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Perspectives on Animal Biosciences

Should animal fats be back on the table? A critical review of the human health effects of animal fat

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Abstract. Humans hunt or raise a wide variety of animals for meat, which vary from free-range to intensively reared. These animals form a valuable part of human nutrition. Their tissues, including the fat, contain vitamin and other essential nutrients necessary for health. However, animal fat from ruminants and other land mammals is usually regarded as saturated. The purpose of this review is partly to examine the basis for the saturated fat hypothesis of cardiovascular disease given more recent research, to examine the human health effects of animal fats, and partly to draw into one place the diverse knowledge about animal fat and the effects of fat on metabolism. Mechanistic understanding of the initiation of the fatty streak and atherosclerosis calls into question the avoidance of ruminant or porcine fat. Due to high levels of oleic acid, a low n-6 : n-3 fatty acid ratio in some groups, and the presence of specific micronutrients including vitamins and essential fatty acids, animal fats are of benefit in human nutrition. Animal fats can be obtained in minimally processed form making them a convenient source of energy and micronutrients.

Additional keywords: cardiovascular disease, docosahexaenoic acid (DHA), ketogenic, obesity, saturated fat.

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Introduction

What butter and whiskey will not cure there's no cure for – Irish Proverb

'For example, in Framingham, Mass, the more saturated fat one ate, the more cholesterol one ate, *the more calories one ate*, the lower the person's serum cholesterol.' – William Castelli, 3rd Director of the Framingham Heart Study (1992).

Humans have used animals and animal products for food including fish, seafood, insects, birds, reptiles, and mammals since time immemorial. These are either caught wild, are harvested as free-range animals, or are raised at varying degrees of intensity for a wide range of markets. They are a source not only of nutrition but also of gustatory pleasure, and many are symbols or are eaten during special occasions. But, with high rates of cardiovascular disease (CVD) and, more recently, high rates of obesity in the West, first fat of all kinds and then saturated fat have been put under the microscope as aetiological agents in chronic disease. Many observers have noted that the trend of usage of animal fats has been in the opposite direction to the rise in CVD or obesity (Yudkin 1957; Antar *et al*. 1964; Kritchevsky 1976; Enig *et al*. 1978; Blaxter and Webster 1991; Eisenmann 2003; Carlson *et al*. 2011; Chapman *et al*. 2011). Furthermore, with the discovery of the effects on CVD of industrial trans fats, animal fats have made a resurgence in the popular literature, on the internet, and in low carbohydrate diet books (Taubes 2001, 2007). The diet wars of the 1960s and 1970s have reappeared (Yudkin 1964; Keys 1971), with a renewed focus on the effects of sucrose and fructose in obesity, CVD, cancer and type 2 diabetes as opposed to fat (Miller *et al*. 2011; Hoenselaar 2012; Lustig *et al*. 2012; Basu *et al*. 2013). There is a renewed popularity of low carbohydrate high fat diets, as well as the scientific study of them (Foster *et al*. 2003; Volek *et al*. 2003; Yancy *et al*. 2004). Indeed, it now appears that genes contribute to whether one will drop out of a low calorie diet depending on whether it is low fat or high fat (Grau *et al*. 2009). Despite these

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changes in society, high quality food has always featured animal fats because of their taste and during the past 40 years there has been no deviation from that practice (Escoffier 1921; Bocuse 1988; Carluccio and Contaldo 2012). The purpose of this review is to investigate whether there are any health benefits in putting animal fats back on the table.

One justification for the unrestricted use of animal fats is the archaeological, ethnographic, and historical evidence that for 1–2 million years before the invention of agriculture humans were omnivorous hunter-gatherers consuming animal tissues including fat (Richards and Trinkaus 2009; Sponheimer and Dufour 2009; Stiner and Munro 2011; Ungar and Sponheimer 2011). Some humans still occupy this niche, and their hunting and gathering habits have been documented (Murdock 1967; Cordain *et al*. 2002*a*; Rouja *et al*. 2003). Organs and fat were generally preferred to lean meat by these hunter-gatherers who were well aware of the value of eating animal fat: the side effects of eating only lean meat have been replicated in the laboratory and they include diarrhoea and unsatisfied hunger (Stefansson 1912; McClellan and Du Bois 1930; Phinney 2004). During human evolution, how much fat was eaten on a daily or yearly basis is a matter for speculation, and would depend on a host of factors. Given the nausea limit in human responses to large amounts of fat (Man and Gildea 1932), one suspects as much fat as could be stomached. These ancestral patterns of food use do not prescribe any particular modern diet or lifestyle but they do show the likely human nutritional adaptations and responses to food, and point to the nutrients that need to be obtained from food (Cordain *et al*. 2005; Lindeberg 2009).

Saturated fat and cardiovascular disease

The degree of saturation of animal fat

Although animal fats are described as saturated and containing cholesterol, apart from butter and some fatty fish, animal fat is best described as monounsaturated either by content or by function (Table 1) for its effect on serum cholesterol. First, dietary cholesterol makes a second order contribution to serum cholesterol, that is, its effect is proportional to the square root of dietary intake, leading to minor changes in serum cholesterol, its importance has been debunked, and it has long been ignored in prediction of CVD risk (Keys *et al*. 1965, 1974). Second, as can be seen from the table, the major component of the triacylglycerol (TAG, triglycerides) of animal fat is monounsaturated fatty acid (MUFA), mostly oleic acid, irrespective of how solid the fat is at room temperature, and in some cases oleic acid consists of more than 50% of all fatty acids (FA). Even when oleic acid is less than 50% of all the FA, there are other MUFA and FA that do not affect overall serum cholesterol. As an example from one of the hardest animal fats, approximately only 27% of tallow from pasture-fed beef is cholesterol-increasing saturated fatty acid (CISFA) (Yang *et al*. 1999*b*), i.e. chain length of 12–16 carbons, and which would raise serum cholesterol, 1% is polyunsaturated, ~4% is conjugated linoleic acid (CLA), and the rest is either MUFA or is the saturated fatty acid (SFA) stearic acid that causes the same effect on total serum cholesterol (TSC) as MUFA (Keys *et al*. 1965; Grande *et al*. 1970; Bonanome and Grundy 1988; Tholstrup *et al*. 1994*a*, 1994*b*; de Roos *et al*. 2001; Mensink *et al*. 2003). By comparison, in butter from pasture-fed cows, 42% of the fat is CISFA (Couvreur *et al*. 2006) and would raise serum cholesterol despite butter having a total of more than 60% SFA. Butter differs from other animal fats in having a large amount of short- and medium-chain SFA, which are rapidly oxidised by the liver instead of being stored in adipose tissue or transported by lipoprotein cholesterol particles (Bach and Babayan 1982; DeLany *et al*. 2000) – the amount of palmitate in butter is similar to other animal fats. The distinguishing features of most animal fats, compared with most plant oils, is the low variability in proportion of palmitate to the total amount of FA, compared with the large range in proportion of other FA, the relatively large proportion of FA with odd number of carbons in the acyl backbone or with variable numbers and locations of unsaturated bonds, and the low to very low levels of n-6 polyunsaturated fatty acids (PUFA), especially in ruminant fat.

The effects of fat on human blood lipids

Fat and cholesterol are carried by chylomicrons and lipoprotein cholesterol particles in circulation, and because serum cholesterol has been associated with risk of CVD, fat intake has been implicated in CVD, although detailed analyses show results contrary to this expectation. The effect of different FA on the average TSC of the sample, its sub-fractions, fasting triacylglycerides (FTG) and the number and size of low density lipoprotein cholesterol (LDL-C) particles have been determined on largely inactive people in studies in metabolic wards. The description of these average changes in TSC and FTG have been studied for more than 50 years, they are well known and are predictable using the Keys equation (Man and Gildea 1932; Havel *et al*. 1955; Ahrens *et al*. 1957; Havel 1957*a*, 1957*b*; Keys *et al*. 1957, 1965; Albrink and Man 1959; Kuo and Carson 1959; Grande *et al*. 1970; Acheson *et al*. 1988; Tholstrup *et al*. 1994*a*, 1994*b*; de Roos *et al*. 2001; McDevitt *et al*. 2001; Mensink *et al*. 2003; Matthan *et al*. 2004; Chapman *et al*. 2011; Miller *et al*. 2011). These changes can be summarised by saying, first, that substituting MUFA and stearic acid for starch causes no change in the average serum cholesterol of a population sample, although LDL-C concentration decreases while high density lipoprotein cholesterol (HDL-C) concentration increases. Second, average serum cholesterol is increased as the proportion of CISFA increases and is decreased as the proportion of PUFA increases. The increases due to CISFA are twice the size of decreases due to PUFA for each unit of CISFA or PUFA. Third, HDL-C and FTG of an individual are inversely related, so high FTG is usually correlated with both low HDL-C and a pattern of low fat plus high carbohydrate intake. High FTG is strongly correlated with small dense LDL-C, to expanded waistlines and to other features of the metabolic syndrome, which is strongly predictive of increased risk of CVD (Castelli 1986; Boerwinkle *et al*. 1994; Gardner *et al*. 1996; Stampfer *et al*. 1996; Lamarche *et al*. 1997; Barrows and Parks 2006; Roberts *et al*. 2008). While serum cholesterol and, particularly, LDL-C concentrations of the individual are used to calculate risk of CVD, of more importance to the mechanistic development of CVD is the size and number of LDL-C particles in circulation and the composition of cholesteryl-esters (cf. below).

An overview of fat and cholesterol transport is shown in Fig. 1 and shows five major phases that are each affected by dietary and

Table 1. Percentage fatty acid composition of a range of fats and oils

SCF, subcutaneous fat. Other, dependent on species, mainly other monounsaturated fatty acids and small amounts of long-chain polyunsaturated fatty acids (PUFA) and odd-numbered SFA in land animals, conjugated linoleic acid in ruminants, and long-chain n-3 PUFA in salmon

Fatty acid	<C12:0	C12:0	C14:0	C16:0	C18:0	C18:1	C18:2 (n-6)	C18:3 (n-3)	Other	Reference
Animal										
Butter pasture	10.8	3.5	10.9	24.3	11.2	21.6	1.26	0.70	15.74	Couvreur *et al.* (2006)
Butter corn silage	11.9	3.8	11.8	31.0	10.3	19.4	1.55	0.22	10.03	Couvreur *et al.* (2006)
Beef SCF pasture	–	–	3.3	23.4	11.1	43.6	0.70	0.42	17.48	Yang *et al.* (1999*b*)
Beef SCF feedlot 100 days	–	–	3.4	26.2	13.7	41.7	1.00	0.13	13.87	Yang *et al.* (1999*b*)
Deer bone marrow	–	–	0.8	16.3	4.7	54.1	2.35	1.49	20.20	Cordain *et al.* (2002*b*)
Antelope SCF	–	–	3.6	24.0	34.3	24.1	1.73	1.14	11.13	Cordain *et al.* (2002*b*)
Elk SCF	–	–	5.5	34.7	23.3	17.5	1.61	1.12	16.18	Cordain *et al.* (2002*b*)
Free-range pig backfat	–	–	1.1	19.0	8.1	56.4	8.73	0.56	6.11	Rodríguez-Sánchez *et al.* (2010)
Wild boar intramuscular fat	–	–	0.9	24.0	10.3	41.1	12.04	0.42	11.24	Razmaite *et al.* (2011)
Free-range chicken	–	–	0.8	26.5	6.3	39.6	14.40	1.64	10.76	Givens *et al.* (2011)
Intensive chicken	–	–	1.1	21.3	6.0	36.8	22.87	3.75	8.18	Givens *et al.* (2011)
Intensive duck intramuscular fat	–	0.4	0.5	23.4	7.5	43.5	13.49	0.64	10.57	Chartrin *et al.* (2006)
Atlantic salmon (farmed-fed fish meal)	–	–	4.2	12.6	2.4	12.0	2.39	1.19	65.22	Sanden *et al.* (2011)
Margarines										
Corn/soy stick	–	–	–	10.5	7.8	48.4[A]	27.8	2.5	3.0	http://nutritiondata.self.com/facts/fats-and-oils/635/2 (verified 20 March 2014)
Canola Harvest soft spread	–	1.5	0.1	9.2	2.3	54.3	18.0	8.4	6.2	http://nutritiondata.self.com/facts/fats-and-oils/10038/2 (verified 20 March 2014)
Plant										
Canola oil	–	–	–	4.2	1.5	58.6	21.4	10.9	3.4	Ackman and Sebedio (1981)
Cocoa butter	–	–	–	26.2	35.8	33.6	2.7	0.8	0.9	Lipp *et al.* (2001)
Coconut oil	21.3	48.2	14.6	6.9	2.0	4.5	1.4	0.1	1.0	Bézard *et al.* (1971)
Olive oil	–	–	–	12.1	2.7	71.8	10.2	0.7	2.5	Van Niekerk and Burger (1985)
Palm oil	–	–	1.1	43.7	4.5	39.3	10.1	0.2	5.3	Van Niekerk and Burger (1985)
Peanut oil	–	–	–	11.2	3.7	41.1	35.5	0.1	8.4	Van Niekerk and Burger (1985)
Shea butter	–	–	–	3.4	40.8	46.3	6.6	0.1	2.8	Di Vincenzo *et al.* (2005)
Soybean oil	–	–	–	9.5	4.9	21.9	52.6	7.9	3.2	Van Niekerk and Burger (1985)
Sunflower oil	–	–	–	6.1	5.6	19.3	67.0	0.1	1.9	Van Niekerk and Burger (1985)

[A]One-third of this was trans C18:1.

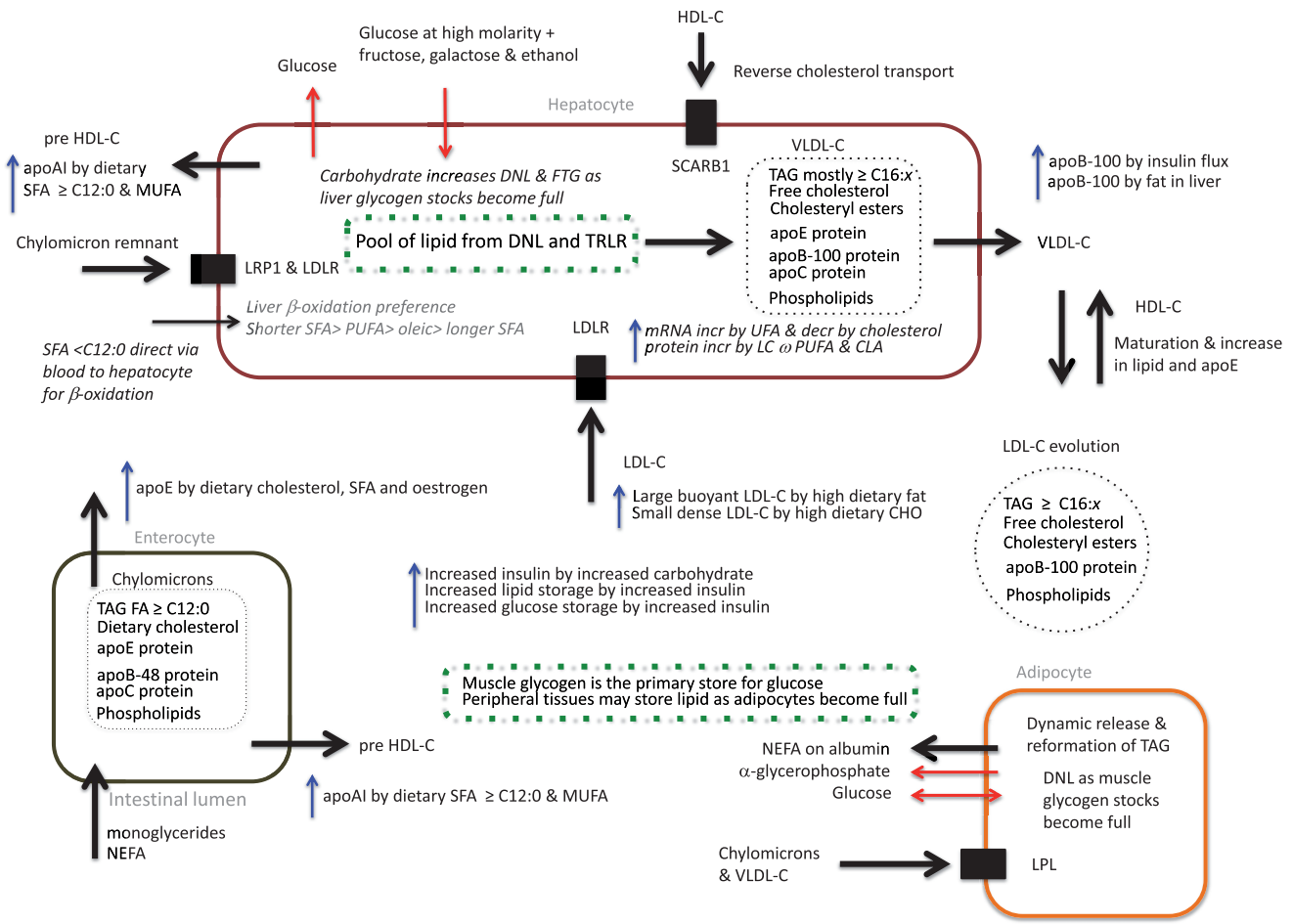

Fig. 1. The main dietary influences on the transport of fatty acids in the body. Bold arrows represent transport of lipids, either in lipoprotein cholesterol particles or bound to albumin. Narrow arrows represent transport of carbohydrate or polar lipids dissolved in serum. Blue arrows represent increases in proteins or particles relevant to blood cholesterol resulting from dietary manipulation. SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; NEFA, non-esterified fatty acid; UFA, unsaturated fatty acid; LC, long-chain; CLA, conjugated linoleic acid; CHO, carbohydrate; DNL, *de novo* lipogenesis; TRLR, triglyceride-rich lipoprotein remnant; TAG, triacylglycerol (triglycerides); FTG, fasting triglycerides; apo, apolipoprotein; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low density lipoprotein cholesterol; LDLR, low density lipoprotein receptor; LRP1, low density lipoprotein receptor-related protein 1; SCARB1, scavenger receptor B1; LPL, lipoprotein lipase.

genetic factors. These phases are (1) the entry of FA into enterocytes and the formation of chylomicrons, (2) the transport of fat and cholesterol via chylomicrons in the circulation to tissues, (3) the processing of chylomicron remnants by the liver and the formation of very low density lipoprotein cholesterol (VLDL-C) in the liver, (4) the transport of fat and cholesterol via VLDL-C and its remnant, LDL-C, to tissues, and (5) the release of FA from adipocytes to be carried on albumin to tissues via the blood (Chapman *et al*. 2011). Starting with the enterocytes, for cholesterol and fat transport, the HDL-C fraction requires apolipoprotein (apo) A series molecules and the huge chylomicrons require apoB-48, apoC and apoE (Utermann 1988; Chapman *et al*. 2011). After being carried to all tissues via the circulation the remnants of chylomicrons are processed by the liver. Dietary FA shorter than 12 carbons are not carried by chylomicrons but are dissolved in blood and carried to the liver via the Portal vein (Bach and Babayan 1982). At the liver, the VLDL-C fraction, composed of fat and cholesterol from chylomicron remnants and from that synthesised in the liver, requires apoB-100, apoC, and apoE for transport (Utermann 1988). As these mature to LDL-C, the apoC and apoE proteins and cholesterol are lost to HDL-C, leaving only apoB-100 as well as progressively depleted LDL-C (Chapman *et al*. 2011). The longer the LDL-C particle stays in circulation the smaller and denser it becomes. HDL-C is part of the reverse transport of cholesterol, carrying it back to the liver where it is recycled (Fielding and Fielding 1995). Particles with apoE are taken up faster than particles with only apoB, because apoB can only be processed by the LDL receptor (LDLR) (Ishibashi *et al*. 1994). Thus chylomicrons and VLDL-C have a faster level of clearance from the circulation than LDL-C. Finally, when insulin levels decline, fat stored in adipocytes is released as non-esterified fatty acids (NEFA, also free fatty acids) transported on albumin (Cahill 2006; Hodson *et al*. 2008; Marinou *et al*. 2011).

The characteristic LDL-C particle number and LDL-C particle size distribution of an individual are affected by both genetics and

diet. Each LDL-C particle has a single apoB molecule associated with it, and apoB expression is affected by insulin flux and the amount of lipid in the liver (Elam *et al*. 1999; Veniant *et al*. 1999), and so APOB gene expression and hence the number of LDL-C particles is partly driven by carbohydrate intake. It is also inversely related to the amount of apoE in circulation (Smit *et al*. 1988; Utermann 1988), and although there is a major genetic effect on apoE expression due to variation at the apolipoprotein E (APOE) coding sequence, apoE expression is positively correlated with dietary cholesterol, oestrogen and SFA (Utermann *et al*. 1979; Srivastava 1996; Srivastava *et al*. 1996).

There are three overall patterns of LDL-C particle size distribution in humans, stable pattern A is biased to larger less dense particles, stable pattern B is biased to smaller denser particles, and unstable pattern A, where individuals have pattern A at high fat levels and pattern B at low fat levels (Campos *et al*. 1995; Krauss and Dreon 1995; Dreon *et al*. 1999). Stable pattern B is governed by mutations at the LDLR (Austin *et al*. 1988; Nishina *et al*. 1992; Zhu *et al*. 2007), which causes delays in LDL-C clearance resulting in smaller, denser particles. Unstable pattern A is due to variation at the APOE locus, where the ε4 allele requires high fat levels to show pattern A (Dreon *et al*. 1995; Krauss and Dreon 1995), and reductions in LDL-C due to low fat diets are not accompanied by reductions in number of LDL-C particles. This is partly because the apoE*E4 protein has a higher affinity for low-density lipoprotein receptor related protein 1 as well as for VLDL-C than the E2 and E3 proteins (Egert *et al*. 2012), so chylomicrons are cleared at a faster rate and VLDL-C matures to LDL-C at a faster rate and so over its lifespan a lipoprotein cholesterol particle will be in the LDL-C form for longer for carriers of this allele.

High levels of CISFA cause the strongest increase in LDL-C particle size but unsaturated lipids also appear to maintain increased LDL-C particle size but to a lesser extent (Dreon *et al*. 1998; Kratz *et al*. 2002). Stable pattern B individuals respond to an increase in CISFA by increasing the number of small dense LDL-C particles in circulation, as seen by an increase in apoB levels (Krauss and Dreon 1995), because the genetic lesion is a reduction in recycling of LDL-C particles. Discordance between LDL-C and apoB concentrations in the blood is an indicator of these differences in LDL-C pattern, and discordance in apoB and LDL-C affects strongly the risk of CVD, with apoB level being the more accurate indicator (Dreon *et al*. 1995, 1998; Sniderman *et al*. 2012).

Unsaturated fatty acids (UFA) are known to increase the expression of the LDLR gene and, in addition, long-chain n-3 and n-6 PUFA and CLA increase the availability of the LDLR protein compared with CISFA (Fernandez and McNamara 1989; Yu-Poth *et al*. 2005; Dorfman and Lichtenstein 2006). This is consistent with the well known reduction of LDL-C concentration with increased UFA. A similar effect is expected for dietary stearic acid because its effects on serum cholesterol fractions are not statistically significantly different to that of oleic acid, it is associated with a reduction in concentration of apoB-100, and it is rapidly converted to oleic acid in the liver where the LDLR gene is expressed (Bonanome and Grundy 1988; Tholstrup *et al*. 1994*a*; Mensink *et al*. 2003).

Although LDL-C concentration of the blood is the most common risk factor used in prediction of CVD, the concentration of LDL-C per mL of blood is a combination of both the number of LDL particles per mL and the amount of cholesterol contained in each particle. That is, a particular LDL-C concentration of the blood could be made up of many particles each containing a small amount of cholesterol or few particles each containing a large amount of cholesterol. However, what counts for heightened risk of CVD is the number of LDL particles per mL in circulation rather than LDL-C concentration *per se* (Sniderman *et al*. 2012). Two individuals with the same LDL-C can have vastly different risks for CVD if one has many small dense particles with small amounts of cholesterol while the other has far fewer particles each carrying much larger amounts of cholesterol. LDL-C particles come in a range of densities. The larger the LDL-C particle the higher the concentration of free cholesterol and lipid, the lower the concentration of protein and cholesteryl-esters, the younger it is, and the longer it takes either for the apoB on the surface of the particle to be glycosylated, or for the particle to cross the vascular endothelium or to oxidise (Tribble *et al*. 1992; Reaven *et al*. 1994; Younis *et al*. 2013).

The development of cardiovascular disease

Plaque formation and atherosclerosis, which is at the heart of CVD, is mechanistically initiated by the peroxidation of PUFA in the cholesteryl-esters of LDL-C, and the first evidence of this was discovered 60 years ago (Glavind *et al*. 1952). The favoured PUFA for incorporation into cholesteryl-esters is linoleic acid (C18:2 n-6), the most common n-6 PUFA (Esterbauer *et al*. 1992). Restricting PUFA in the diet and providing high levels of oleic acid results in its replacement in cholesteryl-esters by oleic acid, the latter of which does not peroxidise (Nestel *et al*. 1992; Abbey *et al*. 1993; Sandker *et al*. 1993; Reaven *et al*. 1994). The PUFA-based cholesteryl-esters of LDL-C are peroxidised when they cross the endothelium, resulting in stepwise damage to apoB-100 on the surface of the LDL-C particle, which results in the LDL-C particle being taken up by macrophages, where the cholesterol accumulates (Brown and Goldstein 1983; Steinberg *et al*. 1989; Esterbauer *et al*. 1992; Stocker and Keaney 2004). The resulting foam cells form the basis of the atherosclerotic plaque. HDL-C particles act as antioxidants in this cascade, and in addition, do cross the vascular endothelium and accept cholesterol from foam cells, reversing the process, returning cholesterol to the liver where it is converted to bile salts (Brown and Goldstein 1983; Fielding and Fielding 1995). The smaller HDL_3 particles are most efficient at this process, and their numbers are increased through consumption of CISFA (Nestel *et al*. 1992; Kontush *et al*. 2003). This mechanism explains to some extent why HDL-C is an independent risk factor to LDL-C for CVD (Castelli *et al*. 1986; Stampfer *et al*. 1996; Chapman *et al*. 2011; Miller *et al*. 2011). Antioxidants such as Vitamins E and C can slow the damage, but they only delay the peroxidation on the scale of minutes not hours (Esterbauer *et al*. 1992), consistent with the demonstrated weak effect of antioxidant use in cohort trials and the failure of antioxidant therapy to control atherosclerosis in random control trials (Jha *et al*. 1995; Knekt *et al*. 2004). Once the plaque forms, inflammatory immunological processes are engaged (Stocker and Keaney 2004), and anti-inflammatory and anti-platelet treatment can reduce the risk of vascular death (Bousser *et al*.

2011). The tendency for LDL-C to cross the vascular endothelium is increased if it is small dense LDL-C. High levels of CISFA are important when they increase the number of small dense LDL-C molecules, otherwise the damage is done by peroxidation of PUFA, and both factors can be rescued by having MUFA as the dominant FA.

The epidemiology of cardiovascular disease and saturated fat

These factors help to explain the success of the traditional Mediterranean diet and lifestyle, which has been described as largely lacto-vegetarian (Keys 1995). The Mediterranean diet and lifestyle as originally described, is a high lipid (40% of total calories) low protein (10%) diet based on olive oil, vegetables, fruit, whole-grain cereals and legumes, wine, nuts, full fat cheese, fish, and meat, especially pork fat and offal (Keys *et al*. 1970; Keys 1995). The fat in this specification is dominated by MUFA, with low levels of linoleic acid (2% of total calories), a ratio of n-6 to n-3 PUFA of ~2, and with modest levels of SFA (8% of total calories) (Keys and Kimura 1970; Keys *et al*. 1970, 1980). Given the composition of olive oil and other plant oils, this suggests a substantial part of the lipid (perhaps a third) was from animal sources. What counts is degree of adherence to that traditional Mediterranean diet and lifestyle (de Lorgeril *et al*. 1994, 1999; Trichopoulou *et al*. 2003; Scarmeas *et al*. 2006; Féart *et al*. 2009; Sofi *et al*. 2012), no single food group is the magic bullet, although there was evaluation of which particular factors are critical that might alleviate the effects of a Western diet and lifestyle (Keys 1980; Hertog *et al*. 1993; Sandker *et al*. 1993; Evans *et al*. 1995; de Lorgeril *et al*. 2002).

Altering the effects of large amounts of SFA on serum cholesterol by replacing it with large amounts of PUFA to control TSC and reduce CVD, which was the subject of a large random controlled trial (Multiple Risk Factor Intervention Trial Research Group 1982), was not envisaged as an option to control CVD and was explicitly criticised before it was performed (Keys *et al*. 1974). The trial was unsuccessful because it showed no significant change in rates of CVD in the trial versus the control sample. Worryingly, this trial showed increased rates of cancer in the test group compared to the control (Blaxter and Webster 1991). Indeed, although treatment of CVD has greatly improved over the last 50 years, the incidence has stayed the same over that time and reductions in serum cholesterol have played a small (11%) role in postponing deaths from CVD (Hunink *et al*. 1997; Ford *et al*. 2007; Gouda *et al*. 2012). Smaller trials showed some progress in treating CVD where the lipid composition approximated that of the Mediterranean diet by providing to participants rapeseed (canola) oil hydrogenated to a margarine that was dominated by MUFA, with more SFA and a lower ratio of n-6 to n-3 PUFA than olive oil (de Lorgeril *et al*. 1994, 1999).

Although they can be flawed, nutritional surveys have found little evidence to link reported fat consumption of any kind and CVD within countries (Siri-Tarino *et al*. 2010), and meta-analyses of random controlled trials have shown small or no benefit to replacing saturated fat with carbohydrate or unsaturated fat (Multiple Risk Factor Intervention Trial Research Group 1982; Micha and Mozaffarian 2010; Hooper *et al*. 2011). Average longevity, a key statistic in comparisons of different diets and lifestyles, does not increase when SFA is replaced by either carbohydrate or UFA (Hooper *et al*. 2011). Nevertheless, these surveys have extra-ordinary statistical power, covering many hundreds of thousands of people. Any association to SFA that is seen is variable and only at the very highest levels of consumption, which is consistent with the known mechanisms of the effect of CISFA on LDL-C structure in some individuals. On the other hand, very high body mass index (BMI: kg/m^2) is reliably and consistently linked within populations to all forms of CVD (Keys *et al*. 1980; McGee and Diverse Populations Collaboration 2005), a marker of increased food consumption or decreased movement. Indeed, waist circumference and waist to hip ratio are stronger physical correlates to CVD than BMI by itself (de Hollander *et al*. 2012) and the relative risk of a large waist circumference easily exceeds the relative risk found for high consumption of SFA and is similar to being in the top quintile for non-HDL-C or the bottom quintile for HDL-C (Chapman *et al*. 2011; Hooper *et al*. 2011). In food overconsumption studies, excess fructose rather than excess glucose leads to an increase in intra-abdominal fat and hence expanded waist circumferences (Stanhope *et al*. 2009).

The within-cohort argument against animal or saturated fat became much weaker once the effects of trans fats in margarines derived from partial hydrogenation of C18 PUFA in vegetable oils were separated from animal fats. Animal fats and margarines had initially been grouped together in analyses, as representatives of fats that were solid at room temperature. These margarines contained substantial amounts of elaidic acid (C18:1 trans 9) (Hunter 2001; Hayes and Pronczuk 2010). The effect of industrial trans fat on risk of heart disease is powerful, the dose response predictable (Hu *et al*. 1997), the results marked (Willett *et al*. 1993; Dorfman *et al*. 2009; Mozaffarian *et al*. 2009), and industrial trans fats are the only fat to double the risk of CVD, all other fats change the risk by a small percentage. Consequently, cities in the United States have banned trans fats from publically prepared food (http://www.nbcnews.com/id/16051436/ns/health-diet_and_nutrition/t/new-york-city-passes-trans-fat-ban/#.UVpxVBm8yTw, accessed 1 April 2014). In effect, C18 trans MUFA, derived from the partial hydrogenation of C18:2 and C18:3 PUFA, show decreased HDL-C but similar LDL-C levels to CISFA (de Roos *et al*. 2001; Matthan *et al*. 2004), which explained to some extent the previously observed emergence of a pattern of low HDL-C, high LDL-C and high FTG seen in some populations (Castelli 1986). Many margarines have a large amount of PUFA, which would contribute to peroxidisable cholesteryl-esters, providing a double hit. Indeed, once trans fats were controlled, risk of CVD declined with increased number of beef, lamb, and pork stews consumed per week, implying a beneficial effect of these animal fats on CVD (Willett *et al*. 1993). Many manufacturers now create margarines with lower trans fat levels through interesterification of completely hydrogenated fats and unhydrogenated oils (Hunter 2001; Hayes and Pronczuk 2010). But there is always some level of trans fat due to the refinement of vegetable oils, while there would still be a high level of linoleic acid (Table 1).

Most of the epidemiological evidence for the role of fat in CVD comes from comparisons between countries and from the

changes in food usage over time within countries. As noted above, if one were to use the evidence of changes in food usage, then animal fat consumption declined and plant oil consumption increased as CVD and obesity rates increased, which argues against the role of animal fat in CVD or obesity (Yudkin 1957; Antar *et al*. 1964; Oddy and Yudkin 1969; Kritchevsky 1976; Enig *et al*. 1978; Eisenmann 2003; Carlson *et al*. 2011; Chapman *et al*. 2011). Comparisons between countries are controversial, called ecological comparisons, because many factors change from one country to the next, and such comparisons result in incorrect inferences due to correlations based on mean values (Robinson 1950; Evans 2011). Moreover, the early ecological comparison of six countries was criticised for biased selection of countries, which had led to the reporting of very strong relationships between fat and CVD (Keys 1953; Yerushalmy and Hilleboe 1957; Yudkin 1957). Nevertheless, much of the prestige of the argument against SFA is based on a later version of that ecological comparison, the Seven Countries study, in which individuals within 16 cohorts were evaluated, which showed that *within* each cohort, smoking, blood pressure, and serum cholesterol were each important risk factors for CVD (Keys *et al*. 1980). Importantly, however, food intake of each individual was not measured, but gross food composition was determined for a representative sample of 30–50 households, and then cross-cohort correlations were made between average nutrient composition and average rates of CVD (Keys *et al*. 1980). This was justified on the basis of the known relationship between average fat composition of a ration and average serum cholesterol of individuals consuming that ration – that individual cholesterol values are too variable for accurate inference (Keys *et al*. 1980). Indeed, the first study of serum cholesterol and atherosclerosis at autopsy had shown no correlation between individual values for these two variables (Lande and Sperry 1936). The Seven Countries study is the basis for the Mediterranean diet and lifestyle.

What are the alternative explanations for the extremely high rates of CVD that occurred in the East Finland cohort in the Seven Countries study (Keys *et al*. 1980), if one were to assume that they were not due to SFA. There, the East Finland cohort had the highest proportion of saturated fat in the diet and nearly twice the incidence of coronary heart disease (CHD) compared with any other cohort, the SFA derived mainly from milk fat. The overall ration also had low levels of linoleic acid as a proportion of calories and a low ratio of n-6 to n-3 FA (Keys and Kimura 1970; Keys *et al*. 1970). First, the West Finland cohort had the same median TSC value as the East Finland cohort (Keys *et al*. 1970; Stengard *et al*. 1995) but had only a third the rate of age adjusted CHD compared with the East Finland cohort. Furthermore, West Finland had a higher average TSC than the Zutphen (Netherlands) or US Railroad cohorts, and the same or more SFA as a proportion of calories than either of those, but less CHD than either Zutphen or US Railroad. Second, the East Finland cohort had the most calorie intake per kilogram bodyweight, but this was not substantially greater than West Finland. East Finland did consume 32% more calories per kilo bodyweight than the Crete cohort (lowest CHD rate), and although both consumed ~40% of calories as fat, this implies substantially more fat in total (Keys *et al*. 1970). Third, the East Finland cohort was located in Karelia (Keys *et al*. 1958), then an isolated and icebound region for most of the year while the West Finland cohort was centred near Turku and included a substantial proportion of Swedes (Karvonen *et al*. 1970). During winter the rations were reduced to milk and other dairy products, bread, and potatoes with small amounts of other foodstuffs (Roine *et al*. 1958), hardly well balanced but hardly a death sentence, given the benefits of dairy product consumption for CVD and the metabolic syndrome (Evans *et al*. 1995; Elwood *et al*. 2010; Livingstone *et al*. 2013). Indeed, there was little difference between East and West Finland in their diets, apart from a small increase in diversity in the West, and reduced vitamin C, vitamin E, and iodine in the East. Finnish researchers in the 1950s suspected differences in iodine and subsequent goitre as a likely cause of the difference in CHD between the two Finnish samples (Roine *et al*. 1958; Uotila *et al*. 1958). Hypothyroidism is a known cause of elevated FTG with decreased particle size of the VLDL fraction (Nikkilä and Kekki 1972; Abrams *et al*. 1981; Castelli 1986), although these days vitamins C and E would also be thought important due to their antioxidant effects (Esterbauer *et al*. 1992). Fourth, the East Finland cohort was centred on the town of Ilomantsi, 3 km from the Finno-Russian border in an area in which Russians had seized territory and displaced Karelians had been repatriated by the Finnish government to other parts of Finland (Karvonen *et al*. 1970). While the report stated that the cohort itself consisted of a minimum of displaced persons, the stress associated with such events, which may have involved family members, should not be underestimated. Stress is a well known factor in CVD, especially stress where one is powerless to alter events (Marmot *et al*. 1997). None of the other cohorts experienced a similar event associated with the Second World War. Last, Karelians are a minority ethnic group and have one of the highest frequencies of the APOE ε4 allele in Europe (Fullerton *et al*. 2000). The APOE gene shows a North/South cline in the frequency of the ε4 allele in Europe, evidence of natural selection, while the lowest frequencies of ε4 of any population are found on the islands and shores of the Mediterranean (Corbo and Scacchi 1999; Singh *et al*. 2006; Lappalainen *et al*. 2010). Carriers of the ε4 allele have a 40% increased risk and homozygotes for this allele have approximately double the risk of CHD compared with the APOE ε3 homozygotes in Western countries (Menzel *et al*. 1983; Song *et al*. 2004; Mooijaart *et al*. 2006). While it may be coincidental that the age-adjusted death rates for CHD in East Finland and Crete were very similar to the frequencies of homozygotes for APOE ε4 in these two cohorts, APOE genotype has been shown to affect CHD in the East and West Finland populations of the Seven Countries study (Stengard *et al*. 1995). The response of APOE ε4 to SFA versus MUFA is significantly different to the response of APOE ε3, with SFA-dominated fats resulting in a substantially elevated LDL-C profile for this allele (Moreno *et al*. 2009; Egert *et al*. 2012). Given that APOE ε4 is ancestral (Hanlon and Rubinsztein 1995; Fullerton *et al*. 2000), may be a thrifty allele (Corbo and Scacchi 1999) and that the East Finland population was actually consuming the most calories per kilogram bodyweight, there is evidence of a genetic component to the observations and the differences between cohorts. Obviously, there would be other genes involved in blood lipids and response to fat consumption, not just APOE but would also include mutations such as the Karelian form of the LDLR gene (Vuorio *et al*. 1997), which would have a role in differences between populations (Teslovich *et al*. 2010). Taken together, any

or all of these factors could be working to explain this ecological comparison.

Perhaps the final word on fat and cholesterol should be given to William Castelli (see quote at the beginning) on individuals living in the real world. In the real world there is only a tenuous link at best between consumption of SFA and serum cholesterol, with other factors overriding the relationship. For example, 'The two factors that jump to mind are exercise and weight. In Framingham, for example, we found that the people who ate the most cholesterol, ate the most saturated fat, ate the most calories, weighed the least, and were the most physically active' (Castelli 1992). As noted at the start, the more SFA consumed the lower the serum cholesterol, and in the Framingham Heart study (Castelli *et al*. 1986), not only did lower serum cholesterol and lower BMI equate to lower risk of CVD, but higher HDL-C, consistent with higher consumption of SFA, was shown to have protective effects.

Components of animal fat with known health benefits

The most important health benefit of fat is that it is a carrier for the vitamins A, D, E, and K and the precursors β-carotene and cholesterol. The transport of these into the body partly through active transport and passive diffusion in fat has been recently reviewed (Reboul and Borel 2011). Deficiency disorders for these vitamins are well known, blindness, rickets, and bleeding disorders are the well attested results of frank deficiency, but low levels of these vitamins are associated with bone weakness, osteoporosis, calcification of the arteries, CHD, type 2 diabetes, depression and other mental disorders (Rimm *et al*. 1993; Schaafsma *et al*. 2000; Holick 2007; Beulens *et al*. 2010; Flore *et al*. 2013). Animal tissues, especially organs such as the liver and adipose tissue, and dairy products are a valuable source for several of these fat soluble vitamins. Although the importance of fat soluble vitamins is extremely well known, with recommendations to consume less fat and less animal tissues on the one hand or absence of these foods in some developing countries on the other hand, vitamin supplementation is often needed.

The fat and other tissues of a wide variety of land animals, not just oily fish, contain long-chain n-3 PUFA (Table 2). Given the pollution of the ocean by methyl mercury, ocean fish consumption needs to be modulated to achieve the benefits of eating oily fish (Mozaffarian and Rimm 2006). These PUFA are part of the phospholipid fraction, hence their presence in substantial amounts in tissues such as brain, liver, and egg yolks. Long-chain n-3 PUFA have a wide range of well attested health benefits, primarily in brain development in young children and as an important modulator of immune system function, especially the inflammatory response (Simopoulos 1991). As inflammation is central to many chronic disorders of aging and obesity, this subject is important and is regularly reviewed (MacLean *et al*. 2006; Schmitz and Ecker 2008; Simopoulos 2008; Nicholson *et al*. 2013). Although α-linolenic acid (C18:3 n-3) is found in leafy green vegetables, some nuts and some oil seed, it appears that only animals or algae can synthesise the long-chain n-3 PUFA docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) (Sprecher 2002). The sequence of reactions and rate-limiting steps are shown in Fig. 2. The human metabolism has a trivial ability to increase DHA given extra α-linolenic acid in the diet (Bézard *et al*. 1994; Brenna 2002; Burdge and Calder 2005; Harper *et al*. 2006), although levels of DHA in the serum of self-reported vegans is higher than expected, which if accurate suggests regulation of DHA levels and enhanced endogenous synthesis of DHA in the absence of dietary intake (Welch *et al*. 2010). The starting ratio of shorter-chain n-6 to n-3 PUFA in the diet largely determines the ratio of longer-chain PUFA that are synthesised, and the ratio stored in tissues or cholesteryl-esters is

Table 2. Amount of tissue from a range of representative animal sources to provide 250 mg of essential long-chain n-3 fatty acids

Amount is the amount of tissue required to obtain 250 mg of long-chain n-3 polyunsaturated fatty acids in the diet consisting of varying ratios of docosahexaenoic acid (DHA), eicosapentaenoic acid and n-3 docosapentaenoic acid depending on species and tissue

Species	Management	Tissue	Amount	Reference
Antelope	Wild	Brain	2.7 g	Cordain *et al*. (2002*b*)
Sardine	Wild	Muscle	6.3 g	Usydus *et al*. (2012)
Salmon	Farmed	Whole	16.7 g	Sanden *et al*. (2011)
Pig	Intensive (linseed supplemented)	Backfat	59 g	Enser *et al*. (2000)
Lamb	Pasture	Subcutaneous fat	89 g	Nuernberg *et al*. (2005*b*)
Pig	Intensive (unsupplemented)	Backfat	101 g	Enser *et al*. (2000)
Chicken	Intensive (flaxseed supplemented)	Breast, skin on	109 g	Jia *et al*. (2010)
Egg	Cage/DHA supplemented	Yolk/whole egg	<2[A]–3 large eggs	Cachaldora *et al*. (2008); Anderson (2011)
Pig	Intensive (unsupplemented)	Liver	113 g	Enser *et al*. (2000)
Chicken	Intensive (flaxseed supplemented)	Wing, skin on	137 g	Jia *et al*. (2010)
Chicken	Intensive	Breast, skin on	219 g	Jia *et al*. (2010)
Lamb	Pasture	Longissimus	260 g	Nuernberg *et al*. (2005*b*)
Chicken	Intensive	Wing, skin on	316 g	Jia *et al*. (2010)
Pig	Intensive (unsupplemented)	Sausages	448 g	Enser *et al*. (2000)
Beef (Simmental)	Pasture	Longissimus	676 g	Nuernberg *et al*. (2005*a*)
Beef	Pasture	Perirenal fat	735 g	Staerfl *et al*. (2011)
Chicken	Intensive	Leg skin off	880 g	Givens *et al*. (2011)
Beef (Charolais)	Feedlot	Longissimus	1.3 kg	Mandell *et al*. (1997)

[A]Chickens supplemented with DHA in their rations.

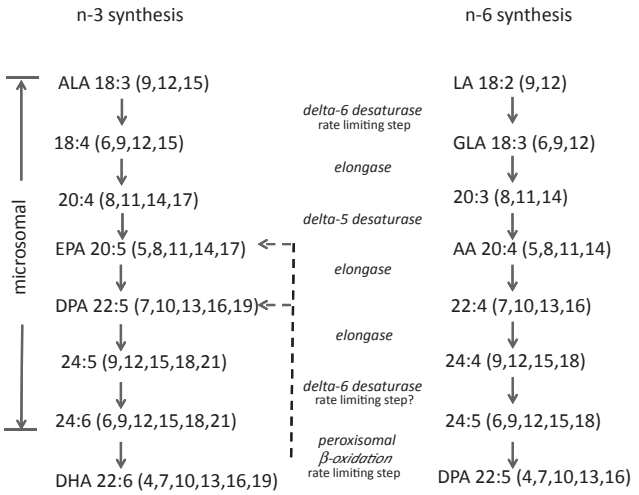

Fig. 2. The steps in synthesis of long-chain n-3 and n-6 polyunsaturated fatty acid (PUFA) in mammalian tissues. Humans have a trivial ability to synthesise DHA from ALA (see text). The main rate-limiting steps apply to both n-3 and n-6 PUFA. The last rate-limiting step involves the translocation of PUFA from the endoplasmic reticulum to the peroxisomes. Degradation usually occurs backwards to the previous PUFA in the pathway, except for 24 : 6 (n-3) and 22 : 6 (n-3), the latter of which degrades to either 22 : 5 (n-3) or 20 : 5 (n-3). ALA, α-linolenic acid; LA, linoleic acid; GLA, gamma-linolenic acid; EPA, eicosapentaenoic acid; AA, arachidonic acid; DPA, docosapentaenoic acid; DHA, docosahexaenoic acid. Information taken from Sprecher (2002).

therefore a reflection of the intake ratio of these fats (Zock *et al*. 1997). Nevertheless, there is human genetic variation in the genes of these pathways, which bias processing towards n-3 PUFA over n-6 PUFA (Tanaka *et al*. 2009). High levels of circulating long-chain n-3 PUFA, especially DHA, therefore, generally requires a dietary source in humans, essentially from fat of other animals, with evidence of little additional benefit beyond a threshold intake of ~250 mg per day (Mozaffarian and Rimm 2006). EPA is interconverted to DHA via the intermediate n-3 docosapentaenoic acid (DPA) but not from n-6 DPA, and n-3 DPA is a long-chain PUFA found in ruminant tissues. However, the ratio of the n-6 to n-3 PUFA in the tissue depends largely on the food source of the animal, with grass-fed ruminants having approximately a 2 : 1 ratio of n-6 to n-3 FA, much lower than for grain-fed ruminants (Yang *et al*. 1999*b*; Couvreur *et al*. 2006; Sinclair 2007), compositional effects seen in other species as well (Sinclair *et al*. 2010). Given the decline and pollution of fisheries (Costello *et al*. 2012; Halpern *et al*. 2012) there are other ways of ensuring a sufficient amount of long-chain n-3 PUFA, especially since many populations, perhaps under the advice to cut back on saturated fat have reduced their consumption of animal fat and are deficient in DHA and EPA (Givens 2010). Better data on DHA, n-3 DPA, and EPA concentrations in a variety of animal tissues under different management systems would be welcome.

The ratio of n-6 to n-3 PUFA (OMR) in animal fats may make an important contribution to human health although it is not clear whether these are all direct effects or whether they are partial effects due to food overconsumption and obesity. Several studies have shown that a high OMR in tissues or cholesteryl-esters is associated with several diseases including cancers such as prostate, bowel and breast cancer, CVD, autoimmune diseases and inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease (Godley *et al*. 1996; Harvei *et al*. 1997; Gogos *et al*. 1998; Simonsen *et al*. 1998; Yang *et al*. 1999*c*; Simopoulos 2008; Murff *et al*. 2011). Intake of many types of fat have been examined, with a suggestion of a threshold of n-6 PUFA, and reduced rates of disease for fats or oils low in n-6 PUFA, including animal fat (Zock and Katan 1998; Freedman *et al*. 2008; Alexander *et al*. 2010; Brennan *et al*. 2010; Dong *et al*. 2011; Gilsing *et al*. 2011; Liu *et al*. 2011; Psaltopoulou *et al*. 2011; Chajes *et al*. 2012). Moreover, supplementation with long-chain n-3 FA fails where there are high rates of consumption of n-6 PUFA. Many plant oils have OMR >10, some with OMR >100 (Table 1). It has been estimated that the general consumption in Western countries is OMR ~15, while more traditional diets have much lower OMR, and the traditional Greek diet, on which the Mediterranean diet was modelled, had an OMR of 2–4 (Keys and Kimura 1970; Keys *et al*. 1970; Simopoulos 2008). In general, for the shorter 18-carbon n-3 and n-6 FA, animal fat can have much lower OMR than plant oils, especially if their rations are low in n-6 PUFA. For longer-chain n-3 and n-6 FA the ratio also depends on the tissue and the species. Ruminant fat has low PUFA due to bio-hydrogenation in the rumen, and from animals on pasture has OMR $\leq$2 (Table 1) and increased levels of α-linolenic acid, which suggests that ruminant fat has a role in reducing not just the amount of n-6 PUFA but also the OMR. However, the West and other countries with high rates of obesity have high rates of these diseases, and being obese greatly increases the risk of these disorders including increased rates for higher levels of intra-abdominal fat (Connolly *et al*. 2002; Key *et al*. 2004; Pischon *et al*. 2008; Renehan *et al*. 2008). In overfeeding, it is primarily dietary fat that is stored, due to the high metabolic cost of converting dietary glucose to lipid in humans, ~0.33 Mj per Mj of lipid deposited, although some samples of obese people showed a greater ability to convert carbohydrate to fat than non-obese people (Acheson *et al*. 1988; Pasquet *et al*. 1992; McDevitt *et al*. 2001; Stanhope *et al*. 2009). So analyses of the fat of obese individuals will usually show a high ratio of n-6 to n-3 fat in countries where seed oils are the dominant source of lipids. This acts to confound the analysis. Is it just that increased food consumption has resulted in higher BMI, which of itself predisposes the individual to these disorders, or is it truly the type of fat? Mechanistic studies of n-3 and n-6 fats show their role in respectively inhibiting and promoting inflammation and tumour growth (Xia *et al*. 2005; Kobayashi *et al*. 2006), while high levels of n-6 fats may inhibit the action of delta-9 desaturase (Yang *et al*. 1999*b*), critical for desaturating SFA. So while controlling bodyweight may be the more important strategy, reducing the level of n-6 PUFA to bring down the OMR of the diet appears worthwhile.

In addition to long-chain n-3 PUFA, ruminant fat contains various types of CLA, a series of bioactive compounds with well known positive effects on human health. CLA are derived from PUFA in animal feed that had been bio-hydrogenated in the rumen. Most of the CLA in the animal's tissues are from vaccenic acid (C18:1 trans-11) absorbed from the rumen that is converted to the CLA rumenic acid (C18:2 cis-9 trans-11) by the host through the action of delta-9 desaturase, and a minor component of the CLA is produced by the rumen flora and absorbed by the host as one of a range of CLA (Griinari and

Bauman 1999; Pariza *et al*. 2001). The richest source is ruminant milk fat (Parodi 1997), but CLA are found in all ruminant fat depots including substantial amounts in bone marrow (Cordain *et al*. 2002*b*), a traditional source of food for pre-agricultural humans (Morin 2007). CLA is produced from both n-6 and n-3 PUFA, so animals on grain versus pasture do not produce less CLA, just the kind of CLA is altered. On grain compared with pasture, most of the CLA is still cis-9, trans-11 C18:2 but there is a reduction of trans-11, cis-13 C18:2 and an increase in trans-7, cis-9 C18:2, trans-10, cis-12 C18:2, and cis-9, cis-11 C18:2 (Daley *et al*. 2010; Aldai *et al*. 2011). This is apparently due to changes in the bacterial composition of the rumen in response to changes in pH as a result of the amount of fibre and energy density of the feed (Daley *et al*. 2010). These CLA isomers have different 3-D structures and there is some evidence for different biological activities, with the cis-9, trans-11 C18:2 isomer seen as the most beneficial (Pariza *et al*. 2001). This CLA isomer is synthesised directly by humans from vaccenic acid (trans-11 C18:1), through the action of delta-9 desaturase in the liver and other tissues. CLA came to prominence in screens to find carcinogenic molecules in grilled steak (Ha *et al*. 1987), and they were targeted because they are trans fats. However, it proved to be one of the most anti-carcinogenic molecules in cell culture assay. In addition, due to the concern with trans fats of industrial hydrogenation, especially elaidic acid, any trans fat receives a great deal of interest, and the health benefits of CLA have been thoroughly studied and intensively reviewed (Parodi 1997; Pariza *et al*. 2001; Dilzer and Park 2012). A wide range of favourable health outcomes have been found, including anti-cancer and anti-obesity effects, improvements in glucose tolerance, cardiovascular health, bone density, immune system function and inflammation, and gut health. Much of this work is now focussed on CLA as a pharmaceutical preparation or food additive, consisting of the main isomers cis-9, trans-11 C18:2 and trans-10, cis-12 C18:2, with dosages from 0.5 to 7 g per day (Dilzer and Park 2012). Given the concentration of CLA in dairy foods or ruminant fat, therapeutic doses of CLA could be obtained from moderate consumption (e.g. 100 g of full fat matured cheese) of dairy products or ruminant fat (Fogerty *et al*. 1988; Mushtaq *et al*. 2010).

There are minor components of animal fat that have unverified human health benefits (Parodi 1997, 2004). In animals, fat is a metabolically active energy store, as adipose tissue, or a nutritive substance, as in milk. Apart from the major TAG and NEFA that constitute the fat, there are minor components of the fat such as phospholipids and sphingolipids that constitute part of the lipid structural element of cell membranes, the non-fat components of the adipocyte, or the fat micelles that constitute milk fat. Few health benefits have been identified for these except that phospholipids and sphingolipids do include long-chain n-3 FA (Lehninger 1982). Pathways involving ceramide and sphingomyelin, components and downstream metabolites of sphingolipids, are known to be involved in several pathogenic metabolic processes involved in cancer cell proliferation as well as insulin resistance (Holland *et al*. 2007). Butyrate (C4:0), a short-chain SFA, forms a substantial part of dairy fat. Butyrate is generated by fermentation from plant fibre and resistant starch in the colon of humans and is the preferred source of fuel for colon cells (Scheppach 1994), and increased levels of butyrate as a result of improved diet quality may reduce risk of colon cancer (Steinmetz and Potter 1991; Van Munster *et al*. 1994; Mathers *et al*. 2012). Although most butyrate from dairy fat is absorbed from the small intestine and metabolised in the liver, there is clear speculation about the potential role of dairy butyrate in not just colon but other cancers, not by surviving into the large colon but by increased levels delivered via the circulation (Parodi 1997, 2004). The human health effects of dairy derived butyrate, ceramide, and sphingomyelin, as well as other minor components of animal fat, have not been extensively studied.

Health effects of fat as a macronutrient and energy source

Calorie restriction, not lipid restriction, has been shown to affect longevity in a wide range of species (Fontana *et al*. 2010) but longevity studies of humans by humans are obviously impractical (Hursting *et al*. 2010), the benefits are questioned relative to sanitation and modern medicine (Everitt and LeCouteur 2007), and a recent trial in primates failed to find an effect (Mattison *et al*. 2012). It is well known that a low fat, low protein whole-plant diet, when supplemented with the essential nutrients vitamin B_{12} and long-chain n-3 PUFA, has been associated with reduction of the thickness of cardiac arteries (Ornish *et al*. 1998). While this gives enormous prestige to low fat whole-plant diets, reduction of the thickness of cardiac arteries can also be achieved using calorie restriction of a high quality diet, including meat, eggs, and dairy products, thereby consuming animal fat (Fontana *et al*. 2004, 2007). Furthermore, starvation itself also causes a reduction in thickness of cardiac arteries in addition to generalised tissue wasting, as was found in the Minnesota Semistarvation Experiment of humans. There, a more than 50% reduction in calories to an extremely low fat ration of root vegetables, cabbage, cereals, and a few grams of animal protein per week also showed substantial negative physical and physiological effects (Keys 1950; Taylor and Keys 1950). In calorie-restricted individuals, when protein was reduced to maintenance levels and replaced isocalorically with other macronutrients, the level of insulin-like growth factor-1 (IGF-1) dropped substantially (Fontana *et al*. 2008). This longevity marker, which is associated with cancer, diabetes, and dementia, including Alzheimer's disease (Paolisso *et al*. 1997; Arai *et al*. 2001; Carro *et al*. 2002; Trejo *et al*. 2002; Longo and Finch 2003; Pollak *et al*. 2004; Carro and Torres-Aleman 2006; Fontana *et al*. 2010; Guevara-Aguirre *et al*. 2011; Duron *et al*. 2012; Rajpathak *et al*. 2012), is raised the least by lipids and most by protein consumption (Thissen *et al*. 1994). A study of raw food enthusiasts consuming 40% of calories as lipid and a maintenance level of 0.7 g/kg of protein (Rand *et al*. 2003), ~10% of calories, showed similar low levels of IGF-I without apparent calorie restriction (Fontana *et al*. 2008). This macronutrient composition is similar to the original description of the Mediterranean diet on Crete (Keys *et al*. 1970).

Although calorie restriction is a niche activity in the West, there is some evidence of increased longevity for communities that eat less food not less fat. Studies of the 'Blue Zones', areas of the world with proven enhanced aging, increased proportions of centenarians, and reduced morbidity from aging (Fraser and Shavlik 2001; Poulain *et al*. 2004), show first a huge range in

average fat consumption, from <10 to >40% of calories (Willcox *et al*. 2007, 2009; Appel 2008; Pes *et al*. 2013), relatively low levels of protein, a diet that is plant-based but not vegan, with differences in staple foods and wide variations in the amount of saturated fat consumed. The individuals generally consume substantially fewer calories than in the West, and have traditions of eating until one was not quite full. There is little evidence of deficiency in essential nutrients (Polidori *et al*. 2007; Willcox *et al*. 2007; Buffa *et al*. 2010). It is by no means certain that the individuals are calorie restricted, and claims to that extent are a source of controversy, because the calorie and protein intake in some of these groups is consistent with their smaller size (Keys and Kimura 1970; Willcox *et al*. 2007; Pes *et al*. 2013). Nevertheless, these individuals consume on average substantially fewer calories than in the West, and less than individuals in surrounding regions (e.g. Sardinia vs Italy, Okinawa vs Japan). Furthermore, despite the lower calorie intake, the individuals were far more physically active than the average in the West, although their activity is not usually associated with particularly hard work but instead represents activity all day long (Fraser and Shavlik 2001; Willcox *et al*. 2009; Pes *et al*. 2013). Fat appears not to be important in explaining increases in longevity in these Blue Zones. Moreover, a study of Ashkenazi centenarians in the US showed that a non-significant smaller proportion of the centenarians reported eating a low fat diet (Rajpathak *et al*. 2011) compared with an age-matched cohort from NHANES I – the only statistically significant difference was that fewer of the men smoked. Eating less in the English-speaking West is an unpalatable recommendation that goes against centuries old traditions of 'eat, drink and be merry, for tomorrow you die', entrenched overconsumption of food, and the social prestige of large amounts of lean meat (Dickson Wright 2011).

While fat *per se* is not negatively associated with longevity, it is positively associated with digestion and gut performance. Low fat high carbohydrate diets of a high glycemic index have been associated with symptomatic gall bladder disease (Tsai *et al*. 2005) likely due to reduced cycling of cholesterol through bile salt release. Although fat or oil are often stated as affecting gastrooesophagial reflux disease, a systematic review of the literature failed to find an effect of fat consumption (Dent *et al*. 2005). In addition, fat has a unique ability to stimulate colonic contraction, not found for carbohydrate or protein, and these contractions are essential to the voiding of faeces (Wright *et al*. 1980). Indeed, remedies for constipation before the Second World War recommended, in addition to 'roughage', water and the avoidance of diuretics, the consumption of fat such as bacon fat, butter, or olive oil, especially if the faeces was small and dry (Hutchison 1936), and for spastic colon no fibre and large amounts of the above listed fat was recommended. This is not a recommendation that is in any current medical guideline. Yet several pieces of evidence show that it is valid. First, infants take in no fibre, so amount of fibre is not a variable. Animal fats in the formula result in stools that are softer, larger, and that are easier to pass than plant fats (Forsyth *et al*. 1999), and babies also grow better when the source of the fat is from animal rather than plant sources (López-López *et al*. 2001). The exact reasons for these effects are not known, but these effects are thought to be due partly to the characteristic stereoisomeric structure of animal fats compared with plant fats (Hunter 2001), and the presence of long-chain PUFA. Second, in a study of a large number of Swiss citizens, the small percentage of individuals with great difficulty in passing faeces were statistically more likely to have a high fibre diet than a low fibre diet (Curtin *et al*. 1998). Although individuals on a high fat diet were less likely to report difficulty in passing faeces this was not statistically significant. Third, animal fat also contains a substantial proportion of stearic acid. Up to 20% of stearic acid, depending on the stereoisomeric location of the FA, is not absorbed by the enterocytes compared with 0–2% for other FA (Bracco 1994). The unabsorbed stearic acid will crystallise in the lumen of the gut as the pH increases and be excreted as a calcium soap (Owen *et al*. 1995). This reduces the energy of the diet, and changes the consistency and increases the mass of the faeces (Dougherty *et al*. 1995). This is not to argue that dietary fibre is unimportant, rather that dietary fibre is often not sufficient to cure constipation and other ailments of the colon and rectum. Constipation underlies many of the diseases of the bowel, and it is long known to be a precursor to diverticulitis, varicose veins, and haemorrhoids, among other disorders (Burkitt 1973; Cleave 1974). Colorectal cancer is related to diet quality, risk is reduced through the consumption of vegetables, fruit and resistant starch (Macquart-Moulin *et al*. 1987; Steinmetz and Potter 1991; Van Munster *et al*. 1994; Archer *et al*. 1998; Topping and Clifton 2001; Mathers *et al*. 2012), and fat consumption has not been shown to be linked to its occurrence in large meta-analyses (Nelson *et al*. 1999; Liu *et al*. 2011). As an aside, colorectal cancer has been linked to red meat, preserved meat and beer consumption, which may implicate methods of preparation and preservation of food involving known factors such as nitrosamines and heterocyclic amines (McMichael *et al*. 1979; Potter 1999; Aune *et al*. 2013; Egeberg *et al*. 2013).

The macroscopic structure of a fat and its stereoisomeric composition of TAG and their abundances makes a substantial difference to the organoleptic and processing characteristics of that fat (Bracco 1994), there are differences between species and between plants and animals (Hunter 2001), but whether these make a substantial difference to health is not clear. A TAG is composed of a glycerol molecule covalently bound to three FA, numbered sn-1, sn-2 and sn-3 from the bottom to the top – which can be imagined as a glycerol molecule displayed vertically on the left-hand side of a visual image with the three FA displayed horizontally, bound to the hydroxyl groups of the glycerol molecule. The specific sn-x structures and varieties of TAG affect the properties of a fat. For example, beef tallow and cocoa butter have similar but not identical mouthfeel, and the property of melting on the tongue is due mainly to the reduced types of TAG and their specific combinations in cocoa butter (Bracco 1994). During digestion, lipases hydrolyse the bonds at the sn-1 and sn-3 position, resulting in a monoglyceride and two free FA, and the monoglycerides are taken up more efficiently. However, this preference is only likely to affect monoglycerides of stearic acid (Bracco 1994), since >99% of all the other FA are taken up irrespective of the sn-x position that they occur in. These monoglycerides preferentially form the backbones for new TAG in the host (Zock *et al*. 1996). Plant oils tend to have more PUFA in the sn-2 position than animal fat (Hunter 2001), which would then result in PUFA being preferentially incorporated into reformed TAG in the individual. Given the discussion on a high

OMR and reactive oxygen species (see above and below) this may have unfortunate effects on stored and structural lipid in the individual. Stereoisomeric modifications of palmitic acid in a normal diet in adults appeared to make no significant difference to the HDL-C or LDL-C concentrations in the blood (Zock *et al*. 1995). However, in a review of the literature on interesterification, (Hayes and Pronczuk 2010) report that a large amount of stearic acid in the sn-2 position had negative effects on the relative HDL-C and LDL-C profile. As stearic acid is generally not found at high frequency in the sn-2 position in natural fats, and is usually considered as hypocholesterolemic (see above), they considered this a concern for manufactured fats. Furthermore, they report that interesterified fats alter the HDL-C and LDL-C ratios and concentrations in the serum of both infants and piglets away from the pattern seen when they are fed their mother's milk (Hayes and Pronczuk 2010), which generally has SFA at the sn-2 position (Hunter 2001). This is a concern given the known improvement in growth of infants on animal versus plant fats (López-López *et al*. 2001). Finally, the overall structure of a fat may affect its digestion. For example, butter is a water-in-oil emulsion, compared with the lipid contents of the gut, which after secretion of bile, becomes an oil-in-water emulsion. This has been hypothesised to explain the result of a shorter period of elevated lipemia after a meal using butter compared with olive or sunflower oils, with an increased number of chylomicrons and faster processing of chylomicron remnants, a positive physiological result (Mekki *et al*. 2002). The alternative explanation is that the cholesterol and SFA in butter increased the expression of apoE (see above), resulting in more chylomicrons that were processed more efficiently by the body. Animal fats as a constituent of adipose or muscle tissue or dairy products and plant fats or oils in the form of nuts, seeds or oily fruits are absorbed slowly compared with refined cooking oils or fats added to food, due to the structures and digestibility of the items (Berry *et al*. 2008; Damasceno *et al*. 2011; Michalski *et al*. 2013; Garcia *et al*. 2014).

Where lipids are the overwhelming energy source then there is substantial generation of ketone bodies, and there are some benefits to be had from the metabolism of ketone bodies (Veech *et al*. 2001; Volek *et al*. 2008). The ketone bodies β-hydroxybutyrate and acetoacetate are deliberately generated from FA and are not a consequence of incomplete glucose metabolism via the tricarboxylic acid cycle (Krebs 1966; Krebs *et al*. 1971). These are a form of energy from fat that is directly soluble in aqueous solution rather than either being carried as NEFA attached to albumin or TAG carried via serum cholesterol or chylomicrons, and are the only metabolite from FA that can be directly metabolised by the brain (Cahill 2006). In a further parallel to serum glucose, levels of ketone bodies are regulated by insulin, so that a pulse of higher levels of ketone bodies increases insulin thereby reducing release of lipid from adipocytes (Hawkins *et al*. 1971). It is thought that ancestral human diets would have generated ketone bodies for parts of the day or for days (Krebs *et al*. 1971; Veech *et al*. 2001; Volek *et al*. 2008), because they are metabolites associated with starvation (Cahill 2006). Although levels of serum ketone bodies have not been measured in traditional hunter-gatherers, there is evidence from contemporary study of some hunter-gatherers of absence of food for days (Stefansson 1912; Marlowe 2005). In addition, measurements on Western volunteers of both sexes show the generation of ketone bodies a few hours after moderate to high fat meals if no snacks are taken (Marinou *et al*. 2011). As blood glucose and insulin levels gradually decline after a meal, levels of NEFA increase in the circulation, and the ketone bodies acetoacetate and β-hydroxybutyrate start to rise (Cahill 2006; Hodson *et al*. 2008; Marinou *et al*. 2011). The metabolism of ketone bodies requires less oxygen to generate the same physiological output and generates fewer free radicals (Sato *et al*. 1995), so is less damaging to tissues (Halliwell 2006), than the metabolism of serum glucose. In the presence of both serum glucose and ketone bodies, less glucose is used (Kashiwaya *et al*. 1994) suggesting that the body will protect its glucose sources in the presence of ketone bodies. In these mild ketotic states, the amount of acetocarnitine and ubiquinone-10 (Coenzyme Q_{10}), the latter through its obligate relationship to the uncoupling proteins, are increased in tissues including the liver, heart, brain, and skeletal muscle (Pearson and Tubbs 1967; McGarry *et al*. 1975; Echtay *et al*. 2000; Sullivan *et al*. 2004). These are two important anti-oxidants in the body whose levels appear to decline with age and are associated with the decline of function of mitochondria due to age-related oxidative damage (Shigenaga *et al*. 1994; Hiatt 2001).

High fat low carbohydrate low to moderate protein diets, often called ketogenic diets, have been shown to reverse the metabolic syndrome and non-alcoholic fatty liver disease without medication and address a range of other biological indicators (Hite *et al*. 2011; Peréz-Guisado and Munoz-Serrano 2011*a*, 2011*b*). These diets have not only led to weight loss without direct calorie restriction they have resulted in improvement in the risk factors associated with CVD when animal and other fats are used (Foster *et al*. 2003; Volek *et al*. 2003; Herron *et al*. 2004; Sharman and Volek 2004; Volek and Sharman 2004; Yancy *et al*. 2004, 2010; Brinkworth *et al*. 2009; Sacks *et al*. 2009). Moreover, trials of ketogenic diets in the treatment of final stage cancer patients and in experimental systems (Tisdale *et al*. 1987; Breitkreutz *et al*. 2005; Zuccoli *et al*. 2010; Ho *et al*. 2011; Klement and Kaemmerer 2011; Schmidt *et al*. 2011; Chang *et al*. 2013) have occurred, with some interesting results of reduction in tumour size, reduction of cachexia, or delay of initiation of cancer. Ketogenic diets continue to be used to treat some classes of epilepsy (Freeman *et al*. 1998; Kossoff *et al*. 2006; Neal *et al*. 2008), and have been suggested for other mental disorders or dementias including Alzheimer's disease and Parkinson's disease (VanItallie and Nufert 2003; Kim *et al*. 2007; Kossoff and Hartman 2012). A random controlled trial of an additive to the normal diet, AC-1202, consisting of short- and medium-chain TAG derived from coconut oil and that are metabolised to ketone bodies, has shown some improvement in Alzheimer's disease sufferers from ketone body production (Henderson *et al*. 2009). Therapeutic doses were 20 g per day, which generated similar levels of ketone bodies to a low carbohydrate diet. Butter fat consists of >10% of short-chain FA and a further 15% of the medium-chain SFA of C12:0 and C14:0, which are rapidly oxidised in the liver (Bach and Babayan 1982; MacDougall *et al*. 1996; DeLany *et al*. 2000) and would therefore generate increased levels of ketone bodies in a high fat but not necessarily low carbohydrate diet.

Finally, at the opposite extreme, consumption of large amounts of sugar, refined carbohydrate and food overconsumption in general can lead to obesity, high serum glucose and hyperinsulinaemia. The effects of high serum glucose and hyperinsulinaemia, hall marks of type 2 diabetes, are well known and are associated with a wide range of chronic diseases of Western civilisation (Kuusisto *et al*. 1997; Xu *et al*. 2004; Friberg *et al*. 2007; Xue and Michels 2007; Johnson *et al*. 2009; Orgel and Mittelman 2013). High serum glucose is functionally related to the glycosylation of protein, which increases the rate of aging of tissues. High serum glucose is also functionally related to the increased glycosylation of small dense LDL-C and subsequent damage to apoB-100 molecules within the blood stream (Younis *et al*. 2013), contributing to atherosclerosis. Serum glucose is needed for cancer cell growth, as cancerous cells are switched to obtaining energy from aerobic glycolysis, the Warburg effect. Cancerous cells use the intermediates of the glycolytic pathway to generate FA and other biosynthetic intermediates within the cell so as to generate cell membranes and organelles and thereby allow cell growth and division, and this is what most of the glucose is used for (Warburg 1956; Wang *et al*. 2012). Paradoxically, these cells do not derive much energy from either ketone bodies or β-oxidation of FA, irrespective of the circulating level of FA. Carbohydrate sources vary in their ability to maintain high serum glucose and promote insulin resistance, with recent research showing that fructose, and by association sucrose, have a much higher ability to promote insulin insensitivity and, consequently, a prolonged elevation in serum glucose than glucose itself (Stanhope *et al*. 2009). Individuals respond differently to these two factors, leading to correlations between disorders. For example, diabetic individuals are more likely to have CVD, or a cancer, or either vascular dementia or Alzheimer's disease (Stamler *et al*. 1993; Luchsinger *et al*. 2001). Non-diabetic individuals with Alzheimer's disease are more likely to have high serum glucose and hyperinsulinaemia, even though BMI is not associated to Alzheimer's disease. Some of these disorders have historically been blamed on high fat consumption using evidence from ecological comparisons, but the evidence from high fat ketogenic diets (cf. above) suggests instead that these disorders are due to food overconsumption rather than fat overconsumption. Obviously, animal fat is not a panacea for all ills, but avoidance of animal fat is no panacea either.

Recommendations for animal industries

If humans are to consume animal fat then the best quality fat should be produced (Kelly *et al*. 2001; Tume 2004; Givens 2005; Shingfield *et al*. 2013). This review suggests that this results in some clear selection and production/nutrition goals for animals. These goals are that where possible animals should be produced with a low OMR, that long-chain n-3 PUFA should be increased, that higher levels of oleate or stearate and lower levels of palmitate should be encouraged, but that increased n-6 PUFA content need not be encouraged.

The composition of the fat of monogastric animals is changed by the feed they eat. Farmed fish are known to have lower levels of long-chain n-3 PUFA and many of the most valuable fish are fed combinations of fish meal. Some research suggests that farmed fish such as salmon have the ability to generate their own long-chain n-3 PUFA when the diet is limiting (Sanden *et al*. 2011). Approximately 35–45% of chicken and other poultry fat is MUFA, between 22 and 27% of the fat is CISFA, 13–26% of fat is PUFA depending on species and method of rearing, but there can be large changes in long-chain n-3 PUFA if the ration contains higher levels of α-linolenic acid (Chartrin *et al*. 2006; Jia *et al*. 2010; Givens *et al*. 2011). In pigs there are smaller changes in stearic acid, MUFA and PUFA with different rations and genotypes than in chickens but CISFA are ~27% of the fat and can as low as 21% for free-range pigs (Rodríguez-Sánchez *et al*. 2010; Razmaite *et al*. 2011; Barea *et al*. 2013). The value of the OMR is dependent on the food source. Interestingly, genetic modification of pigs with the nematode delta-3 desaturase results in animals with a lower OMR even if fed diets high in n-6 PUFA (Ren *et al*. 2011). This has not yet been reported in other food animal species.

Ruminants have low levels of PUFA in their fat due to biohydrogenation of dietary PUFA (Doreau and Ferlay 1994) although there are differences in ruminants in the amount of oleate depending on genetics and feed source (Yang *et al*. 1999*a*). One of the major effects on ruminant fat is the ratio of stearate to oleate, which depends on the location of the fat within the body: the closer to the surface the higher the oleate and the lower the stearate (Meng *et al*. 1969; West and Shaw 1975; Morin 2007; Staerfl *et al*. 2011). Despite the difference in total SFA between free-range chicken, pig and ruminant fat, they contain very similar levels of CISFA, in a range ~25%. Although the level of PUFA in ruminant fat is much lower than in monogastric fat, the OMR is still dependent on the ration or type of feed, with lower OMR achievable on feed if higher levels of n-3 fats are used (Bobe *et al*. 2007). Changing the OMR in ruminant feed will affect the OMR of PUFA available for human consumption, and this would be a benefit. Whether the feeding of cattle in feedlots will grow or decline in the future will be affected by a range of factors including amount of methane produced per kilogram meat produced, the cost of feedlot rations compared with the cost and requirement for biodiesel and other fuels, and the availability of rangeland for pasture for ruminants.

The palatability of animal foods is affected by the amount and composition of its fat, but at present, in Western countries like Australia, a lot of emphasis is placed on reducing the amount of fat in livestock. Palatability and eating quality of meat is related to increased fat content, as reported in tests of consumers, but consumers in many Western countries actively select leaner cuts when meat is presented raw (Wood *et al*. 1999; Thompson 2004; Dransfield *et al*. 2005; Polkinghorne and Thompson 2010; Utrilla *et al*. 2010). Although it is suggested that this reduction in meat fat will improve human health, as this review has shown, this claim is dubious. This demand for leaner meat has led to some distortions in selection and production goals. From poultry to cattle, animals are selected for more meat and less fat (Abasht *et al*. 2006; Lagarrigue *et al*. 2006; Givens *et al*. 2011), and meat is presented with more fat trimmed from the cuts. This has led to fat being discarded and, in some cases, excess animal fat burned for fuel (Fairlie 2010), which is wasted production. Selecting animals for more meat, greater efficiency, greater productivity, and less fat has occasionally resulted in negative consequences for the

animals themselves, such as reductions in fertility and fecundity, dystocia, porcine stress syndrome, Rendement Napole, or skeletal problems (Carlson *et al*. 1980; Hanset *et al*. 1982; Enfält *et al*. 1997; Grobet *et al*. 1997; Pitchford 2004). Changing the selection goal of more meat and less fat may well be intractable, however, as it is partly a response to consumer preference, and consumer preference can take decades to change.

Nevertheless, it is not impossible for consumer sentiment to change, a newspaper article titled 'Butter crisis spreads in Norway' (Anonymous 2011) reported that due to a high fat low carbohydrate diet craze Norway ran out of butter in the lead in to the Christmas period. New formulations of products, such as Christmas Puddings and Chicken Liver Pate, are appearing on Australian supermarket shelves with ingredients including animal fats and margarines made from edible animal tallow (change observed between December 2012 and April 2013) that previously had potato starch as stabiliser or vegetable shortening only. Prominent medical professionals are starting to say that it is better to control sugar, especially fructose and thereby sucrose (Lustig *et al*. 2012), and that controlling dietary saturated fat is irrelevant, so it may be that the wheel has started to turn. Animal industries should be aware of these trends and need to take advantage of them when they arise, because changing selection goals or production practises does not occur overnight. More emphasis should be placed on healthy fat from animals, not just from fish, but also from livestock of all kinds.

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