*-3 PUFAs and any problems overcome (Jacobsen & Bruni-Let 2006).

Margarines and other spreads enriched with *n*-3 PUFAs are a useful vehicle for increasing intakes of these fatty acids. Currently, such products that have been enriched with ALNA from linseed oil are available. Increasing the amount of ALNA, at the expense of LA, in margarine and fat spreads increases the chance of oxidation, as the number of unsaturated double bonds in the molecule is greater. Manufacturers add antioxidant compounds to spreads to combat this problem; it is also important that good manufacturing processes are adhered to as a number of other factors, including temperature, can influence risk of oxidation, and such factors must be controlled for (Upritchard *et al.* 2005).

It is also possible to manipulate the fatty acid composition of foods of animal origin by changing the diets of livestock, resulting in foods with a fatty acid profile more conducive to human health (Givens & Gibbs 2006). Such work forms the focus of two workpackages within the European Union (EU)-funded *Lipgene* project, which is endeavouring to find out more about the aetiology and the role of diet in the development of the metabolic syndrome. The project also aims to produce plant and animal foods (*i.e.* seed oils, meat and milk) with a modified fatty acid composition, which have the potential to reduce the prevalence of the metabolic syndrome and relieve some of the public health pressures associated with it (see Buttriss & Nugent 2005; Nugent 2005).

Novel sources of unsaturated fatty acids

Micro-organisms, such as fungi, are capable of synthesising PUFAs. The production of PUFAs from micro-organisms has been extensively reviewed by Sanders & Theobald (2006). Zygomycetes, a group of lower fungi, can accumulate the *n*-6 PUFA GLA. The zygomycetes fungus, *Mortierella alpina*, is capable of synthesising AA, and this has been grown in culture and commercially exploited. The 'single cell' derived oil end-product typically contains 49% AA by weight. Such sources of AA are currently being used in infant formulas and sold as dietary supplements. *M. alpina*, if supplemented with LA, is capable of synthesising EPA rather than AA, but this is a costly and lengthy exercise and therefore not economically viable.

Marine algae, notably microalgae, are capable of synthesising long chain *n*-3 PUFAs, and are the primary source of EPA and DHA present in oil-rich fish, as these fatty acids pass up the food chain following consumption by fish. Dinoflagallates can be grown in culture and used commercially to produce long chain *n*-3 PUFAs, but care must be taken to select strains that do not produce toxins. The dinoflagallate species, *Crypthecodinium cohnii*, is commercially exploited to produce an oil that is 40–45% DHA and virtually devoid of EPA. Again, this oil is used in infant formulas and also dietary supplements. Thraustochytrids are another microalgal source of long chain *n*-3 PUFAs, and *Schizochytrium spp.* are able to synthesise large amounts of DHA and also the *n*-6 fatty acid DPA (22:5*n*-6). DHA produced from this source has been approved for use in foods, and single cell oils produced from micro-organisms are considered to be suitable for vegetarians and vegans.

In the EU, these 'single cell' oils produced from micro-organisms are considered novel foods as they do not have a significant history of consumption within the EU before May 1997. All novel foods must undergo a pre-market assessment for safety before they are permitted for consumption within the EU. Certain single cell oils have been assessed and passed by the UK's Advisory Committee on Novel Foods and Processes and, as a result, are considered safe and their use permitted within the EU. The US Food and Drug Administration has also given certain single cell oils 'generally regarded as safe' status. While it is economically viable to produce both AA and DHA of a high purity from micro-organisms, it is not currently possible to produce EPA in economical amounts.

Genetic engineering of oil seed crops that synthesise LA or ALNA is another avenue that is being explored in a bid to find a sustainable and economically viable source of long chain *n*-3 PUFAs. Higher plants are capable of synthesising PUFAs (predominantly *n*-6 PUFAs and to a lesser extent, *n*-3 PUFAs) but not long chain PUFAs of carbon chain length of 20 or more. The addition of biosynthetic genes from micro-organisms encoding for the synthesis of long chain *n*-3 PUFAs into suitable oil seed crops is currently being explored (see Graham *et al*. 2004; Napier & Sayanova 2005). Genes encoding for elongase and desaturase enzymes involved in the biosynthesis of EPA and DHA have been identified and isolated in fungi and algae, and inserted into suitable oilseed crops (*e.g.* linseed). The synthesis of both AA and EPA from endogenous LA and ALNA has been successful in transgenic crops, but yields of EPA in particular have been low.

Current research is attempting to increase yields of EPA in transgenic plants. The ultimate goal of the genetic engineering of oil seed crops is the synthesis of DHA; additional genes capable of elongating and desaturating EPA are required for this. Such genes have been identified and functionally characterised, but there are a number of constraints that need to be overcome in order that transgenic oil seed crops can accumulate DHA. Such research will form the focus of much anticipated research, including work being conducted within the *Lipgene* project (Napier & Sayanova 2005). There is also the potential to genetically modify micro-organisms to produce specific unsaturated fatty acids. Despite the health benefits it might provide, currently there is a lot of resistance to genetic engineering in Europe, and it may be some time before the practice is accepted by the public and the potential benefits realised.

5.4 Implications of optimising intakes of unsaturated fatty acids

It will be clear that there are several, valid reasons why we should be looking at increasing our intakes of certain fatty acids. However, there are concerns that pressing for intakes of unsaturated fatty acids to increase may, inadvertently, bring about other problems, if the public health message is not clear and consistent. What is required by the majority of the public is a shift in the proportions of the fatty acids that make up our diet, alongside a decrease in total fat consumption. MUFAs, *n*-6 and *n*-3 PUFAs should be substitutes for dietary SFAs in our diets, rather than consumed in addition. If too much emphasis is placed on the health benefits of the 'good fats', then the risk is that people may actually increase their total fat intakes, while believing that they are making positive dietary changes for their future health.

Some concern has been expressed about the potential for intakes of *n*-6 PUFA to exceed the upper limit set for individuals of 10% of energy intake, despite there being very little epidemiological evidence that considers the risks of consuming diets high in PUFAs. To date, much of the concern has been based on the fear that high intakes of PUFA might lead to a pro-oxidant environment that may increase risk of CHD and cancer. A small minority of individuals already consume high amounts of PUFAs, at levels close to the recommended upper limit for individuals. The fear is that the upper limit might be exceeded if *n*-6 PUFA intakes were to increase further. However, this is not of great concern for the majority of the population as average intakes of *n*-6 PUFA are just below the population recommendation of 6.5% of energy. Indeed, it has been suggested that provided intakes of total fat are below the recommended 35% of energy, it is virtually impossible to reach *n*-6 PUFA intakes of 10% or higher (Astorg 2004).

As previously mentioned, although fish oil supplementation provides a useful source of long chain *n*-3 PUFA, most nutritionists and dietitians prefer to advocate dietary sources of nutrients. In this instance, product reformulation (*e.g.* to incorporate oil-rich fish such as salmon in fish-based ready meals) and enrichment of foods with these fatty acids (*e.g.* eggs and meat through modifications to animal-feeding practices) can be rational alternative approaches. It is of some concern that fatty acids are added to foods not usually associated with fat, such as orange juice or bread, as this may confuse customers about the natural sources of these fatty acids, and consequently make it harder for them to learn how to make appropriate substitutions elsewhere in

Key points:

Unsaturated fatty acids and public health

- There is no legal requirement to include information about either total fat or the types of fatty acids on a food label. However, if information is provided, legislation determines the format to be used.
- There is currently no specific legislation to control the use of health claims relating to the fatty acid content of foods. However, an EU Directive is expected imminently which will formally set down the criteria that a product will have to meet in order to make any nutrition or health claim.
- The UK recommendations on fat intakes are in line with those around the world. However, as a population, we need to increase our consumption of long chain *n*-3 PUFAs and decrease SFA intakes.
- Food technologists are looking at ways in which the fatty acid profile of a food can be modified in order to bring dietary improvements without requiring a major change in dietary habits.
- Public health messages surrounding the optimum intakes of fatty acids must be clear and consistent to ensure that a favourable change in the fatty acid profile of the UK diet occurs.

their diet. Such initiatives require clear labelling supported by a strong public health message; it is not sufficient simply to draw attention to the presence of the 'good fat' using colourful messages on the front of pack.

It is also essential that upper limits of intake are considered as, over the course of a day, individuals may inadvertently consume a substantially higher amount of long chain *n*-3 PUFAs by incorporating a number of enriched foods into their diet. In the UK, there is currently no recommendation for a safe upper limit for of *n*-3 PUFAs, as historically intakes have been so low that there has been little concern of overdose. In the USA, a maximum level of intake has been set as 3 g per day, and it is very important that this issue is also given consideration in the UK.

Health implications of the n-6 to n-3 ratio

If the general public take on advice to increase consumption of *n*-3 PUFAs, the ratio of *n*-6 to *n*-3 PUFAs in our diets is likely to decrease. As has been mentioned previously, it has been suggested that the ratio of *n*-6 to *n*-3 fatty acids in the diet may be an important risk factor for CHD. This hypothesis is mainly derived from ecologic data that suggest that as intakes of *n*-6 PUFAs have increased and intakes of *n*-3 PUFAs have decreased over the past 150 years, there has been a parallel increase in the incidence of CHD in the developed world (see Simopoulos 1999; Kris-Etherton *et al.* 2000). Both *n*-6 and *n*-3 PUFAs compete for the same enzymes involved in fatty acid desaturation and elongation (see *What are unsaturated fatty acids?*), so it is thought that an increase in dietary *n*-6 PUFA in the diet may lead to an increase in the production of prothrombotic rather than antithrombotic metabolites, increasing the risk of CHD (Chan *et al.* 1993; Freese *et al.* 1994; James *et al.* 2000). Furthermore, if intakes of LA are high, there may be a reduced capacity for ALNA conversion to the cardioprotective fatty acids EPA and DHA.

However, few studies have investigated the influence of the relationship between *n*-3 and *n*-6 fatty acids and risk of CHD and, as yet, the ratio of *n*-6 to *n*-3 fatty acids associated with a reduced risk of CHD has not been determined. Indeed, some question whether it is physiologically relevant. Mozaffarian *et al.* (2005b) have recently reported no influence of EPA and DHA intakes relative to *n*-6 PUFAs on risk of CHD in men. Similarly, another recent large cohort study has reported no significant increase in CVD death in men with the highest *n*-6 to *n*-3 ratio when compared with those men with the lowest (Laaksonen *et al.* 2005). What is becoming increasingly clear is that both *n*-3 and *n*-6 PUFAs have independent health effects in the body, and as intakes of the *n*-6 PUFAs are within the guidelines for a healthy diet, concerns about the *n*-6 to *n*-3 ratio are driven by low intakes of *n*-3 rather than high intakes of *n*-6. In fact, it may not be that useful to talk in terms of a ratio, as this might bring about a reduction in intakes of *n*-6, which would be unnecessary and even undesirable. If the population were to meet the guideline intakes for the unsaturated fatty acids, the ratio would automatically be 5:1, so perhaps it would be more useful to talk in terms of absolute amounts, rather than in terms of a ratio that is very difficult to interpret.

6. Conclusions

Unsaturated fatty acids are now a nutritional hot topic, and their presence in foods has attracted both public and industrial interest. There are undeniable benefits, in terms of CVD prevention, that can be obtained if dietary SFAs are reduced, and some of the remainder sub-

stituted with both MUFAs and PUFAs. There are also a number of new and emerging areas where dietary unsaturated fatty acids may play a role in affecting an individual's risk of developing other diseases, including diabetes, inflammatory conditions such as rheumatoid arthritis or asthma, and perhaps even cancer. What we are currently lacking is the cumulative evidence that is needed to begin to make specific dietary recommendations. No doubt over the next decade, increasing numbers of trials will be conducted and will hopefully shed some more light on these newer aspects of unsaturated fatty acids in health and disease, so that appropriate public health messages can be developed. However, it is looking increasingly likely that intakes required for improvements in some disease risk factors are substantially higher than those that could be feasibly obtained from the diet. This raises the issue that supplementation might be the only way to achieve these high intakes, an approach that is not automatically favoured by most nutritionists or dietitians.

New developments in the determination of optimal fatty acid status aside, there are currently many other issues surrounding fatty acid intakes that have to be faced. In the UK, intakes of the long chain *n*-3 PUFAs are substantially below recommended intakes, and this may have implications for heart health. As the best sources of the long chain *n*-3 PUFAs are oil-rich fish and currently only 27% of the population consumes oil-rich fish, it is unlikely that the situation will change unless there is a massive shift in food preferences. One possible solution lies in food technology. Currently, food technologists are looking at ways in which the fatty acid profile of a food can be modified in order to bring about dietary improvements without requiring a major change in dietary habits. Foods commonly consumed in the UK diet, such as milk, eggs, meat and spreads, are targets for fatty acid enrichment, where the fatty acids are added either during processing or at an earlier stage in the food's production. Alternatively, novel sources of the long chain *n*-3 PUFAs that might form the basis of future food ingredients are being investigated.

It is clear that this is a fast-moving area of nutrition research. It may also be influenced by our understanding of natural human genetic variation and the interplay between these polymorphisms and our diet. We have already seen examples where individuals carrying specific gene variants respond differently to dietary interventions; advances in this area may ultimately allow more tailored and targeted diets. However, such developments are a long way off and in the meantime, it is vital that public health messages surrounding the optimum intakes of fatty acids must be clear and consistent to ensure that a favourable change in the fatty acid profile of the UK diet occurs.

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Appendix 1

Food groups in the National Diet and Nutrition Survey – main contributors to fat intake are highlighted in bold

Cereals & cereal products	Pasta; rice; **pizza**; **white bread**; wholemeal bread; soft grain bread; other bread; wholegrain & high fibre breakfast cereals; biscuits; fruit pies; buns, cakes & pastries
Milk & milk products	**Whole milk**; **semi-skimmed milk**; skimmed milk; cream; other milk; **cheese**; **cottage cheese**; fromage frais; yogurt; other dairy desserts; ice cream
Eggs & egg dishes	Eggs; egg dishes
Fat spreads	**Butter**; **block margarine**; **soft margarine**; **polyunsaturated margarine**; **polyunsaturated oils**; **otheroils & cooking fats**; **polyunsaturated low fat spread**; **other low fat spread**; **polyunsaturated reducedfat spread**; **other reduced fat spread**
Meat & meat products	**Bacon & ham**; **beef**, **veal & dishes**; **lamb & dishes**; **pork & dishes**; **coated chicken & turkey**; chicken & turkey dishes; liver, liver products & dishes; **burgers & kebabs; sausages**; **meat pies & pastries**; **other meat & meat products**
Fish & fish dishes	**Coated and/or fried white fish**; other white fish & dishes; shellfish; **oil-rich fish**
Vegetables (excluding potatoes)	Raw carrots; other raw & salad vegetables; raw tomatoes; peas; green beans; baked beans; leafy green vegetables; carrots – not raw; tomatoes – not raw; vegetable dishes; other vegetables
Potatoes & savoury snacks	**Potato chips**; **other fried or roast potatoes & products**; potato products – not fried; other potatoes & potato dishes; **savoury snacks**
Fruit & nuts	Apples & pears; citrus fruits; bananas; canned fruit in juice; canned fruit in syrup; other fruit; nuts & seeds
Sugar, preserves & confectionery	Table sugar; preserves; sweet spreads, fillings & icings; sugar confectionery; **chocolate confectionery**
Drinks	Fruit juice; soft drinks; alcoholic drinks; tea; coffee; water
Miscellaneous	Powdered beverages; soups; sauces; condiments and artificial sweeteners