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OMEGA-3 FATTY ACIDS IN HEALTH AND DISEASE: THE SCIENCE BEHIND THE HEADLINES

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Stories of the health benefits of oily fish, fish oil supplements and omega-3 fats appear regularly and frequently in the media, along with occasional 'scare' stories. Such reports may elicit scepticism from health professionals about the health benefits and can cause confusion amongst consumers. There is, however, plenty of good quality science in this area and the evidence base in support of the healthful image of oily fish, fish oils and omega-3 fats is fairly strong. This article will provide a general overview of the topic and will identify literature sources from where more information can be obtained.

Omega-3 fatty acids are a family of naturally occurring polyunsaturated fatty acids. The term 'omega-3' refers to a structural characteristic of the family, denoting the position of one of the double chemical bonds within the fatty acid stricture (1,2) and is often written as ω-3 or n-3. The omega-3 family includes alpha-linolenic, eicosapentaenoic and docosahexaenoic acids. Eicosapentaenoic acid and docosahexaenoic acid are abbreviated as EPA and DHA, respectively. Although obviously retaining the characteristic omega-3 feature, these fatty acids have different structures, different dietary sources and different functions, but they are metabolically related to one another (Figure 1).

Alpha-linolenic acid cannot be synthesized by animals, including humans, but is synthesized by plants; it is one of the two classically essential fatty acids. In the human body alpha-linolenic acid can be converted into EPA and DHA (Figure 1), although the extent of this conversion, especially to the end product DHA, seems to be quite poor (3). However, this conversion has not been well explored in different subgroups of the population, but may be greater in women than in men (3) and may be partly determined genetically (4).

The apparently limited ability of humans to form DHA has led to some discussion as to whether DHA should be considered to be an essential fatty acid too. Because it is made in plants, some seeds, nuts and seed oils (such as rapeseed oil) contain significant amounts of alpha-linolenic acid (1). Flaxseeds and flaxseed oil have the highest content of alpha-linolenic acid. Increased intake of alpha-linolenic acid can increase the amount of EPA in blood and blood cells (3). However, conversion of alpha-linolenic acid to EPA is decreased if intake of the essential omega-6 fatty acid linoleic acid is high, because of metabolic competition between the two fatty acids. EPA and DHA are found in seafood and in the highest amounts in 'fatty' or 'oily' fish like salmon, mackerel and sardines (1). In the absence of significant consumption of oily fish, alpha-linolenic acid is the major omega-3 fat in the diet; adults in the UK typically consume about one gram of alpha-linolenic acid each day, this contributing about 90 percent of dietary omega-3 fatty acids.

Intake of the omega-6 linoleic acid is about 10-fold greater than this. In non-fish consumers, intake of EPA+DHA is likely to be less than 0.1 gram per day. One meal of oily fish can provide one to three grams of EPA+DHA, depending upon the type of fish, so eating oily fish can greatly increase intake of EPA and DHA and regular fish consumers have a higher content of these two fatty acids in their blood, blood cells and tissues compared with non-fish eaters.

In the UK less than 25 percent of adults eat oily fish regularly (5). Fish oil supplements provide EPA and DHA, which contribute about one-third of the fatty acids in a standard fish oil capsule. Thus, a standard one gram capsule would provide about 0.3 grams of EPA+DHA. More concentrated 'fish oils' are available which have a higher content of EPA and DHA and there is a pharmaceutical grade omega-3 preparation called Omacor which is highly concentrated, being approximately 90 percent EPA+DHA. Fish oil supplements can substantially increase intake of EPA and DHA and people who regularly use these supplements have a higher content of these two fatty acids in their blood, blood cells and tissues than those who do not use supplements and do not eat fish. As far as human health is concerned, EPA and DHA are the most important omega-3 fatty acids, although alpha-linolenic acid is important in those who do not consume pre-formed EPA from fish or supplements.

Interest in the health benefits of omega-3 fats can be traced back to epidemiological studies in Greenland Inuits, where the observed very low rate of mortality from coronary heart disease was ascribed to the high intake of EPA and DHA from seal, whale and fish (6). This link between high omega-3 intake and low cardiovascular morbidity and mortality was confirmed in other Inuit populations and in the Japanese and has also been demonstrated

Professor Calder has a long-term interest in the metabolism and functionality of fatty acids, particularly with regard to inflammation and immunity, chronic disease, and nutrition support.

across the range of habitual intakes in Western populations (6). The explanation for the cardioprotective effect of EPA+DHA is beneficial modification in the profile of cardiovascular risk factors such as serum triglycerides, blood pressure, endothelial dysfunction, inflammation and thrombosis (6, 7). The efficacy of EPA+DHA in lowering serum triglycerides is such that some formulations are licensed as triglyceride-lowering medications. The improved risk profile for cardiovascular disease that occurs with increased intake of EPA+DHA most likely slows or limits the process of atherosclerosis, the build-up of the fatty plaque within the blood vessel wall. However, a small number of large secondary prevention trials demonstrated that EPA+DHA reduced mortality, especially as a result of myocardial infarction, in people with existing advanced atherosclerosis (8). This has focused attention on actions of EPA and DHA on heart cell electrophysiology and on atherosclerotic plaque stability as likely mechanisms at play in people with existing disease (8). Some recent trials have failed to reproduce the previously documented protective effects of EPA+DHA on mortality; the reason for this is not clear, but may relate to some significant differences between the recent and the earlier trials and some failures in the design of the recent trials (9).

Omega-3 fatty acids have an anti-inflammatory action that may be useful in treating some chronic diseases where inflammation is part of the pathology (10, 11). The anti-inflammatory effect of EPA+DHA stems from their ability to interfere with the production of the classic pro-inflammatory eicosanoids (prostaglandins and leukotrienes) produced from omega-6 arachidonic acid. In addition, EPA yields eicosanoids that are typically biologically weak, while resolvins produced from EPA and DHA and protectins produced from DHA seem to be very potent inflammation resolving agents (10,11). Thus increased exposure to EPA and DHA results in an environment that is not only less inflammatory, but which favours resolution ('turning off') of inflammation (12).

Some regions of the brain and the eye have a very high content of DHA which plays specific roles in membrane structure, enabling appropriate signalling mechanisms to operate, for example when the eye receives a visual stimulus (13). Because the brain and eye develop early in life, it is essential that a baby receives sufficient DHA from its mother before birth (i.e. across the placenta) and after birth (i.e. in breast milk) in order to optimise visual and neurological function (14,15). There is some evidence that the importance of omega-3 fats on aspects of brain function goes beyond these very early fundamental developmental aspects. For example, a small number of studies have highlighted the potential for omega-3 fatty acids to contribute to enhanced mental development (16) and improved childhood learning and behaviour (17) and to reduce the burden of psychiatric illnesses in adults (18), although these remain less certain areas of possible action which require more scientific support. There may also be a role for omega-3 fatty acids, DHA in particular, in preventing neurodegenerative disease of ageing (19).

Another area that has emerged where omega-3 fatty acids may have an important role is in nutrition support, either enterally or parenterally. Lipids traditionally used in nutrition support are based on soybean oil which is rich in the omega-6 fatty acid linoleic acid. This may not be optimal and one alternative is the partial replacement of soybean oil by fish oil. Parenteral fish oil has shown benefit in neonates with liver failure, in adults post-surgery (mainly gastrointestinal) and, in some studies, in critically ill adults (20). Fish oil has been included in combination with other nutrients in various enteral formulae which have benefits in post-surgical patients, in patients with mild sepsis or trauma and in patients with acute respiratory distress syndrome, acute lung injury or severe sepsis (20).

Overall, there is a substantial scientific evidence base to support important roles of omega-3 fatty acids in growth and development, in lowering risk of many chronic human diseases and in contributing to the therapeutic regimen in those with advanced disease or requiring nutrition support. All the effects of omega-3 fatty acids that have been described are likely to be dose-dependent, but clear dose response data has not been identified in most cases. Nevertheless, much progress is being made in understanding the effects of omega-3 fatty acids and the mechanisms of action involved (21). It is likely that the coming years will see significant progress in this area, with new actions being described and existing actions being better understood.

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Questions relating to: *Omega-3 fatty acids in health and disease: the science behind the headlines.*
Type your answers below and then **print for your records.** Alternatively print and complete answers by hand.

Q.1	Which fatty acids are included in the omega-3 family and what links them all?
A	
Q.2	Why is alpha-linolenic acid the major omega-3 fatty acid in the diet?
A	
Q.3	Explain what influences the levels of eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) in our blood cells.
A	
Q.4	Describe how omega-3 supplements can be of benefit.
A	
Q.5	Give an historical example of how omega-3 intake can effect cardiovascular morbidity.
A	
Q.6	Why do omega-3s have an anti-inflammatory action?
A	
Q.7	Describe the role that DHA plays in aspects of brain function.
A	
Q.8	Why are omega-3s important in nutrition support?
Q.9	Summarise the importance of omega-3 fatty acids in health and disease and what influences their effect.

Please type additional notes here . . .