

## The Fatty Acid Profile: Dietary Intake and Beyond

Fatty acid testing can provide a great deal of information allowing for individualized interventions. Varying patterns can help to identify not only essential fatty acid deficiency or excess, but also signs of insulin resistance, hypertriglyceridemia, proinflammation, or omega-3 dominance. Metamatrix offers four fatty acid tests, which measure key omega-3 and omega-6 polyunsaturated fatty acids (PUFAs), trans fatty acid (TFA), as well as indicators of optimal balance.

### Early Signs of Insulin Resistance

Elevated plasma triglycerides and free fatty acids are considered a hallmark of insulin resistance. Modulating dietary and supplemental fats may improve insulin resistance.<sup>1</sup> Improved insulin action is represented by a pattern of higher omega-3 fatty acids, lower omega-6/omega-3 ratios, low saturates, and possibly increased monounsaturates.<sup>2</sup>

Insulin action is blunted when cell membranes have a higher concentration of saturated fatty acids. Palmitic acid (C16:0) in particular has been found to play a critical role in insulin resistance.<sup>3</sup> It appears insulin resistance, resulting in high levels of palmitic and stearic acids, inhibits delta-9 desaturase. Delta 9 desaturase converts saturated fatty acids to monounsaturated fatty acids (Figure 1).

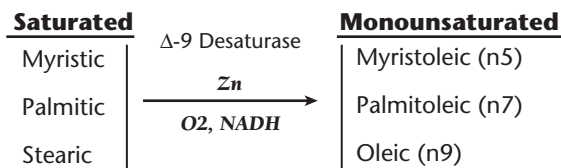


Figure 1. Saturated fatty acids are converted to monounsaturated fats in the presence of Delta-9 desaturase. Zinc, oxygen, and NADH (from vitamin B3) are cofactors in this reaction.

Insulin stimulates endogenous fatty acid synthesis, thereby increasing palmitic, stearic, and arachidic fatty acids. In a Metamatrix fatty acid profile, a patient with insulin resistance displays a pattern of high long chain fatty acids (palmitic, stearic and arachidic acids) while short chain (capric, lauric, and myristic) and very long chain saturated fatty acids (behenic, lignoceric, and hexacosanoic) are low. When viewing the bar graphs in the saturated fats section from afar, one can see this pattern, similar to a 'greater than sign' (Figure 2), where long chain fatty acids are very high, yet short chain and very long chain fatty acids are low.

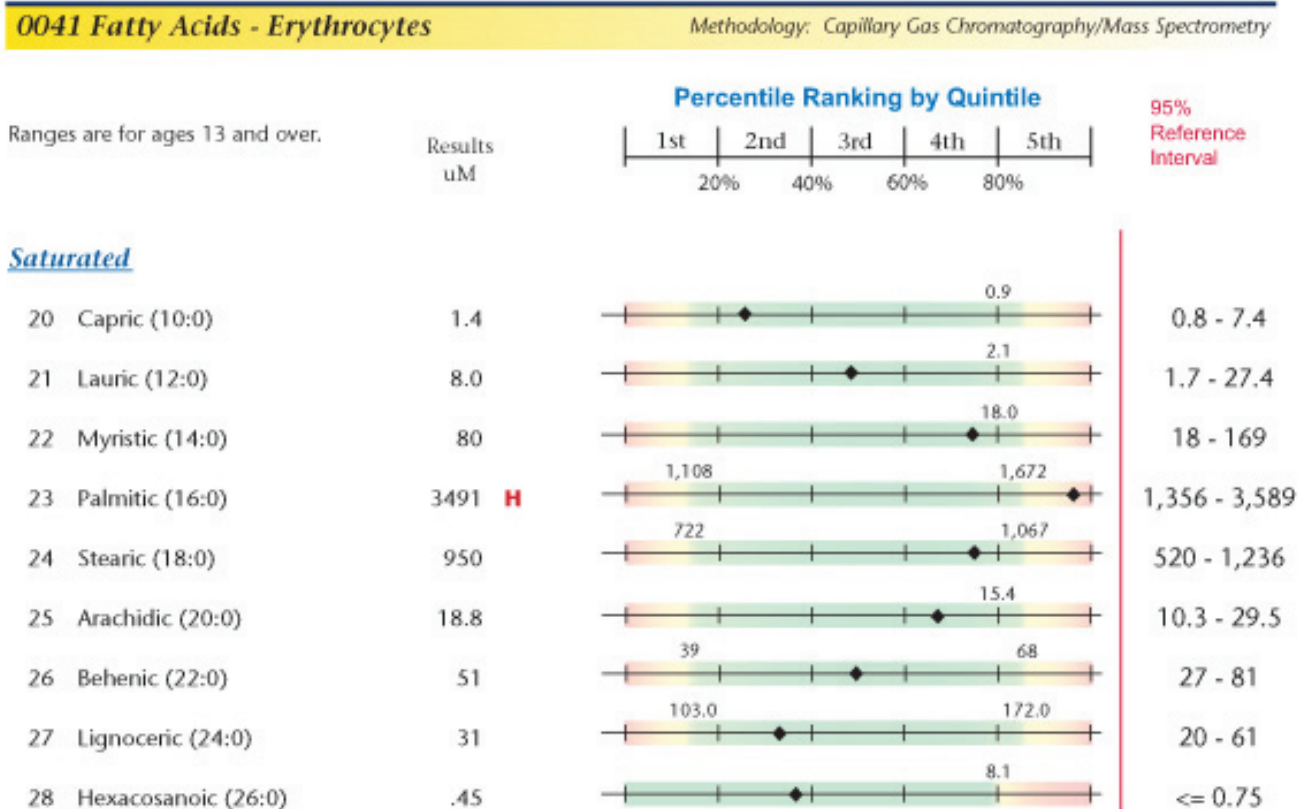


Figure 2. Saturated Fatty Acids Profile

Higher levels of polyunsaturated fatty acids, especially those with a chain length of 20-22 carbons, are generally associated with improved insulin sensitivity.<sup>1</sup> Delta-6 desaturase (D6D) acts on polyunsaturated fatty acids. Because Delta-6 desaturase activity is induced by insulin, insulin resistance may impair its effect.<sup>4,5</sup> Thus, those with insulin resistance may have low levels of arachidonic acid and long chain omega-6 fatty acids.

Increased levels of arachidonic acid (AA) have been shown to down regulate glucose transporters (GLUT4), and increase insulin resistance, while omega-3 fatty acids offer a protective effect.<sup>6,7</sup> In the presence of insulin, GLUT4 receptors move to the plasma lipid membrane and pump glucose into the cell. The receptors recycle back to their pre-insulin position when blood insulin levels fall. Research also shows that improvement of delta-6 desaturase improves glucose control in those with diabetes.<sup>3</sup> Higher levels of omega-3 fatty acids of 20-22 carbons may be the most beneficial in maintaining insulin action.<sup>1,8</sup> Attention should also be paid to the EPA/DGLA ratio, which is low in insulin resistance and cardiovascular disease. While fats should be balanced, therapies directed at insulin resistance should also include chromium, niacin, and removing high glycemic foods from the diet.

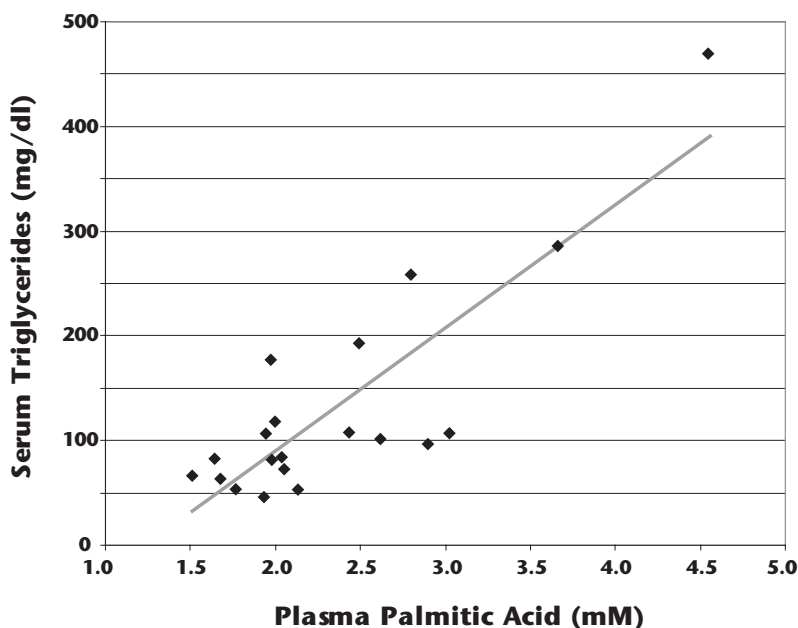
Initial insulin elevation in pre-diabetics appears to increase PUFA production via increased delta-6 desaturase activity; however AA elevation over time will itself contribute to further insulin resistance, thereby reducing all long chain PUFAs, including the protective omega-3 fatty acids. Therefore, increasing the intake of omega-3 fatty acids while normalizing omega-6 fatty acids in addition to other appropriate dietary and supplemental interventions, appears to be a powerful and effective treatment for insulin resistance.

Increased intake of trans fatty acids is associated with increased risk of cardiovascular disease and diabetes. The detrimental effects of trans fats have been found to increase low-density lipoprotein (LDL), triglycerides, lipoprotein (a), and the total cholesterol/ high-density lipoprotein (HDL) ratio, while decreasing LDL particle size and HDL levels.

### *Non-Specific Hypertriglyceridemia*

In hypertriglyceridemia there will be a general shift to the right of all saturated and monounsaturated fatty acids. Plasma palmitic acid has a positive linear correlation with serum triglycerides (**Figure 3**). Increased levels of palmitic acid have been associated with increases in IL-6 in coronary endothelial cells.<sup>9</sup>

Higher omega-3 levels have been shown to reduce triglycerides.<sup>7</sup> Research of over 4,000 middle aged men found plasma triglycerides to be inversely related to saturated, monounsaturated and omega-3 polyunsaturated fatty acids of 20 carbons or more, and positively associated with shorter chain fatty acids.<sup>10</sup>

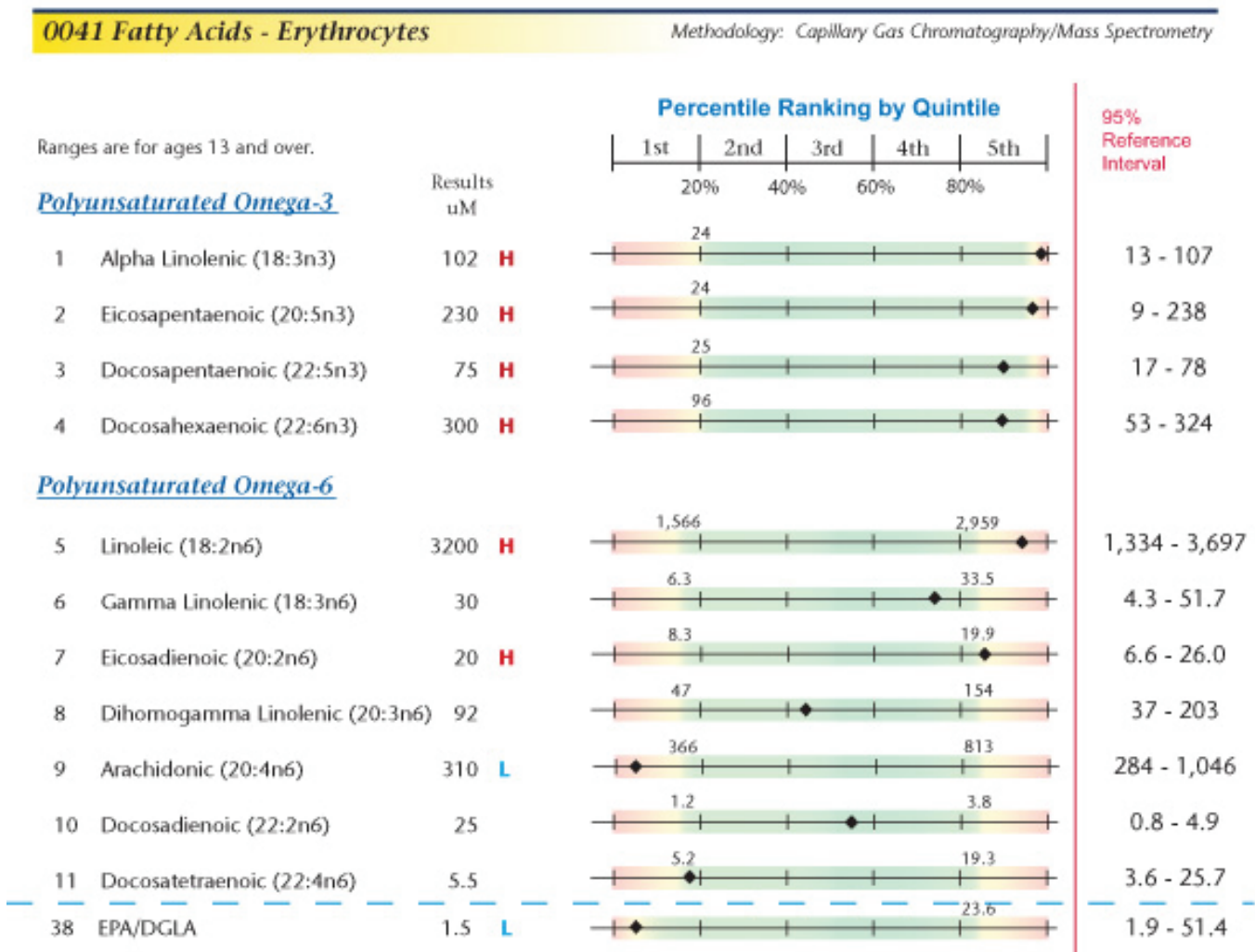


**Figure 3.** Hypertriglyceridemia is related to endogenous fatty acid synthesis and clearance. As the principal product of the fatty acid biosynthetic pathway, palmitate represents endogenous synthesis, and the level of palmitate in plasma reflects serum triglyceride levels. The trend line shows a strong linear relationship.

In hypertriglyceridemia, there is typically an associated decrease of lipoprotein lipase activity.<sup>11</sup> Therapies such as niacin have been shown to reduce triglycerides.<sup>11</sup> Other therapies that increase HDL cholesterol may also be of benefit such as garlic and B<sub>5</sub>. A dietary emphasis on restriction of sugar and other refined carbohydrates should be strongly considered, as the associated release of insulin in response to these foods will stimulate the further production of triglycerides. Inflammation is closely associated with hypertriglyceridemia. Several ratios comparing fatty acid precursors of pro- and anti-inflammatory eicosanoids can help the clinician determine the role of inflammation in hypertriglyceridemia and treat accordingly. These ratios include EPA/DGLA, which compares the two anti-inflammatory PUFA precursors of series 3 to series 1 eicosanoids, and AA/EPA a ratio of the pro-inflammatory series 2 to series 3 eicosanoids. These ratios are pivotal in the creation of individualized therapies designed to balance omega-3 and omega-6 fatty acids.

### Omega-3 Dominance

Low dietary omega-3 PUFAs can lead to increased inflammatory responses and can contribute to the development and exacerbation of inflammatory diseases. Conversely, excessive or unbalanced supplementation of omega-3 PUFAs can actually suppress immune function, leading to increased infections and poor wound healing. The patient identified in **Figure 4** below shows an omega-3 dominant profile. In addition, consumption of any PUFAs without adequate antioxidant intake can lead to increased production of free radicals, which is exacerbated by a low vitamin E level.<sup>2</sup>



**Figure 4.** This pattern was found in a 54 year old male who, prior to specimen collection, had been eating salmon 4-5 times per week for 1.5 months plus supplementing with 2,000 mg of fish oil and 600 mg of flax oil per day. All four members of omega-3 fatty acids are found in the fifth quintile. Fifth quintile linoleic acid with arachidonic acid in the first quintile shows a significant suppression of delta-6 desaturation. The AA/EPA ratio is in the first quintile, but not yet 2 standard deviations from the mean. However, continuing this level of omega-3 oil supplementation can further suppress AA formation to generate a very low AA/EPA ratio. There are no clear adverse clinical consequences at this stage, but the data provides a warning of the potential for crossing into clinically suppressed AA status and various consequences of sustained high peroxisome status, so supplementation of omega-3 enriched oils should be monitored.

## ***In Conclusion***

Metamatrix has several tests that evaluate fatty acid levels and ratios, including plasma, erythrocytes, and bloodspot. The erythrocyte and plasma tests include extensive data on individual fatty acids, including; polyunsaturated, monounsaturated, saturated, and trans fatty acid levels, as well as several ratios including; LA/DGLA, AA/EPA, EPA/DGLA, and Triene/Tetraene. The easy-to-use bloodspot test can be collected by the patient and measures key omega-3 and omega-6 PUFAs, as well as trans fats, and calculates indicators to establish an optimal balance. Fatty acid profiles are an ideal way to track patient progress or response to treatment and can help clinicians determine if he/she is giving too much or too little fatty acid supplementation. Clinical management of fatty acid supplementation is aided by testing for antioxidant status as well. This can be done by measuring markers of oxidant damage, such as lipid peroxides and urinary 8-hydroxy-2'-deoxyguanosine. Simply having these pieces of information can make a significant difference in your ability to guide your patient in diet and supplementation recommendations while modulating their inflammatory cytokines.

## ***References***

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