The health benefits of omega-3 polyunsaturated fatty acids: a review of the evidence

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Abstract

The UK dietary guidelines for cardiovascular disease acknowledge the importance of long-chain omega-3 polyunsaturated fatty acids (PUFA) – a component of fish oils – in reducing heart disease risk. At the time, it was recommended that the average n-3 PUFA intake should be increased from 0.1 to 0.2 g day^{-1}. However, since the publication of these guidelines, a plethora of evidence relating to the beneficial effects of n-3 PUFAs, in areas other than heart disease, has emerged. The majority of intervention studies, which found associations between various conditions and the intake of fish oils or their derivatives, used n-3 intakes well above the 0.2 g day^{-1} recommended by Committee on Medical Aspects of Food Policy (COMA). Furthermore, in 2004, the Food Standards Agency changed its advice on oil-rich fish creating a discrepancy between the levels of n-3 PUFA implied by the new advice and the 1994 COMA guideline. This review will examine published evidence from observational and intervention studies relating to the health effects of n-3 PUFAs, and discuss whether the current UK recommendation for long-chain n-3 PUFA needs to be revisited.

Introduction

In 1994, the Committee on Medical Aspects of Food Policy (COMA) published a report bringing together evidence on various nutritional determinants of heart disease risk (Department of Health, 1994). One aspect was the beneficial impact of fish oils, and their constituent long-chain omega-3 polyunsaturated fatty acids (n-3 PUFA), on platelet aggregation and tendency towards thrombosis. The daily recommendation emerging from this particular discussion, i.e. 0.2 g long chain n-3 PUFA, is yet to be revised. Since 1994, extensive evidence has been published on the health benefits of fish oils and their constituent fatty acids; docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Interestingly, there is more to n-3 PUFAs than their well-recognized role in ameliorating the risk of heart disease. This review will examine the impact of n-3 PUFA on cardiovascular disease, inflammatory disease, brain function and mental health with a view to exploring whether the current UK guideline is still appropriate. This discussion is particularly relevant since the Food Standards Agency (FSA), following advice from the Scientific Advisory Committee on

Nutrition (SACN, 2004), changed its advice on oil-rich fish to recommend a weekly consumption for the general population of one to four portions per week (up from one to two portions) and, for pregnant and lactating women, up to two portions a week. If translated into long-chain n-3 PUFA, this would increase the recommended range to 0.45 to 0.9 g day^{-1}. The restriction for pregnant women was intended to safeguard them from possible heavy metal or dioxin contamination. In the present review, biomedical literature was accessed through a MEDLINE search (January 1989–June 2003). Search terms included fish oil, omega-3 fatty acid, cardiovascular disease, inflammation, immune function, dementia, cognitive function, arthritis, systematic review and randomized-controlled trial (RCT).

Definition and nomenclature of n-3 PUFA

Fatty acids typically have an even number of carbon atoms, in the range of 16–26. Fatty acids with only single bonds between adjacent carbon atoms are referred to as 'saturated', whereas those with at least one C=C double bond are called 'unsaturated'. The PUFA have two or more double bonds and are named according to the position of these bonds and the total chain length. For example, DHA (22:6) is an omega-3 (n-3) fatty acid with 22 carbon atoms and six double bonds (Fig. 1). The term 'n-3' indicates that, counting from the methyl (CH_3) end of the molecule, the first double bond is located between the third and fourth carbons. As the degree of unsaturation in fatty acids increases, the melting point decreases which confers the attribute of fluidity on n-3 PUFA.

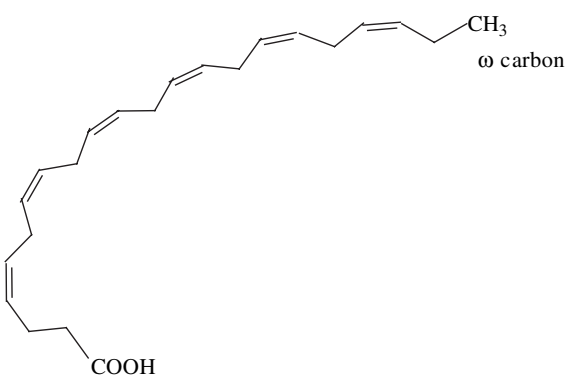

Figure 1 Diagram of the structure of docosahexaenoic acid (DHA; 22:6, n-3).

The DHA and EPA are synthesized from the n-3 precursor α-linolenic acid (ALA; 18:3), whereas long chain n-6 PUFA such as arachidonic acid (AA) are synthesized from the precursor linoleic acid (LA; 18:2). The ALA and LA are essential to the human diet because neither is synthesized endogenously by humans, and the n-3/n-6 families cannot be interconverted. In theory, the ability to convert ALA to EPA and DHA means that humans have no need for an exogenous supply of these fatty acids. However, there are two reasons why this may not be strictly true. First, the biosynthetic pathways of both the n-3 and the n-6 families share an enzyme called δ-6-desaturase. This enzyme, which is vital for the conversion of ALA to DHA and EPA, has a preference for ALA but the presence of high levels of plasma LA (caused by high n-6 PUFA intakes) can shift its actions towards the n-6 pathway (Budowski, 1988). The result is inhibition of the pathway that converts ALA to EPA and DHA (Gerster, 1998) and possible low plasma levels of these fatty acids. Secondly, it has long been suspected that the conversion of ALA to DHA is inefficient. Studies comparing supplementation using linseed oil (ALA) vs. fish oil (EPA + DHA) have demonstrated that whereas linseed oil produces a moderate increase in platelet EPA, fish oil produces a large rise in both platelet EPA and DHA (Sanders & Roshanai, 1983). The absence of EPA and DHA in the diet is unlikely to lead to clinical deficiency but it is possible that people with enhanced requirements could be disadvantaged by this type of diet.

Cardiovascular disease

Cardiovascular disease (CVD) is one of the most common in the Western world; its complex aetiology involving both genetic and acquired factors. Public health messages about diet and CVD have tended to focus on saturated fatty acids (SFA) and n-6 PUFA. More recently, the messages have included the positive role of n-3 PUFA.

Observational studies

The lower rate of CVD seen in fish-eating communities, e.g. the Japanese, prompted investigation into how fish and its nutritional components might lower the risk of CVD. Bulliyya (2002) compared fish-eaters ($n = 500$) with non fish-eaters ($n = 500$) in a study based in South Indian villages. Mean high-density lipoprotein (HDL) concentrations were consistently but modestly higher, whereas low-density lipoprotein (LDL) concentrations were lower in the fish-eaters compared with the non fish-eaters. There was also an improvement in the HDL : LDL ratio. Similar effects on HDL were noted by Dewailly *et al.* (2003) in their comparison of three ethnic groups in Quebec. Interestingly, the Inuit – regular fish-eaters – demonstrated the lowest CVD risk despite a high prevalence of obesity and smoking.

Good epidemiological data were reported by Hu *et al.* (2002) who followed 84 688 women enrolled into the Nurses' Health Study for 16 years. Deaths related to CVD were 50% lower in women who consumed fish five times per week, and even a fish intake of one to three times per month was associated with over 20% reduction in CVD events. The same authors (Hu *et al.*, 2003) studied a subgroup of diabetic women from the Nurses' Health Study and discovered an even stronger inverse relationship between fish intake and CVD, with more than 60% risk reduction for the highest fish intake, and approximately 30% reduction for women eating one to three fishmeals per month. A Cochrane review has confirmed that fish oil lowers triglycerides in people with type II diabetes (Farmer *et al.*, 2003) and this is likely to be the mechanism for how CVD risk is reduced in this group.

Although habitual fish consumption appears to offer protection against CVD, the benefits are influenced by the type of fish consumed. Fatty fish (e.g. tuna, mackerel, trout, salmon) provide more DHA and EPA and confer greater cardio-protection than white fish (Oomen *et al.*, 2000).

Clinical trials

Although observational studies can reveal associations between dietary factors and disease, RCT are needed to establish a causal relationship. However, it is not easy to interpret the evidence because of differences in n-3 PUFA dose, DHA : EPA ratio, duration of intervention and reported outcomes. Bucher *et al.* (2002) conducted a meta-analysis of 11 RCT, which involved a total of 7951 patients in the intervention groups and employed supplementation levels of 0.3–6.0 g day^{-1} for EPA, and 0.6–3.7 g day^{-1} for DHA. The study selection and assessment of quality was conducted by two independent investigators under strict guidelines. Two of the studies included in the Bucher analysis are described below as they are particularly well-known. The meta-analysis concluded that n-3 PUFA could reduce overall mortality, mortality because of myocardial infarction (MI) and sudden death in patients with CHD. When comparing the relative benefits for different types of patients, Bucher *et al.* (2002) calculated that 250 patients with a low CHD risk would need to be supplemented with n-3 PUFA for $1\frac{1}{2}$ years to prevent one premature death. The respective figure for high-risk patients was much lower at 24.

It is generally accepted that n-3 PUFA have their most useful role in secondary prevention of CVD. The largest trial conducted is the GISSI Interven-zione study (GISSI, 1999) involving 11 324 subjects who had survived an acute MI. Subjects, who were followed for 3.5 years, were assigned to one of four groups: (i) 0.88 g day^{-1} n-3 PUFA (1 : 2, EPA : DHA) alone; (ii) n-3 PUFA + 300 mg day^{-1} vitamin E; (iii) vitamin E alone; (iv) no treatment. The subjects given n-3 PUFA showed a significant reduction in cardiac events. Inclusion of vitamin E offered no additional protection.

In the Diet and Reinfarction Trial (DART), 2033 men aged <70 years, who had survived an acute MI, were randomized to receive one of three types of advice: (i) a reduction in total fat intake with an increase in the ratio of PUFA : SFA; (ii) an increase in fatty fish intake; (iii) an increase in fibre intake (Burr *et al.*, 1989). The subjects advised to eat fatty fish, around two to three portions per week, had a 29% reduction in 2 year all-cause mortality compared with those given alternative advice. Interestingly, a repeat of this study in 3114 men with angina (Burr *et al.*, 2003) found no beneficial effect of dietary advice on mortality after 3–9 years; men

advised to eat more fish experienced a higher risk of cardiac death. The authors acknowledged that the results were unexpected and contradicted most other literature in the field.

Inflammatory disease

There is growing evidence from animal and human studies that n-3 PUFA have an immunomodulatory effect (for review, see Calder, 1996). This has prompted researchers to investigate the usefulness of n-3 PUFA in treating inflammatory conditions such as rheumatoid arthritis (RA), Crohn's disease, ulcerative colitis, psoriasis, asthma, lupus and cystic fibrosis (CF).

Inflammatory bowel disease

Evidence for the beneficial effects of fish oils in chronic inflammatory bowel disease is conflicting and largely inhibited by small study populations. The RCT using fish oils at varying concentrations have reported either a significant improvement in active mild-to-moderate ulcerative colitis (Aslan & Triadafilopoulos, 1992) or modest but insignificant effects (Lorenz *et al.*, 1989). Others have found no effect on rate of relapse (Middleton *et al.*, 2002).

Asthma

The effect of n-3 fatty acids on asthma is also unclear. A Cochrane review (Woods *et al.*, 2003) aimed to evaluate the effect of fish oil supplementation on asthma, searching widely to find nine RCT of appropriate quality up to October 2002; most conducted in adults. Whereas some found improvements in symptoms and medication use, there were no significant consistent effects. Neither was any risks found, suggesting that it would be safe for individual asthma sufferers to try fish oil therapy alongside conventional treatment.

Cystic fibrosis

A Cochrane review examined the evidence for the use of n-3 PUFA in CF, searching widely to find six RCT up to May 2002, only two of which were deemed of acceptable quality (Beckles Willson *et al.*, 2003). The authors concluded that n-3 PUFA intake benefited the patients with CF, however, the size of the interventions (31 patients in total) limited the scope of the findings. Few adverse effects were noted.

Rheumatoid arthritis

The RA is only inflammatory condition for which there is good evidence for the potential therapeutic benefits of n-3 PUFA, perhaps because there is a clear mechanism involving a modulation of the immune system to reduce the action of inflammatory compounds (Darlington & Stone, 2001), and a number of RCT have now been published. Fortin *et al.* (1995) conducted a meta-analysis of 10 clinical trials of fish oil supplementation in RA representing 395 patients in both control and intervention groups. They concluded that, while there was a significant reduction in the number of tender joints and in duration of morning stiffness after 3 months of therapy, no effect was seen on indices of disease activity or progression of RA. A later nonsystematic review (Cleland *et al.*, 2003) described 14 double-blind RCT of fish oil in RA representing a dosage range of 1.0–7.1 g day^{-1} EPA + DHA (mean dose 3.3 g day^{-1}) with a duration of 12–52 weeks. A variety of improvements in clinical outcome was reported which included reduced duration of morning stiffness, reduced number of tender or swollen joints, reduced joint pain, reduced time to fatigue, increased grip strength and decreased use of non-steroidal anti-inflammatory drugs (NSAID). Cleland *et al.* (2003) opined that the evidence for benefits from n-3 PUFA in the *management* of RA is robust. However, the Scottish Intercollegiate Guidelines Network (2000) guideline on the management of early RA expresses doubt about the practicality of fish oil therapy because high doses would be needed and this may be difficult to take and expensive. In a typical fish oil, long chain n-3 PUFA comprise 20–30% of the fatty acids, thus providing 1–1.5 g of EPA + DHA per 5 mL portion. Thus, to achieve the average dosage quoted in Cleland *et al.* (2003), a patient would have to consume 15 mL of fish oil per day.

Brain development and function

In palaeontology, there is a school of thought that our ancestors enjoyed a diet rich in marine foods (Crawford, 1992). Perhaps then it is no surprise that the human nervous system contains a significant amount of DHA.

Role of n-3 PUFA in brain development

Information on what function DHA might have in the brain was gleaned from animal experiments. Young monkeys given a diet deficient in n-3 PUFA (Reisbick *et al.*, 1997) demonstrated poor visual acuity and increases in stereotypical behaviour suggesting that brain development had been impeded. It is believed that n-3 PUFA enable fluidity in neuronal membranes and help regulate neurotransmitters (Yehuda *et al.*, 1999), both crucial for optimal brain function.

Creating deficiency in humans would be unethical, but valuable work on the cadavers of premature babies has demonstrated a rapid accretion of DHA and AA in foetal brain tissue during the third trimester of pregnancy (Clandinin *et al.*, 1980). The additional foetal requirement for long chain PUFA is met by the placenta, but women with low n-3 PUFA stores, perhaps due to multiple pregnancies or a vegetarian diet, can pass on this suboptimal status to their newborns (Otto *et al.*, 1997). Increasing n-3 PUFA intake during pregnancy can enhance maternal DHA status, potentially benefiting the foetus. Connor *et al.* (1996) reported that pregnant women who consumed regular amounts of sardines or fish oil increased their own plasma DHA levels and transferred additional n-3 PUFA to their foetuses.

After birth, the fatty acid status of the mother continues to impact on her newborn via the delivery of breast milk; a naturally rich source of DHA (Crawford *et al.*, 1981). Breast milk reflects the habitual fatty acid intake of the mother, e.g. the breast milk of vegans contains relatively low levels of DHA (Sanders, 1999), whereas mothers who regularly eat fish produce breast milk with a high DHA content (Jørgensen *et al.*, 2001). The fatty acid composition of breast milk has changed over the last few years in Western countries and now tends towards a higher n-6 : n-3 ratio. This is most likely due to low fish intakes combined with an increased consumption of margarine and vegetable oils (Makrides *et al.*, 1995).

Early diet and later indicators of brain function

Given the importance of DHA in early brain development, it seems logical that a poor n-3 status would have an adverse effect on infants. Whereas this appears to be the case in animal models (Wainwright, 2002), strong evidence in humans is lacking. A number of RCT has examined whether supplementing the diets of infants with DHA and AA can benefit visual acuity and cognitive development. This review has insufficient space to do justice to the issue, which has been covered by two Cochrane reviews. The first, relating to preterm infants (Simmer, 2003a) which assessed five randomized trials, concluded that DHA supplementation benefited preterm infants in the first 4 months of life but there was insufficient evidence for the months beyond this. It is possible that, after 4 months, the preterm infant is able to synthesize sufficient AA and DHA to support normal development. The review refuted the concern that DHA supplementation could lead to adverse effects on growth. The second Cochrane review, relating to term infants which included eight randomized trials (Simmer, 2003b), found no significant benefits for n-3 PUFA in terms of visual acuity or general development, although there was a possibility that information processing could be improved by giving long chain PUFA. A number of commercial infant formulae now contain AA and DHA, whereas a position statement (Koletzko *et al.*, 2001) has called for term infant milk to contain 0.2% of total fatty acids as DHA with a higher amount for preterm.

Some authors have examined the relationship between n-3 PUFA status in infants and later development. Jørgensen *et al.* (2001) found a correlation between maternal fish consumption and better infant visual acuity, whereas Daniels *et al.* (2004) found that mothers who ate fish four times a week during pregnancy had babies with higher developmental scores at 18 months compared with those who ate no fish. Ghys *et al.*

(2002) and Bakker *et al.* (2003) attempted to relate foetal n-3 PUFA status to later intelligence quotient (IQ) in cohorts of infants, but no associations were found. Instead IQ was significantly related to a range of other factors, e.g. maternal intelligence, highlighting the confounders, which can obscure any relationship between nutrition and brain function. However, Helland *et al.* (2003) did find a relationship between n-3 PUFA and infant IQ. In a double-blind RCT pregnant women were supplemented with 1.18 g DHA and 0.8 g EPA per day as cod liver oil from week 18 until delivery. When the infants were followed up at 4 years of age, those whose mothers had received the supplementation scored significantly higher in tests of mental processing. This potentially exciting outcome needs to be confirmed by other studies.

Mental health

Behavioural disorders

It has been suggested that imbalances in fatty acid status could be linked to behavioural and learning disorders such as attention deficit hyperactivity disorder (ADHD), dyslexia, dyspraxia and autism (Richardson & Ross, 2000).

The ADHD is characterized by inattentive, impulsive and hyperactive behaviour and affects around 2–4% of children. Interest in n-3 PUFA arose when ADHD patients were found to have lower plasma levels of EPA and DHA compared with normal children (Stevens *et al.*, 1995). However, the limited evidence from RCT fails to demonstrate a consistent benefit for intakes of 0.34–0.67 g DHA + EPA, perhaps due to wide differences in supplementation regimes.

Depression and bipolar disorder

Evidence for the role of n-3 fatty acids, particularly DHA, in the aetiology and treatment of depression and other mental disorders has been reviewed elsewhere (Freeman, 2000; Mischoulon & Fava, 2000). It is hypothesized that a relationship exists between a poor n-3 PUFA status and an increased risk of depression. In a nine country study, Hibbeln (1998) demonstrated a significant correlation between high annual fish consumption and a low prevalence of major depression. Tanskanen *et al.* (2001) studied a sample of 3204 Finnish adults finding a significant correlation between low fish consumption and depressive symptoms. A survey of 4644 New Zealand adults found that fish consumption was significantly associated with higher self-reported mental health status (Silvers & Scott, 2002). Whereas population comparisons are interesting, they are insufficiently controlled to elucidate a cause and effect relationship between n-3 PUFA and depression. More convincing are studies, which have found reduced n-3 PUFA levels in the tissues of depressed patients (Maes *et al.*, 1999) and a relationship between low n-3 status and severity of symptoms (Adams *et al.*, 1996). Once again these data cannot establish causality as it is possible that depression, or related drug treatments, could influence fatty acid status.

Evidence from supplementation trials, although limited, suggests that n-3 PUFA are useful in the treatment of depression at dosages of 0.2–9.6 g EPA + DHA. Elderly patients treated with DHA-supplemented phosphatidylserine demonstrated significant reductions in depressive symptoms compared with a placebo group (Cenacchi *et al.*, 1993). In a double-blind RCT of EPA, patients with unipolar depressive disorder experienced significant improvements in symptoms after 4 weeks of treatment (Nemets *et al.*, 2002). A well-known intervention in 30 patients with manic depression (Stoll *et al.*, 1999) used a daily dose of 6.2 g EPA + 3.4 g DHA in a 4 month, double-blind RCT. Significant improvements were seen in nearly every outcome measure particularly with respect to depressive symptoms. However, no effect was seen in an intervention trial on 36 severely depressed patients (Marangell *et al.*, 2003), although it could be that the dose of 2 g day^{-1} DHA was too low.

Postnatal depression has also been linked with a low n-3 PUFA status, which fits with the evidence for high foetal requirements for DHA in the third trimester. Hibbeln (2002) suggests that mothers selectively transfer DHA to their foetuses to support optimal neurological development leaving themselves at risk of depletion if dietary n-3 PUFA

intake is low. In a review of 23 countries, Hibbeln (2002) found that both a lower DHA content in breast milk and lower seafood consumption were associated with higher rates of postpartum depression. However, this evidence has yet to be supported by intervention trials. Llorente *et al.* (2003) supplemented mothers for 4 months after delivery with 0.2 g day^{-1} DHA finding no significant effect on self-rated depression despite increases in plasma DHA status.

Cognitive impairment in later life

Dementia is a common disorder among elderly people. Its prevalence increases with age to more than 30% among those aged 85 years and over (Ott *et al.*, 1995). Large-scale epidemiological studies have identified fish consumption as a potential protective factor against dementia. In a prospective study of 5386 Dutch citizens aged 55 years or older (Kalmijn *et al.*, 1997a), those with a fish consumption of more than 20 g day^{-1} had a reduced risk of cognitive impairment, cognitive decline, dementia and Alzheimer's disease. Another Dutch study of 476 men aged 69–89 years (Kalmijn *et al.*, 1997b) reported that a high LA intake was associated with cognitive impairment after adjustment for confounders, whereas high fish consumption was inversely associated. A recent prospective study (Morris *et al.*, 2003) found a strong inverse link between fish intake and Alzheimer disease. Elderly people who ate fish at least once a week had a 60% lower risk of developing the disease over a 4-year period.

Plasma studies support the evidence that low n-3 levels are associated with dementia. Conquer *et al.* (2000) found lower levels of plasma phospholipid DHA in patients with Alzheimer's disease and other dementias. They also found a significantly decreased level of plasma DHA in a group of elderly individuals who were cognitively impaired but did not have dementia. The authors hypothesized that decreased n-3 PUFA prior to disease onset may be at least partly responsible for the lower levels of plasma DHA and the cognitive decline. A French longitudinal survey supports this view. Heude *et al.* (2003) measured erythrocyte membrane fatty acid composition and cognitive function in 246 elderly people and followed them up 4 years later. Those with high n-6 PUFA and low n-3 PUFA in their erythrocytes were most likely to experience cognitive decline. The next stage to unravelling the relationship between n-3 PUFA and cognitive function in the elderly is an intervention trial, but so far only one small pilot has been published. Terano *et al.* (1999) supplemented 10 elderly Japanese with 0.72 g DHA for 12 months and compared them with an unsupplemented group. A significant improvement in dementia scores was found in the DHA group, but not in controls, after 3 months. The potential usefulness of DHA in this field now needs to be verified by larger intervention studies.

Commentary

The authors suggest that COMA's initial view of the potential benefits of n-3 PUFA has been reenforced by new evidence gathered over the intervening years. The benefits of an increased consumption of EPA and DHA to improve cardiovascular risk factors is widely accepted, whereas understanding of the role of n-3 PUFA in alleviating inflammatory disease is improving. Perhaps the most intriguing area for potential benefits is in brain function and mental health; aspects of a dietitian's caseload where there are often too few evidence-based nutrition solutions. With respect to the evidence relating to pregnancy and the elderly, the issue has perhaps moved on from ensuring an absence of deficiency to creating the right environment for optimal health. The idea that postnatal depression might be prevented by regular consumption of omega-3 rich foods is a powerful one. However, as with the potential benefits of n-3 PUFA to attenuate cognitive decline in the elderly, the observational studies now require convincing support from supplementation trials using different levels of DHA. The inclusion of antioxidants, e.g. vitamin E, in such trials is worth considering since n-3 PUFA are highly unsaturated, making them susceptible to peroxidation. This might explain the absence of an effect in some intervention trials.

Although health benefits might be effected by research studies, it is another matter to reproduce

these in the free-living population, particularly when the n-3 PUFA levels given to subjects often far exceed the modest 0.2 g day^{-1} recommended by COMA and the 0.1 g day^{-1} consumed by the UK population. Certainly, the Food Standard Agency's new stance on oil-rich fish is in the right direction. However, the portion advice now needs to be translated into DHA and EPA levels to clarify the discrepancy between the foodbased advice and the arguably out-of-date COMA guidelines on n-3 PUFA. One to four portions of oil-rich fish per week would translate into a daily EPA/DHA intake of 0.45 to 0.9 g. This may not be an achievable recommendation on fish alone as it is estimated that just one-third of UK adults eat oily fish with an average intake of one small portion per week (British Nutrition Foundation, 1999). Cod liver oil, equally unpopular with the consumer, can provide around 1 g EPA/DHA per 5 mL portion.

It would be helpful if the FSA advice was broadened to give consumers other dietary options for increasing n-3 PUFA intakes. New techniques in food manufacturing have enabled the benefits of fish oils to be conferred on nonfish products. Eggs can be fortified by feeding fish oils or their derivatives to poultry, thus increasing the normal n-3 PUFA content of eggs yolks by up to 18-fold. Commercially available eggs provide around 0.15 g DHA each (see www.dha-in-mind.com). Animal diet manipulation can also be used to augment the n-3 PUFA content of meat, e.g. lamb and pork. Vegetarian sources of n-3 PUFA, such as linseed or rapeseed oil, are a good source of EPA but conversion to DHA is poor (Gerster, 1998). A direct vegetarian source of DHA has been derived from algae (see www.martekbio.com). The addition of neat fish oil to food products, such as baked goods or dairy products, is limited by the alteration in taste which results. One way around this is to purify and microencapsulate the fish oils, then add the resulting flavourless powder to a range of foods. Products fortified in this way are considered to be both bioavailable and have the capacity to increase population intakes of n-3 PUFA (Higgins *et al.*, 1999). An intervention study, which gave fortified bread (providing 0.3 g EPA and 0.2 g DHA per day) to 36 volunteers with hyperlipidaemia, found significant reductions in plasma triglycerides after 4 weeks and increases in plasma HDL (Liu *et al.*, 2001). This emphasizes the value of fortified foods, particularly in populations where consumption of oily fish is low.

Given the health benefits from EPA and DHA intakes in excess of 0.2 g day^{-1} reported by many studies, it could be argued that even the n-3 PUFA intakes implied by the new FSA advice are rather low. While there may be little justification for a general recommendation for n-3 PUFA intakes above 0.9 g day^{-1} to address conditions experienced by a minority of the population e.g. arthritis or depression, there could be reason to target CVD. With the rising incidence of obesity and non-insulin diabetes, more adults could be at risk from CVD. It is perhaps time to re-examine the literature to determine which levels of n-3 PUFA are most appropriate for primary and secondary prevention. Harris *et al.* (2003) suggest that individuals with coronary artery disease can reduce their risk of acute MI by increasing their n-3 PUFA intake to approximately 1 g day^{-1}. Whatever the recommendations might be, it is questionable whether a single n-3 PUFA intake is appropriate for everyone, and distinction may need to be made between recommendations for general health and those to prevent disease.

Calls to increase a particular food or nutrient must be considered alongside any potential risks. Whereas the Cochrane reviews quoted did not emphasize any significant risks from increasing n-3 PUFA intakes, there are concerns that a higher oily fish consumption could impact on intakes of pollutants such as dioxins and heavy metals. Certainly, public health warnings identify tuna, swordfish and marlin as foods to be eaten in moderation because of possible pollution with mercury but if intakes of other oily fish were to increase beyond current UK intakes, it is unlikely that the risk of exposure to toxins would outweigh the potential benefits from n-3 PUFA (Food Standards Agency, 2003). In a review of risks from pollutants, Jarup (2003) suggested that the general population in moderate fish-eating communities 'does not face a significant health risk from methyl mercury'. Over the counter cod liver oil from a range of companies has been found to contain negligible levels of heavy metals

(Koller *et al.*, 1989). The microencapsulated tuna oil used for many types of fortified products is purified to remove pollutants (Nu-Mega, Brisbane, Australia, personal communication). Bourre *et al.* (1991) considered the impact of excessive intakes of n-3 PUFA in the rat model, finding that brain and liver n-6 PUFA were severely reduced, although it is not clear what would be the functional impact of this. It seems that the balance between n-6 and n-3 PUFA is vital, but the average Western diet is a long way from being too high in n-3 PUFA. Data on n-6 : n-3 ratios (Simopoulos, 2001) suggests that the Japanese diet has a 4 : 1 ratio, whereas the figures for the UK and USA are 7 : 1 and 17 : 1 respectively.

Conclusion

There is evidence that an increased intake of long-chain omega-3 PUFA could impact positively on the health of many people. However, more work is needed to clarify and update current UK recommendations to enable more people, even those who do not wish to eat oil-rich fish, to benefit from enhanced intakes of long-chain omega 3 PUFA.

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