THE EQOLOGY™ FULL SPECTRUM FATTY ACIDS REPORT

Date: 05/11/2024 **ID:** EQ424QH6847C

The importance and biological impact of your personal fatty acid blood profile

Background
A healthy human body is dependent upon regular sleep, physical activity and a balanced diet – including the right amounts and composition of energy-sources found in a diet consisting of carbohydrates, proteins and fat. In addition fiber-containing food is also important for a healthy you.

Unsaturated fatty acids are important building-bricks for the cell membrane and intra-cellular organelles in all human cells. The body needs a regular supply of unsaturated fatty acids (where the omega-3 fatty acids are the most important). However, also a regular intake of saturated fatty acids is needed. For a healthy body it is the balance in intake between these two types of fatty acids – the saturated and the unsaturated that counts. In order to stay healthy we should increase the amount of unsaturated fatty acids in our diet – and through that "improve" the balance between intake of the unsaturated omega-6 fatty acids and the unsaturated omega-3 fatty acids. When we measure the ratio between unsaturated omega-6 and omega-3 fatty acids in our blood, this ratio should never be higher than 5 – meaning no more than five times omega-6 than omega-3.

Which functions have the individual fatty acids?
In the following table you will find:
A: A description of the main functions of the most important saturated and unsaturated fatty acids in the human body.
B: An overview of the expected blood-values for these acids found in healthy people.
C: The values / concentrations for the fatty acids measured in the blood sample you have sent to Vitas Laboratory.

Why do we need an "extended" fatty acids report, and how can it be used?
The human body consists of organs and cells with identified, specific tasks. One thing is common for all – both organs and cells – they need regular supply of energy and oxygen. In this context it will be interesting to look into the functions associated with the main fatty acids found in the blood stream, and the range of concentrations that are recognized as the optimal values. For people interested in a healthy lifestyle a knowledge of your own fatty acid concentrations may be helpful in finding the right way of lifestyle, including to choose a diet containing the ingredients associated with potential health benefits – to secure people to stay healthy as long as possible.

Your blood fatty acid

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	Fatty acid	Type	Your values	Recommended range plasma-values	Potential health effects with too high values	
1	Palmitic acid (PA) C16:0	Saturated	23,2	20 - 27	Increased risks for CV diseases	
2	Stearic acid (SA) C18:0	Saturated	16,8	8 - 12	Important for a healthy skin. Often found in skin products	
3	Oleic acid (OA) C18:1	Unsaturated Omega-9	18	15 - 25	Can decrease blood pressure and reduce risks for CV diseases	
4	Linoleic acid (LA) C18:2	Unsaturated Omega-6	24,8	20 - 30	An essential fatty acid – that is important for development of a healthy skin – but can give ulcerative colitis in too high concentrations	
5	Alfa Linoleic Acid (ALA) C18:3	Unsaturated Omega-3	0,31	0,2 – 0,6	Can lower risks for cardiovascular diseases	
6	Gamma Linoleic Acid (GLA) C18:3	Unsaturated Omega-6	0,2	Not defined	Can reduce skin-symptoms with eczema	
7	Dihomo-gam-ma-linoleic acid (DGLA) C20:3	Unsaturated Omega-6	1,7	0,5 – 1,2	Has anti-inflammatory and anti-coagulation effects	
8	Arachidonic acid (AA) C20:4	Unsaturated Omega-6	11	4 – 8	Can reduce risks for CV-diseases. Can improve insulin sen-si-tivity. Can enhan-ce inflammation	
9	Eicosa-pentanoic acid (EPA) C20:5	Unsaturated Omega-3	0,63	1 - 7	Works anti-inflammatory	
10	Docosa-pentanoic acid (DPA) C22:5	Unsaturated Omega-3	1,55	0,8 – 2,0	No obvious health benefits observed	
11	Docosa-hexanoic acid (DHA)	Unsaturated Omega-3	1,81	2 - 7	Structural membrane functions. Important for brain development	

The biological functions of the measured fatty acids

1. **Palmitic acid (PA) C16:0. Saturated fatty acid. Should be low.**

According to the World Health Organization, evidence is "convincing" that consumption of palmitic acid increases the risk of developing cardiovascular disease, based on studies indicating that it may increase the LDL cholesterol levels in the blood. Retinyl palmitate is a source of vitamin A added to low-fat milk to replace the vitamin content lost through the removal of milk fat. Palmitate is attached to the alcohol form of vitamin A, retinol, to make vitamin A stable in milk.

2. **Stearic acid (SA) C18:0. Saturated fatty acid. Important for the skin.**

Cosmetic creams and lotions are often composed of water and oil-based ingredients, which are held together by substances called emulsifiers. Without emulsifiers, the formula would separate, causing oil droplets to float on top of the water. Stearic acid is an emulsifier by itself, but can also be used with triethanolamine. When mixed, the two compounds react and become a paste called 'triethanolamine stearate' that helps to create a loose emulsion which is easily absorbed by the skin – that keep you akin smooth and heathy.

3. **Oleic acid (OA): C18:1. Unsaturated omega-9. In olive oil. Reduce blood pressure.**

Oleic acid is a common monounsaturated fat in human diet. Monounsaturated fat consumption has been associated with decreased low-density lipoprotein (LDL) cholesterol, and possibly with increased high-density lipoprotein (HDL) cholesterol, however, its ability to raise HDL is still debated. Presence of a ratio balancing the two types is considered essential for good health and that relationship remains subject to scientific debate as research continues.

Oleic acid may be responsible for the hypotensive (blood pressure reducing) effects of olive oil that is considered a health benefit. Adverse effects have been documented in some research of oleic acid, however, since both oleic and monounsaturated fatty acid levels in the membranes of red blood cells have been associated with increased risk of breast cancer, although other research indicates that the consumption of the oleate in olive oil has been associated with a *decreased* risk of breast cancer.

4. **Linoleic acid (LA) C18:2. Unsaturated. Important for the skin.**

Linoleic acid is a polyunsaturated fatty acid used in the biosynthesis of arachidonic acid (AA) with elongation and saturation, and thus some prostaglandins, leukotrienes (LTA, LTB, LTC), and thromboxane (TXA). It is found in the lipids of cell membranes. It is abundant in many nuts, fatty seeds (flax seeds, hemp seeds, poppy seeds, sesame seeds, etc.) and their derived vegetable oils; comprising over half (by weight) of poppy seed, safflower, sunflower, corn, and soybean oils.

The consumption of linoleic acid is vital to proper health, as it is an essential fatty acid. In rats, a diet deficient in linoleate (the salt form of the acid) has been shown to cause mild skin scaling, hair loss, and poor wound healing. However, chronic consumption of high levels of LA may be associated with the development of ulcerative colitis.

5. **Alpha Linoleic Acid (ALA) C18:3 (Unsaturated omega-3)**. **Can reduce risks for CV-diseases.**

Although the best source of ALA is seeds, most seeds and seed oils are much richer in an *n*–6 fatty acid, linoleic acid. Exceptions include flaxseed (must be ground for proper nutrient absorption) and chia seeds. Linoleic acid is the other essential fatty acid, but it, and the other *n*–6 fatty acids, compete with *n*–3s for positions in cell membranes and have very different effects on human health. There is a complex set of essential fatty acid interactions.

α-Linolenic acid can only be obtained by humans through their diets because the absence of the required 12- and 15-desaturase enzymes makes *de novo* synthesis from stearic acid impossible. Eicosapentaenoic acid (EPA; 20:5, *n*–3) and docosahexaenoic acid (DHA; 22:6, *n*–3) are readily available from fish and algae oil and play a vital role in many metabolic processes. These can also be synthesized by humans from dietary α-linolenic acid: ALA → stearidonic acid → eicosatetraeonic acid → eicosapentaenoic acid → docosapentaenoic acid → 9,12,15,18, 21-tetracosapentaenoic acid → 6,9,12,15,18, 21-yetracosahexaenoic acid → docosahexaenoic acid, but with an efficiency of only a few percent. This means that using ALA alone will not give you the recommended daily minimum dosage for healthy adults of 250 mg combined EPA and DHA. Because the efficacy of *n*–3 long-chain polyunsaturated fatty acid (LC-PUFA) synthesis decreases down the cascade of α-linolenic acid conversion, DHA synthesis from α-linolenic acid is even more restricted than that of EPA. Conversion of ALA to DHA is higher in women than in men.

Multiple studies have shown a relationship between α-linolenic acid and an increased risk of prostate cancer. This risk was found to be irrespective of source of origin (e.g., meat, vegetable oil). However, a large 2006 study found no association between total α-linolenic acid intake and overall risk of prostate cancer; and a 2009 meta-analysis found evidence of publication bias in earlier studies, and concluded that if ALA contributes to increased prostate cancer risk, the increase in risk is quite small.

According to one scientific review, higher ALA consumption is associated with a moderately lower risk of cardiovascular disease, but wide variation in results across multiple studies highlights the need for additional research before drawing firm conclusions.

6. **Gamma-Linoleic acid (GLA) C18:3 (omega-6). Important for the skin.**

More recently, topical application of borage seed oil (an oil with a high concentration of GLA) has been shown to reduce the symptoms of atopic dermatitis in a double-blind, placebo-controlled clinical trial. Western diets are deficient in omega-3 fatty acids and have excessive amounts of omega-6 fatty acids compared with the diet on which human beings evolved and their genetic patterns were established. The recommended ratio of omega-6 to omega-3 fatty acids in the diet is 4:1 or less. However, the Western diet has a ratio between 10:1 and 50:1. Therefore, although omega-6 fats are essential in the right quantities, most people in the developed world should aim to reduce their omega-6 intake.

7. **Dihomo-Gamma-Linoleic acid (DGLA) C20:3 omega-6. Anti-inflammatory effects.**

Dihomo-γ-linolenic acid (**DGLA**) is a 20-carbon ω–6 fatty acid. In physiological literature, it is given the name 20:3 (ω–6). DGLA is a carboxylic acid with a 20-carbon chain and three *cis* double bonds; the first double bond is located at the sixth carbon from the omega end. DGLA is the elongation product of γ-linolenic acid (GLA; 18:3, ω–6). GLA, in turn, is a desaturation product (Delta 6 desaturase) of linoleic acid (18:2, ω–6). DGLA is made in the body by the elongation of GLA, by an efficient enzyme which does not appear to suffer any form of (dietary) inhibition. DGLA is an extremely uncommon fatty acid, found only in trace amounts in animal products. DGLA production from GLA is enhanced when high levels of alpha-linolenic acid are present, blocking the arachidonic acid pathway.

The eicosanoid metabolites of DGLA are:

- Series-1 thromboxanes (thromboxanes with 1 double-bond), via the COX-1 and COX-2 pathways.
- Series-1 prostanoids, via the COX-1 and COX-2 pathways.

- A 15-hydroxyl derivative that blocks the transformation of arachidonic acid to leukotrienes.

All of these effects are anti-inflammatory. This is in marked contrast with the analogous metabolites of arachidonic acid (AA), which are the series-2 thromboxanes and prostanoids and the series-4 leukotrienes. In addition to yielding anti-inflammatory eicosanoids, DGLA competes with AA for COX and lipoxygenase, inhibiting the production of AA-derived eicosanoids.

Taken orally in a small study, DGLA produced antithrombotic effects. Supplementing dietary GLA increases serum DGLA, as well as serum AA levels. Cosupplementation with GLA and EPA lowers serum AA levels by blocking Δ-5-desaturase activity, while also lowering leukotriene synthesis in neutrophils.

8. **Arachidonic acid (AA) C20:4 omega-6 . Reduce risks for CV-diseases and improve insulin-sensitivity.**

Arachidonic acid supplementation in daily doses of 1,000–1,500 mg for 50 days has been well tolerated during several clinical studies, with no significant side effects reported. All common markers of health, including kidney and liver function, serum lipids, immunity, and platelet aggregation appear to be unaffected with this level and duration of use. Furthermore, higher concentrations of AA in muscle tissue may be correlated with improved insulin sensitivity. Arachidonic acid supplementation of the diets of healthy adults appears to offer no toxicity or significant safety risk. Arachidonic acid recommended range plasma-value to be 4-8.

While studies looking at arachidonic acid supplementation in sedentary subjects have failed to find changes in resting inflammatory markers in doses up to 1,500 mg daily, strength-trained subjects may respond differently. One study reported a significant reduction in resting inflammation (via marker IL-6) in young men supplementing 1,000 mg/day of arachidonic acid for 50 days in combination with resistance training. This suggests that rather being pro-inflammatory, supplementation of ARA while undergoing resistance training may actually improve the regulation of systemic inflammation.

Arachidonic acid is not carcinogenic, and studies show dietary level is not associated (positively or negatively) with risk of cancers. AA remains integral to the inflammatory and cell growth process, however, which is disturbed in many types of disease including cancer. Therefore, the safety of arachidonic acid supplementation in patients suffering from cancer, inflammatory, or other diseased states is unknown, and supplementation is not recommended.

9. **Eicosa-pentanoic acid (EPA) C20:5 omega-3. Anti-inflammatory effects.**

The omega-3 fatty acids EPA and DHA are components of the cell membrane and have a modulating effect on the function of different cells. The following effects for EPA and DHA have been demonstrated in human studies:

- they have an anti-arrhythmic effect (prevent cardiac arrhythmias) both at the level of the atrium and the ventricle
- they stabilize unstable vascular areas that otherwise cause myocardial infarctions («unstable plaques»)
- they slow the progress of changes in the coronary vessels
- they lower triglycerides
- they have a preventive effect against coronary heart disease (CAD)

- they promote blood circulation
- they inhibit platelet aggregation
- they have numerous other positive effects on vascular function, blood pressure, inflammation mediators

The short chain (vegetable) α-linolenic acid (18:3 ω-3) can be obtained by competitive inhibition of the linoleic acid (18:2 ω-6) by the desaturase - and elongase displace enzymes and therefore the production and tissue concentrations of inflammatory arachidonic reduce.

So far, the results of four large clinical intervention studies on a total of over 30,000 people are available: *Diet and Reinfarction Trial* (DART), *Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico-Prevenzione* (GISSI-P), DART -2, and *Japan EPA Lipid Intervention Study.* (JELIS). DART and GISSI-P showed a reduction in total mortality between 20 and 29 percent of sudden cardiac death by about 45 percent and cardiac events after administration of almost one gram of EPA and DHA per day. DART-2 was so poorly collected that no reliable conclusions could be drawn. 18,645 hyperlipidemic Japanese with additional cardiovascular risk factors participated in JELIS for five years. Traditionally, a lot of fish, including EPA and DHA, is consumed in Japan, which results in high levels. These levels were further increased by the administration of 1.8 grams per day of eicosapentaenoic acid. The incidence of sudden cardiac death in JELIS was 40 per 100,000, which is still significantly lower than the incidence of the German general population (see above). Other cardiac events were also rare in JELIS and were further reduced by taking eicosapentaenoic acid.

10. **Docosa-pentanoic acid (DPA) C22:5 omega. No obvious health benefits.**

Supplementation does not appear to be associated with a lower risk of all-cause mortality.

11. **Docosa-hexanoic acid (DHA) C22:6 omega-3. Important for the cell structure.**

Pregnancy and lactation

Foods high in omega-3 fatty acids may be recommended to women who want to become pregnant or when nursing. A working group from the International Society for the Study of Fatty Acids and Lipids recommended 300 mg/day of DHA for pregnant and lactating women, whereas the average consumption was between 45 mg and 115 mg per day of the women in the study, similar to a Canadian study.

Brain and visual functions

A major structural component of the mammalian central nervous system, DHA is the most abundant omega–3 fatty acid in the brain and retina. Brain and retinal function rely on dietary intake of DHA to support a broad range of cell membrane and cell signaling properties, particularly in grey matter and retinal photoreceptor cell outer segments, which are rich in membranes.

A systematic review found that DHA had no significant benefits in improving visual field in individuals with retinitis pigmentosa.

Omega-3 fatty acids during pregnancy and lactation

The placenta provides the growing fetus with 50–60 mg docosahexaenoic acid per day. Omega-3 index values between 2.6 and 14.9% were measured in 25 unselected pregnant women in Germany. Regulatory mechanisms in the placenta try to adjust the fetus to an omega-3 index of 10 to 11%. In mothers with low levels, this leads to the emptying of existing memory. A good supply of

mother with eicosapentenoic and docosahexaenoic acid showed a better result in intervention studies in the following criteria:

- Early Birth are aspirations rarely, if started early with supplementation. Starting after the 33rd week is ineffective, as was shown in intervention studies.
- Postpartum depression rarely occurs in populations that are characterized by high fish consumption or high levels of breast milk in DHA. Intervention studies are ongoing.
- The brain development in children with high levels of eicosapentaenoic acid and docosahexaenoic acid is documented to go faster as compared to children with lower levels of EPA and DHA. However, more interventional omega-3 studies in children are needed to confirm and document such developments and improvements in complex brain functions.
- The intelligence quotient of 4-year-old children, whose mothers supplemented 2 g eicosapentaenoic acid and docosahexaenoic acid daily during pregnancy and during the first three months after birth, was 4 points higher than in a intervention study, which was fairly small with 83 participants, with 106 points Children of mothers ingested corn oil that contains practically no omega-3 fatty acids. This was attributed to the fact that the levels of eicosapentaenoic and docosahexaenoic acid in the umbilical cord blood of the more intelligent children were twice as high.
- Breast milk can be enriched with eicosapentaenoic acid and docosahexaenoic acid via the mother's diet in a dose-dependent manner. The results of the intervention studies are not entirely consistent, but generally show better complex brain performance in children whose mothers supplemented with eicosapentaenoic acid and docosahexaenoic acid during lactation. Individual manufacturers supplement DHA with milk foods.

However, according to a study by the Technical University of Munich, the hope that the targeted intake of omega-3 fatty acids during pregnancy could prevent obesity in children does not seem to be confirmed.

At the end of August 2007, with the support of the EU, a group of scientists held a consensus conference: "New EU Recommendation Suggests Pregnant Women Need Higher Levels of Omega-3". It was recommended to take at least 200 mg / day of DHA in pregnancy, whereby it was pointed out that up to 2.7 g / day of eicosapentaenoic acid and docosahexaenoic acid had been given in intervention studies without any significant side effects. Here, too, there was agreement on the assessment of the value of omega-3 fatty acids in pregnancy, but disagreement regarding the dose.

The consensus conference recommends eating two servings of fatty fish (e.g. salmon or mackerel) per week for pregnant and lactating women, which is also in line with the recommendations of the European Food Standards Agency. Women who eat little or no fish should consider using omega-3 supplements.

Cancers

In observational studies, evidence of a protective effect against prostate cancer was obtained by eating eicosapentaenoic acid and docosahexaenoic acid, while α-linolenic acid may have the opposite effect. Higher levels of eicosapentaenoic acid and docosahexaenoic acid, but not of α-linolenic acid, were associated with a lower probability of prostate cancer. Several intervention studies on the subject are currently being prepared.

However, a 2013 study also found a higher risk of prostate cancer for docosahexaenoic acid.

In other cancers such as colorectal cancer or breast cancer, the higher the level of eicosapentaenoic acid and docosahexaenoic acid in the erythrocytes (red blood cells), the lower the risk of developing the disease. Previous studies that examined fish consumption showed less clear results. Here, too, no final assessment can be made.

By stimulating myeloid-derived suppressor cells (MDSC), polyunsaturated fatty acids can adversely affect the tumor microenvironment depending on ROS production.

Inflammatory diseases with autoimmune component

In inflammatory diseases with autoimmune components, such as rheumatoid arthritis, inflammatory bowel diseases, asthma or primary sclerosing cholangitis, mechanisms of action, such as the reduction of inflammation-promoting mediators, speak for a therapeutic effect. The first intervention studies had positive results, but a final evaluation is still pending as further intervention studies have to be carried out.

In 2013, Yan, Jiang, and co-workers discovered that the anti-inflammatory (anti-inflammatory) effect of omega-3 fatty acids was due to an inhibition of the activation of the NLRP3 inflammasome, with the subsequent caspase-1 activation and secretion of IL-1 β.

Age-related degenerative diseases

Observational studies suggested that an increased content of omega-3 fatty acids in the diet could counteract age-related macular degeneration, but this could not be confirmed in the ARED II study.

Effect on the microbiome

Randomized studies show that omega-3 fatty acids have a beneficial effect on human intestin al microbiome (the «intestinal flora»). While the number of beneficial intestinal dwellers like that of bifidobacteria increases, the number of facultatively pathogenic bacterial strains like that of clostridia decrease.

However, very high doses (> 5 g per day) can lead to gastrointestinal complaints such as diarrhea . However, these high doses can only be achieved through the excessive intake of dietary supplements and generally not through nutrition.

Omega-3 fatty acids in neurology and psychiatry

Omega-3 fatty acids are essential for the structure and function of the brain and eye. Various mechanisms of action relevant for this have been described: changes in dopaminergic function, regulation of hormone systems, changes in intracellular signaling systems, increased dendritic branching and synapse formation and a number of others. This is especially true for docosahexaenoic acid, less for eicosapentaenoic acid and not for α-linolenic acid.

Stroke

A systematic review showed that ischemic stroke is about 30% less common in people who consume omega-3 fatty acids. Omega-3 fatty acid levels do not appear to be associated with the occurrence of hemorrhagic strokes.

Cognitive impairment and Alzheimer's disease

Observational studies in patients with cognitive impairments and Alzheimer's disease showed that eating more fish, but especially higher levels of eicosapentaenoic and docosahexaenoic acid, was associated with a lower risk of loss of cognition and dementia development. A first small intervention study had promising results, others are currently being prepared.

Depression

(Unipolar) depression and bipolar disorder are more common in people with low omega-3 fatty acid intake and / or low levels of eicosapentaenoic acid and docosahexaenoic acid. A low Omega-3 index is a risk factor for future suicide attempts. There are several meta-analyzes of various intervention studies (doses between 1 and 9.6 g / day), the results of which do not match. There seems to be some evidence that what is important for the detection of an antidepressant effect is which of the omega-3 fatty acids was administered to the study participants. It could be demonstrated that EPA has an antidepressant effect when administered more than 1 g / day, while DHA alone shows only a minor to no antidepressant effect. Several combination studies that administered both omega-3 fatty acids in a ratio> 1 of EPA: DHA also showed positive antidepressant effects. However, if the ratio of EPA to DHA was less than 1, no antidepressant effects could be measured. There therefore still seems to be a need for research in order to be able to issue precise instructions for the diet (i.e. monotherapy of individual omega-3 fatty acids versus combination therapy and also the amount of the daily dose used). However, there is a sustained interest in continuing to research in this area, since the results so far are promising insofar as depression has been alleviated or completely eliminated in a number of test subjects. It has been suggested that future studies should be based on omega-3 fatty acid levels.

Schizophrenia

The omega-3 fatty acid levels in patients with schizophrenia are significantly lower than the omega-3 fatty acid levels in the subjects of healthy control groups. In 3 out of 4 intervention studies positive effects were seen and in studies on the effects of eicosapentaenoic acid. Further intervention studies are currently being prepared.

Borderline Personality

Initial data from intervention studies in borderline personalities showed that eicosapentaenoic and docosahexaenoic acid can reduce hostility and aggression as well as depressive symptoms.

Attention-deficit / hyperactivity disorder

Lower levels of omega-3 fatty acids have been found in adolescents and adults with attention deficit hyperactivity disorders than in healthy people.

A cross-sectional study from 2016 concludes that the results of the studies examined with omega-3 preparations are contradictory, but that there are possible indications of a successful treatment of ADHD symptoms.

Cancer

The evidence linking the consumption of marine omega–3 fats to a lower risk of cancer is poor. With the possible exception of breast cancer, there is insufficient evidence that supplementation with omega–3 fatty acids has an effect on different cancers. The effect of consumption

on prostate cancer is not conclusive. There is a decreased risk with higher blood levels of DPA, but an increased risk of more aggressive prostate cancer was shown with higher blood levels of combined EPA and DHA. In people with advanced cancer and cachexia, omega–3 fatty acids supplements may be of benefit, improving appetite, weight, and quality of life.

Cardiovascular disease

Omega–3 fatty acid supplementation greater than one gram daily for at least a year may be protective against cardiac death, sudden death, and myocardial infarction in people who have a history of cardiovascular disease. No protective effect against the development of stroke or all-cause mortality was seen in this population. Eating a diet high in fish that contain long chain omega–3 fatty acids does appear to decrease the risk of stroke. Fish oil supplementation has not been shown to benefit revascularization or abnormal heart rhythms and has no effect on heart failure hospital admission rates. Furthermore, fish oil supplement studies have failed to support claims of preventing heart attacks or strokes. In the EU, a review by the European Medicines Agency of omega-3 fatty acid medicines containing a combination of an ethyl ester of eicosapentaenoic acid and docosahexaenoic acid at a dose of 1 g per day concluded that these medicines are not effective in secondary prevention of heart problems in patients who have had a myocardial infarction.

Evidence suggests that omega–3 fatty acids modestly lower blood pressure (systolic and diastolic) in people with hypertension and in people with normal blood pressure. Some evidence suggests that people with certain circulatory problems, such as varicose veins, may benefit from the consumption of EPA and DHA, which may stimulate blood circulation and increase the breakdown of fibrin, a protein involved in blood clotting and scar formation. Omega–3 fatty acids reduce blood triglyceride levels but do not significantly change the level of LDL cholesterol or HDL cholesterol in the blood. The American Heart Association position (2011) is that borderline elevated triglycerides, defined as 150–199 mg/dL, can be lowered by 0.5-1.0 grams of EPA and DHA per day; high triglycerides 200–499 mg/dL benefit from 1-2 g/day; and >500 mg/dL be treated under a physician's supervision with 2-4 g/day using a prescription product. In this population omega-3 fatty acid supplementation decreases the risk of heart disease by about 25%.

ALA does not confer the cardiovascular health benefits of EPA and DHAs.

The effect of omega–3 polyunsaturated fatty acids on stroke is unclear, with a possible benefit in women.

Inflammation

A 2013 systematic review found tentative evidence of benefit for lowering inflammation levels in healthy adults and in people with one or more biomarkers of metabolic syndrome. Consumption of omega–3 fatty acids from marine sources lowers blood markers of inflammation such as C-reactive protein, interleukin 6, and TNF alpha.

For rheumatoid arthritis, one systematic review found consistent, but modest, evidence for the effect of marine n–3 PUFAs on symptoms such as "joint swelling and pain, duration of morning stiffness, global assessments of pain and disease activity" as well as the use of non-steroidal anti-inflammatory drugs. The American College of Rheumatology has stated that there may be modest benefit from the use of fish oils, but that it may take months for effects to be seen, and cautions for possible gastrointestinal side effects and the possibility of the supplements contain-

ing mercury or vitamin A at toxic levels. The National Center for Complementary and Integrative Health has concluded that «supplements containing omega-3 fatty acids may help relieve rheumatoid arthritis symptoms» and warns that such supplements «may interact with drugs that affect blood clotting».

Developmental disabilities

Although not supported by current scientific evidence as a primary treatment for attention deficit hyperactivity disorder (ADHD), autism, and other developmental disabilities, omega–3 fatty acid supplements are being given to children with these conditions.

One meta-analysis concluded that omega–3 fatty acid supplementation demonstrated a modest effect for improving ADHD symptoms. A Cochrane review of PUFA (not necessarily omega–3) supplementation found "there is little evidence that PUFA supplementation provides any benefit for the symptoms of ADHD in children and adolescents",while a different review found "insufficient evidence to draw any conclusion about the use of PUFAs for children with specific learning disorders".

Fish oil has only a small benefit on the risk of premature birth. A 2015 meta-analysis of the effect of omega–3 supplementation during pregnancy did not demonstrate a decrease in the rate of preterm birth or improve outcomes in women with singleton pregnancies with no prior preterm births. A 2018 Cochrane systematic review with moderate to high quality of evidence suggested that omega–3 fatty acids may reduce risk of perinatal death, risk of low body weight babies; and possibly mildly increased LGA babies. However, a 2019 clinical trial in Australia showed no significant reduction on rate of preterm delivery, and no higher incidence of interventions in post-term deliveries than control.

Mental health

There is some evidence that omega–3 fatty acids are related to mental health, including that they may tentatively be useful as an add-on for the treatment of depression associated with bipolar disorder. Significant benefits due to EPA supplementation were only seen, however, when treating depressive symptoms and not manic symptoms suggesting a link between omega–3 and depressive mood. There is also preliminary evidence that EPA supplementation is helpful in cases of depression. The link between omega–3 and depression has been attributed to the fact that many of the products of the omega–3 synthesis pathway play key roles in regulating inflammation (such as prostaglandin E3) which have been linked to depression. This link to inflammation regulation has been supported in both in vivo studies and in a meta-analysis.

There is, however, significant difficulty in interpreting the literature due to participant recall and systematic differences in diets. There is also controversy as to the efficacy of omega–3, with many meta-analysis papers finding heterogeneity among results which can be explained mostly by publication bias. A significant correlation between shorter treatment trials was associated with increased omega–3 efficacy for treating depressed symptoms further implicating bias in publication. One review found that "Although evidence of benefits for any specific intervention is not conclusive, these findings suggest that it might be possible to delay or prevent transition to psychosis.

Cognitive aging

Epidemiological studies are inconclusive about an effect of omega–3 fatty acids on the mechanisms of Alzheimer's disease. There is preliminary evidence of effect on mild cognitive problems, but none supporting an effect in healthy people or those with dementia.

Brain and visual functions

Brain function and vision rely on dietary intake of DHA to support a broad range of cell membrane properties, particularly in grey matter, which is rich in membranes. A major structural component of the mammalian brain, DHA is the most abundant omega–3 fatty acid in the brain. It is under study as a candidate essential nutrient with roles in neurodevelopment, cognition, and neurodegenerative disorders.

Risk of deficiency

People with PKU often have low intake of omega–3 fatty acids, because nutrients rich in omega–3 fatty acids are excluded from their diet due to high protein content.

Asthma

As of 2015, there was no evidence that taking omega–3 supplements can prevent asthma attacks in children.

Disclaimer

Health advises: Please consult your physician if you plan to do lifestyle changes in combination with use of nutrition and dietary supplements – that will have an impact on ongoing drug-related medical treatment.