

WHAT ARE ORGANIC ACIDS?

Conventional medical doctors use a complete blood count (CBC) and a metabolic panel (MP) as general screening tools to help rule out health problems in their patients. In addition to these standard laboratory tests, functional medicine practitioners use an organic acid test to identify imbalances occurring in the body that may well precede abnormal findings on a CBC or an MP. Organic acids are products of metabolism that can sensitively identify nutrient deficiencies that lead to metabolic roadblocks. Traditionally they were used for detection of neonatal inborn errors of metabolism, including mitochondrial disorders.

Mitochondria are responsible for the oxidation of food energy (carbohydrates, proteins, and fats) into cell energy or adenosine triphosphate (ATP). The production of ATP requires hundreds of chemical reactions, and each reaction must run almost perfectly in order to have a continuous supply of energy. Organic acids can identify impairments in essential cellular functions, such as those occurring in the mitochondria, involving the citric acid cycle or electron transport, as well as beta-oxidation. When specific cellular functions are blocked due to impairment or absence of enzymes or a lack of cofactors, such as nutrients, normally low or absent organic acids spill into urine. Though the majority of research has focused on finding the most extreme inborn errors of metabolism, functional medicine clinicians evaluate organic acids to find more subtle impairments. These disorders can be present at birth or develop as an adult due to stress or lack of essential nutrients.

Polymorphisms (genetic mutations) in enzyme structure can lead to decreased cofactor binding and impair enzyme activity. Increased cofactor nutrients can help to push and sustain appropriate enzyme activity. Individuals with faulty enzyme binding can have increased nutrient needs that will not be revealed by measures of vitamin concentrations in blood.

A case in point is the variants of maple syrup urine disease (MSUD). MSUD is caused by an impairment of the enzyme needed to break down the branched chain amino acids, to their branched chain keto-acid. The enzyme is a branched-chain amino acid dehydrogenase. It can have different degrees of function. For the enzyme to function correctly it needs several B vitamins, primarily thiamin. Polymorphisms within the enzyme can result in severe clinical consequences in infancy or milder variants of MSUD in adults that are often brought on by precipitating conditions such as infection or stress. Thiamin supplementation may improve milder forms by making thiamin more available and thus increasing the enzymes function. A build up of the branched chain keto-acids in the urine can identify an impairment with the branched-chain amino acid dehydrogenase enzyme. Many such inborn errors of metabolism have both severe and mild forms. Table 1 (see reverse) shows the clinical phenotypes of MSUD. Some patients simply need extra thiamin to achieve full enzyme function, something they may not be aware of until they encounter a stress later in life.

Routine testing of organic acids is a relatively newer tool and may not be readily used by mainstream physicians. Abnormal concentrations of organic acids in the urine can provide a functional marker for metabolic effects of micronutrient inadequacies, genetic polymorphisms, impaired enzyme function, toxic exposure, neuroendocrine activity, and intestinal bacterial overgrowth. As such, organic acid testing can indicate the functional need for specific nutrients, diet modification, antioxidant protection, detoxification, and other therapies. Because impairments in some cellular functions may not show up until an increased stress or inadequate nutrient status impairs the enzyme function, an assessment of organic acids is recommended each time the patient has a physical, just like a CBC or MP.

Table 1 NIH Clinical Phenotypes of MSUD*

Variant	Enzyme Activity	Organic Aciduria	Clinical Presentation
Classical MSUD	< 3%	Elevated BCKA's: a-ketoisocaproate, a-ketoisovalerate, a-keto- β -methylvalerate	Symptoms within the first several days of life. Infant death or prominent abnormalities. Developmental delays.
Intermediate MSUD	3-30%	Similar to classic phenotype, though quantitatively less severe	Developmental delays.
Intermittent MSUD	5-20%	Normal BCAAs when well, similar to classic biochemical when ill	Will react with illness, stress, or high protein intake. Normal early growth and development. Age of onset varies.
Thiamin-responsive (10-1000 mg/day)	2-40%	Profiles improve with thiamin therapy (lower levels in urine)	Large doses of thiamin will increase the enzyme activity and break down leucine, isoleucine, and valine. Normal early growth and development. Age of onset varies.

*<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=gene.chapter.msud#msud.T2>