

Fatty Acid Blood Spot Interpretive Guide

Table 1: Signs and Symptoms Associated with Fatty Acid Abnormalities

SIGNS & SYMPTOMS	FATTY ACID ASSOCIATION	ACTION
<i>Emaciation, weakness, disorientation</i>	Caloric deprivation	Add food balanced in fat, protein, and carbohydrate.
<i>Reduced growth, renal dysplasia, reproductive deficiency, scaly skin</i>	Classic essential fatty acid deficiency	Add good quality fats and oils
<i>Eczema-like skin eruptions, loss of hair, liver degradation, behavioral disturbances, kidney degeneration, increased thirst, frequent infections, poor wound healing, sterility, miscarriage, arthralgia, cardiovascular disease, growth retardation</i>	Linoleic acid insufficiency	Add corn or safflower oils
<i>Growth retardation, weakness, impairment of vision, learning disability poor coordination, tingling in arms/legs, behavioral changes, mental disturbances, low metabolic rate, high blood pressure, immune dysfunction</i>	Alpha or gamma linolenic acid insufficiency	Add flax, primrose, or black currant oil
<i>Depression, anxiety, learning, behavioral and visual development, cardiovascular disease risk</i>	Long chain PUFA-dependent neuromembrane function, imbalanced prostanoids	Add fish oils
<i>Cancer</i>	Low stearic/oleic ratio, loss of prostanoid cell controls (RBC only)	Add omega 3 PUFAs Use omega 6 PUFAs with caution
<i>Myelinated nerve degeneration</i>	Increased very long chain FAs	Add high-erucate rape oil mustard seed oils
<i>Fatty liver</i>	Saturated and omega 9 family accumulation in hepatic cells	Restrict alcohol consumption, and increase lecithin and methionine intake
<i>Accelerated aging</i>	High poly-unsaturated acid intake without increased antioxidants	Increase vitamins E and C and the minerals Se, Mn, and Zn
<i>Obesity</i>	Various imbalances resulting from using processed oils (high elaidic with low GLA) like nuts, seeds, and fresh whole grains	Re-establish proper fat-to-protein balance using foods

For more information on fatty acids see

Laboratory Evaluations in Molecular Medicine, Nutrients, Toxicants and Cell Regulators, Chapter Five- *Fatty Acids*

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Polyunsaturated Omega-3

Eicosapentaenoic Acid

Deficiency of *eicosapentaenoic acid (20:5n3)* is likely the most prevalent fatty acid abnormality affecting the health of individuals in western societies. Low levels in plasma or especially in erythrocytes are indicative of insufficiency. Arthritis, heart disease, and general aging result from direct or indirect effects of unchecked inflammatory response.

Eicosapentaenoic acid (EPA) is anti-inflammatory and should balance the levels of pro-inflammatory arachidonic acid. Although EPA can be produced from the essential fatty acid, ALA, dietary intakes of this fatty acid are generally poor. The conversion also requires the action of the $\Delta 6$ desaturase enzyme that may be low due to inadequate Zn, Mg, or vitamins B₃, B₆, and C. Such an enzyme impairment would be indicated if EPA is low and ALA is normal or high. High levels of saturated, monounsaturated, trans fatty acids, and cholesterol also slow the conversion of ALA to EPA (as well as GLA to DGLA).

Docosapentaenoic Acid Docosahexaenoic Acid

The growth and development of the central nervous system is particularly dependent upon the presence of an adequate amount of the very long chain, highly unsaturated fatty acids, *docosapentaenoic (22:5n3)* and *docosahexaenoic acids (22:6n3)* (1,2). Attention deficit hyperactivity disorder (3) and failures in the development of the visual system in EFA deficiencies are two examples of this dependency. Docosahexaenoic acid (DHA) is an important member of the very long chain fatty acids (C22 to C26) that characteristically occur in glycosphingolipids, particularly in the brain. Since this fatty acid is so important in early development, it is worth noting that the levels in breast milk are correlated with the mother's intake of fish oils (4), which are rich sources of both of these fatty acids. DHA intake may also help to lower blood pressure (5).

Polyunsaturated Omega-6

Linoleic Acid

Linoleic acid (18:2n6) is by far the most abundant polyunsaturated fatty acid in most human tissues. Linoleic acid (LA) is an essential fatty acid, and low levels indicate dietary insufficiency, which can lead to a variety of symptoms (see Table 1). Some of these symptoms result from lack of LA in membranes, where it plays a role in structural integrity. Most, however, are from failure to produce eicosanoids, which are cell regulators. LA is the starting point for this pathway. Normal neonatal status of this fatty acid is marginal, if not insufficient (6). Since dietary sources (especially corn oil) are abundant, however, LA may be found above normal. Excessive LA can contribute to inflammation. Supplementation with LA has been shown to increase body weight and essential fatty acid status in patients with cystic fibrosis (7).

Gamma Linolenic Acid

Gamma linolenic acid (18:3n6), abbreviated *GLA*, is the precursor of DGLA, an anti-inflammatory fatty acid, and it's also the precursor of arachidonic acid, a pro-inflammatory fatty acid. It is found in hemp, borage, black currant, and evening primrose oils. It can be produced in human tissues by the action of desaturase enzymes on LA. See Table 1 for clinical associations. GLA corrects most of the biological effects of zinc deficiency (8), highlighting the zinc requirement of the $\Delta 5$ desaturase enzyme.

Dihomogamma-linolenic Acid

Low levels of *dihomogamma-linolenic acid (20:3n6)* result from diets low in both essential fatty acids, LA, and dihomogamma-linolenic acid (DGLA). DGLA is also anti-inflammatory, so an insufficiency of this fatty acid impairs a wide range of cellular functions and tissue responses. When testing reveals low levels of DGLA, supplementation with black currant or evening primrose oils should be considered, but if a history of tumor formation is known, always consider ALA sources (black currant) as well (9).

Arachidonic Acid

Because of the prevalence of corn and corn oil products in feed for cattle and hogs, diets high in these red meats are rich in *arachidonic acid (20:4n6)*. Arachidonic acid (AA) is a 20-carbon or fatty acid that serves as the principal pro-inflammatory fatty acid. Its synthesis is inhibited by non-steroidal anti-inflammatory drugs (NSAIDs). High AA promotes gallstone formation by stimulating mucin production in the gallbladder mucosa (10).

metabolic pattern that can lead to increasing levels of VLCFAs in plasma and erythrocyte membranes. The effect is mediated by hormonal responses, mainly norepinephrine and insulin, and is exacerbated by drugs that modulate energy metabolism such as the antianginal drug, trimetazidine (11).

Trans

The *total C18 trans isomers* include elaidic acid, petroselaidic, and trans-vaccenic acids. The presence of these eighteen-carbon long trans fatty acids in human tissue can disrupt or impair cell membrane function. A patient with high levels of total C18 trans isomers should be told to avoid hydrogenated oils. These fatty acids contain one double bond and thus are included in the unsaturated category. Because of the geometry of the trans bond, however, they behave like saturated fats on the one hand, leading to elevated cholesterol levels (13). On the other hand they mimic unsaturated fats that bind to desaturase enzymes and antagonize the normal production of necessary products. The net effect is to raise plasma LDL cholesterol and lower HDL. It is now the consensus among experts in lipid nutrition that foods containing hydrogenated oils are to be avoided. These fatty acids are also produced by the bacteria in the gut of ruminant animals which is the reason that beef and milk contain small amounts (13%) of elaidic acid. Moderate use of these foods is unlikely to provide trans fatty acids at levels that are of concern.

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Calculated ratios

LA/DGLA Ratio (No. 36)

The ratio of LA to DGLA increases when the $\Delta 6$ desaturase enzyme is inhibited by zinc and magnesium deficiency, elevated insulin, or dietary excess of saturated, monoenoic, or trans fatty acid. Under these conditions, the enzyme cannot convert the substrate (LA) to its product (I8:3v6) fast enough. The production of all desaturation products is affected, including GLA, EPA and AA. These longer chain polyunsaturated fatty acids, then must be supplied from the diet or supplements.

EPA/DGLA Ratio (No. 37)

The balance of 20-carbon or eicosanoic fatty acids is critical for proper supply of the prostanoid and leukotriene 1-, 2-, and 3-series local hormones that control a host of cellular functions and responses. The EPA/DGLA ratio will be low when DGLA is elevated relative to EPA, indicating a need for EPA sources like fish oils. When the ratio is high, sources of DGLA (black currant or evening primrose oil) are indicated.

AA/EPA (Omega-6/Omega-3) Ratio (No. 38)

AA and EPA are the most critical fatty acids for maintaining the ratio of the omega-6 and omega-3 classes because they compete for enzymes that make cell regulators. A high ratio indicates an overabundance of the pro-inflammatory, omega-6 fatty acid, AA. An overabundance of AA is quite common in Western high meat and corn oil diets and can result in an imbalance in the AA/EPA ratio. This is one of the indicators that extra omega-3 fatty acids, including EPA of fish oils, would be beneficial.

Resources

Information on the clinical effects of fatty acids, lipoproteins and glycolipids is rapidly expanding. The following sources are recommended for further study.

Erasmus (17): Excellent general review of structure and function of dietary and physiological fats.

Horrobin (18): Symposium proceedings emphasizing clinical uses of evening primrose oil.

Murray et. al. (19): A brief comprehensive review of the metabolism of fatty acids and related compounds.

Contributing authors to Annual Reviews (20): In depth reviews with extensive references.

Recommended Review Articles:

Fenton WS, Hibbeln J, Knable M. Essential fatty acids, lipid membrane abnormalities, and the diagnosis and treatment of schizophrenia. *Biological Psychiatry*. 47(1):8-21, 2000 Jan 1.

Leaf A, Kang JX, Xiao YF, Billman GE, Voskuyl RA. The antiarrhythmic and anticonvulsant effects of dietary N-3 fatty acids. *Journal of Membrane Biology*. 172(1):1-11, 1999 Nov 1.

Rose DP and Connolly JM. Omega-3 fatty acids as cancer chemopreventive agents. *Pharmacology & Therapeutics*. 83(3):217-44, 1999 Sep.

Valenzuela A, Morgado N. Trans fatty acid isomers in human health and in the food industry. *Biological Research*. 32(4):273-87, 1999.

Youdim KA, Martin A, Joseph JA. Essential fatty acids and the brain: possible health implications. *International Journal of Developmental Neuroscience*. 18(4-5): 383-99, 2000 Jul-Aug.

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12. Duran M., et al., Systemic carnitine deficiency: benefit of oral carnitine supplements vs. persisting biochemical abnormalities, *Eur J Pediatr*, 142(3):224-8 (1984).
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