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USING ORGANIC ACIDS TO DIAGNOSE AND MANAGE RECALCITRANT PATIENTS

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STATEMENT OF PURPOSE
Diseases have reached epidemic proportions with new labels continually emerging. Most are managed with medications, and surgery is used as a last resort. Most medications merely poison an abnormally functioning pathway, thereby terminating the symptom. However, with the growing number of metabolic assays available, identifying the underlying causes of many symptoms is emerging as a reality. Researchers now tell us 95% of cancer and maybe other diseases have only 2 causes—diet and environment.[1]

From this starting point, we have found the correctable causes of a number of diseases that were previously managed through symptom suppression with drugs. This article explains some rudimentary aspects of organic acids and how they relate to uncovering the underlying causes of common symptoms.

TARGET AUDIENCE
This activity is designed to meet the educational needs of physicians and other healthcare professionals who diagnose, treat, and manage recalcitrant patients.

OBJECTIVES
After completing this article, participants should be able to:
1. Explain how organic acids can be used as a diagnostic laboratory tool to provide insight that may be unavailable by other routine avenues.
2. Explain why organic acids are a functional assay superior to serum levels for many nutrients.
3. Name a half dozen organic acids and what they indicate about a patient's health. (*Altern Ther Health Med*. 2006;12(4):44-53.)

DISCLOSURE
The author has disclosed that she has received small honoraria from Carlson Laboratories and MetaMetrix Laboratories in the last 12 months for non-CME presentations.

Organic acids can reveal things about a patient's metabolism that may be crucial to their stalled healing. Unlike vitamins, minerals, amino acids, and fatty acids, there are no essential nutrients in this category. Instead of measuring nutrient concentrations, organic acids actually go one step further, measuring whether the nutrient in question is functioning adequately. For example, Lindenbaum's study in *The New England Journal of Medicine* looked at patients with fatigue and loss of memory.[2] Some participants' serum levels of B12 were found to be normal, and the patients had no anemia or macrocytosis. After they were given B12 injections, they had marked improvement in energy and brain function. It has now been known for more than a decade that metabolic organic acid metabolites are much more sensitive than serum levels.[3] The Lindenbaum study is an example of how organic acids can provide information beyond what mere levels and less sensitive indicators can provide. They can offer a starting point for successfully guiding a patient to wellness.

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Diseases have reached epidemic proportions, with new labels continually emerging. In the last few decades, cancer and cardiovascular disease have become the most common ailments,[4] and common diseases are occurring at younger ages. An 18-year-old with breast cancer is not what we as clinicians expect to see.[5] Additionally, the author is seeing more of formerly less common maladies, such as macular degeneration and Parkinson's disease. Meanwhile, new labels, such as "chronic fatigue syndrome," "metabolic syndrome," "fibromyalgia," "erectile dysfunction," "premenstrual syndrome," "autism," and "reflex sympathetic dystrophy" have emerged. Most medical conditions are managed with medications, and surgery is used as a last resort. The most common mechanism of action of medication is to poison abnormally functioning pathways, thereby ameliorating the symptom. Hence, most medications are blockers, inhibitors, anti-inflammatories, anti-histamines, anti-biotics, anti-fungals, anti-emetic, anti-hypertensive, antiseptics, anti-coagulants, antacids, anti-convulsants, anti-depressants, or anti-neoplastic. But in this era of advanced biochemical knowledge, we have more tools to use to determine the underlying causes—many of which are correctible—of a number of common symptoms and diseases.

Researchers now tell us 95% of cancers and possibly other diseases have only 2 causes—diet and environment.[1] This translates to what we have witnessed in more than 3 decades of medical practice and what research from a variety of sources bears out. There are epidemics of undiagnosed common nutrient deficiencies throughout the United States, which in itself is enough to introduce baffling symptoms in the medical system.

NUTRIENT DEFICIENCIES: A HIDDEN EPIDEMIC

Vitamin D deficiencies are epidemic in 42% to 93% of the population.[6-8] That explains why other diseases that depend in part on replete vitamin D stores are also on the rise—from osteoporosis and cardiovascular diseases to cancer, diabetes, and multiple sclerosis.[9-12] No matter what nutrient is studied, the results confirm epidemics with wide-ranging epidemiologic effects. For example, one study of preschool children aged 2-5 years revealed that 91% were grossly deficient in vitamin E.[13] Half did not even have two-thirds of the recommended daily allowance, which is very low at 11 IU, compared with the dose of 400-800 IU, which alone or with 1 or 2 other nutrients made a dramatic clinical difference in many studies.[14-17]

Vitamins and other nutrients have a clear role in disease prevention and treatment, but we are not routinely assaying them. Undiagnosed vitamin deficiencies are at the root of some of our top causes of disease and death.[18-22] And genetics has a role in appreciating variant enzymes within genetic polymorphisms.[23]

Mineral deficiency is even more prevalent than vitamin deficiency. In a *JAMA* study of more than 1,033 hospitalized patients, researchers, without the physicians' awareness, evaluated the patients for a magnesium deficiency. The researchers found that more than 57% of the patients who were sick enough to be hospitalized had a magnesium deficiency. Ninety-five percent of the physicians had never checked the patients' magnesium levels, and many of the patients died of magnesium deficiency–related symptoms, such as cardiac arrhythmia and sudden cardiac arrest.[24] Furthermore, the test used by the researchers had low sensitivity. They assayed the serum magnesium, which constitutes less than 1% of the body's magnesium. The more appropriate and more sensitive test is intracellular or erythrocyte magnesium.

Government studies show that the average American diet provides only 40% of the daily requirement for magnesium.[25] In the *JAMA* study, researchers studied the serum magnesium levels whenever patient bloods came to the lab for testing of whatever the doctor ordered. They found that 54% of the patients were deficient via the serum assay. A surprising finding in this study was that 90% of physicians never even ordered a magnesium assay.[24]

Magnesium is, among other things, nature's calcium channel blocker, so it is not surprising that the number-one category of prescribed cardiology drugs is calcium channel blockers.[26] Unfortunately, one of the side effects of this category is shrinking of the brain away from the skull and loss of intellect within 5 years of taking it.[27] The repeating distance is 4 times the diameter for calcium channels, so the membrane must be significantly damaged to require them. The fact that the gap junctional proteins on cell surfaces are also compromised explains why cancer incidence is greater in users of this type of drug.[28]

Polypharmacy results in further reduction of magnesium status, which in turn leads to more symptoms, such as hypertension. And the drugs from the practice guidelines for hypertension further deplete magnesium, as well as potassium, coenzyme Q10, zinc, and other nutrients while increasing homocysteine, until there is sudden cardiac death.[29-31] Suppression of symptoms with drugs can hinder the practitioner's ability to find the underlying, correctable causes of disease. This can allow the underlying causes to worsen, while drugs further deplete the patient's nutrient reserves, accentuating deficiencies and symptoms.[32]

ENVIRONMENTAL TOXINS: AN UNAPPRECIATED CAUSE OF DISEASE

The second part of the equation confounds medical diagnoses even more, for the human body now harbors more *xenobiotics* or foreign chemicals than at any other time in history. Even newborn babies are not exempt. When umbilical cord blood of a newborn was examined for only 287 common everyday chemicals (out of more than 60,000), he had on average 200 in his blood at the moment of birth, 180 of which are known carcinogens. This explains researchers' concerns that 1 in 6 children born today have some degree of neurological/behavioral impairment from environmental xenobiotics.[33,34] These included phthalates or plasticizers if his mother had an IV or drank from a plastic water bottle. The top 10 culprits included polybrominated diphenyl ether (PBDE) from flame retardants in mattresses and other furnishings; pesticides from foods and furnishings; polychlorinated naphthalenes from wood preservatives, varnishes, vehicles, incinerators, and factories; and polyaromatic hydrocarbons from burning of gasoline and garbage as well as industrial smokestacks. Some contend that this is why, according to one group's review, the incidence of autism has

increased 10-fold, birth defects and asthma have doubled, leukemia has increased 62% and childhood brain cancers have soared 40% in the last couple of decades.[34] The CDC found phthalates (plasticizer metabolites) in 100% of US humans studied.[35]

Today, newborns are so burdened with xenobiotics that, for the first time, they are not expected to live as long as their parents.[36] The study's authors attributed this to the obesity epidemic, but it has been clearly shown that phthalates create insulin resistance. Additionally, the authors failed to document the proven roles of trans fatty acids, high-fructose corn syrup, olestra, heavy metal toxicity, nutrient-depleted processed foods, and other contributors.[37] Studies have shown that polar bears in the Arctic have osteoporosis from chemicals boosting out calcium from their bones and thyroid disease from the vast array of environmental endocrine disruptors.[38-40] The number-one pollutant from ubiquitously unavoidable phthalates or plasticizers in foods, beverages, medicines, air, construction materials, textiles, and toiletries is an example of just one category of pollutant that can create insulin resistance, obesity, metabolic syndrome, and arteriosclerosis.[41] Phthalates accomplish this and more through a variety of mechanisms as they damage mitochondrial lipid metabolism, genes, membrane signaling, nutrient receptors, and cytokine release and redox.[42-45]

ORGANIC ACIDS

One of the many recognized risk factors for early cardiovascular (heart attack, stroke, thrombosis), neurodegenerative (Alzheimer's, macular degeneration), and other diseases is homocysteine.[46,47] Methylation is important in converting homocysteine to methionine. Methylation is also crucial in keeping DNA from expressing cancer genes, and it is an important process in detoxifying everyday chemicals. Crucial to methylation is the chemistry of folic and B12. But Harvard reports from decades ago showed practitioners that the serum levels for B12, for example, could be normal in spite of clinically serious B12 deficiencies.[2] People with normal serum B12 levels and no megaloblastic erythrocyte changes had improved energy, depression, and thought processes when given B12. A more accurate determination is the urinary organic acid indicator metabolite methylmalonyl-CoA, which requires B12 to break down valine into energy-yielding products, whereas B12 deficiency increases the level of methylmalonic acid in the organic acid assay. Further, organic acid testing is simpler than blood collection, as methylmalonic acid and the other organic acids require only a single urine collection and not a blood draw.

Equally important in methylation is the assay for formiminoglutamate (FIGLU), an intermediate in the deamination of the amino acid histidine. Just as urinary excretion of methylmalonic acid increases with B12 deficiency, the organic acid FIGLU increases with folic acid deficiency. When these are low, it is often beneficial to replete them with readily available non-prescription sublingual nutrients of methylcobalamin and folinic acid, thus bypassing the gut absorption for a while until that has been investigated and repaired.[48] Of course, dietary evaluation and correction is preferable, after ruling out diverse causes, such as medications, cancer, smoking, or alcoholism. One of the greatest contributors to deficiencies of nutrients like B12 and folic acid are medications. Oral contraceptives, hormone replacement therapy, chemotherapy, and anticonvulsant and anesthesia drugs are just a few that deplete folic acid.[32,49] For example, forms of colitis are known to increase the risk of cancer, but this is due in part to the actual medications, like sulfadiazines, which deplete folic acid. DNA that is hypomethylated more easily promotes carcinogenesis and cardiovascular disease.[50-52]

A significant portion of the elderly population is low in B12, contributing to a myriad of subtle symptoms that are attributed to old age and rob patients of vitality and brain power. In another study of patients admitted to an acute medical service, 23%-50% had undiagnosed nutrient deficiencies, and this study was very rudimentary and not a comprehensive assay.[53] One of the most common categories to cause unsuspected B12 deficiency is the H2 acid inhibitors. Omeprazole was the first "blockbuster" drug on the market that turned off gastric acid secretion. In doing so, it produces hypo-chlorhydria in some individuals, and with concomitant intrinsic factor inhibition, there is B12 deficiency. After this drug went off patent, it was deemed safe enough for over-the-counter, non-prescription status, and more people used it, potentially masking the correctable causes of heartburn, like *H pylori*, before they cause age-accelerating atrophic gastritis, ulcers, gastric cancer, or coronary artery disease.[48] Hypomethylation via unsuspected B12 and folic acid deficiency is more common than people realize. Research shows that people who take medications to suppress intestinal symptoms have not just the national increase in gastric cancer over the last 2 decades of 8-fold, but a much higher rate—43-fold.[48]

Another reason hypomethylation is important is in its role as a common cause in exponentially increasing degenerative disease, hyperhomocysteinemia. Elevated homocysteine is a risk factor for cardiovascular disease, stroke, and Alzheimer's, among others.[54] Vascular flow has been improved by correcting elevated homocysteine with B12 and folic acid.[55,56] In other studies, as the homocysteine levels decreased with treatment, there was a reduction in carotid artery thickness 32%, while the group that did not have B12, B6, and folate had a 23% increase in carotid artery thickness.[57] In other studies, treatment produced a decrease in abnormal stress EKGs.[58] Some people with corrected homocysteine methylation have less restenosis after angioplasty,[59] and in 556 post-angioplasty patients, there was a 34% decreased risk for death, myocardial infarction, or restenosis after 1 year.[60] In patients who need more or additional nutrients to correct their hyperhomocysteinemia, the organic acids target the nutrients that need special attention.

Folic acid is commonly deficient, but if the clinician naïvely relies on a serum value, it may merely reflect recent dietary intake, giving a false sense of security. Given that the vast majority of medications (from birth control, antihypertensives, and nonsteroidal anti-inflammatory drugs to chemotherapy, colitis medications, and anticonvulsants, not to mention xenobiotic exposures) can leave the patient with inadequate levels of folic acid, and it is so pivotal in remethylation, it behooves the practitioner to be sure he has a grasp on the functional assessment for

adequate folic acid status, FIGLU, especially for cancer patients.[61] The diet patterns of many Americans, cigarette and alcohol consumption, and intestinal dysbiosis, which interferes with processing of folate to its active form, can be contributing factors in cancers progressing to other cancers and metastases.

DYSBIOSIS MARKERS

A second indispensable category of organic acids shows evidence for abnormal microbial invasion of the gut. The body is capable of making only a limited quantity of certain organic acids. When there is an overabundance of specific ones, this is a clear indication that something other than the body produced them—namely organisms residing in the intestinal tract. For example, tricaballyate, produced by unfavorable gut microflora, contains 3 carboxylic acid groups that have a powerful ability to mimic ethylenediaminetetraacetic acid (EDTA) in chelating metals. Magnesium can be so tightly bound by the claw-like effect of 3-carboxylic groups that it can cause severe magnesium deficiency and calcium or zinc deficiencies as well.[62] In fact, intestinal dysbiosis can be a leading hidden cause of inability to maintain reverse magnesium levels. Many people will never be able to reverse magnesium deficiencies because the practitioner failed to assess the gut first. The gut not only houses a major part of the immune system and the detoxification system for the entire body, but determines absorption, assimilation, and maintenance of nutrients.[48,63,64]

D-arabinitol provides another crucial clue about why some people have trouble getting well.[65] In many patients, the presenting symptoms are so diverse and comprehensive that the practitioner is in a quandary as to how to proceed. When there is biochemical evidence of overload and malabsorption from an inflamed gut, it must be healed first. It does little good to force nutrient corrections, environmental controls, drugs, allergy injections, chelation, or other attempts at treatment if the gut is so inflamed that (1) it cannot absorb nutrients, (2) half the immune system is out of commission, or (3) xenobiotic biotransformation is paralyzed. D-arabinitol not only provides insight about why some patients' medical progress seems indefinitely stranded, it also tells the practitioner where to start.[66,67] The gut must be healed first.

Many people have tried processed-food diets and antibiotics and other *Candida*-fostering medications that leave them with a gut full of yeasts. D-arabinitol, a marker of yeast invasion that normalizes on treatment, is positive even days to weeks before blood cultures are positive.[68] There are many other ramifications of yeast overgrowth that are beyond the focus of this article, such as *Candida* organisms making thiaminase, an enzyme that destroys thiamin, vitamin B1, before it even gets absorbed.[48] This, in turn, leads to baffling cardiovascular and neuropsychiatric symptoms as part of the vicious cycle initiated with deficiencies. When symptoms are treated as a deficiency of a drug, then—as a simple example—the thiamine deficiency goes unrecognized while anti-depressant or cardiac prescriptions cause further nutrient depletions and more symptoms. The result: the self-perpetuating vicious cycle of drug-oriented medicine as opposed to biochemically-oriented medicine, which looks for the cause and cure. In addition, yeasts translocate across the gut wall into the circulatory system. Because of molecular mimicry, the body now makes antibodies to destroy its own thyroid, and this will not stop as long as there is continual antigen drive.[69]

Organic acids relating to bowel health, such as hippuric acid and benzoate, are not as specific. They need to be evaluated in the context of the big picture, as they have other sources besides bacterial overgrowth. For example, if you walk into a newly painted or carpeted room, for every molecule of toluene that reaches the bloodstream, the body couples glycine onto it to make it heavy and polar. This enables it to be dragged out of the liver sinusoids, into the bile, then into the gut for final depuration as hippuric acid. However, benzoic acid (conjugated the same way) is a common component of processed foods (eg, pickled lunchmeats, soda drinks) as well as natural foods (eg, cranberries). That is one reason why it is important to assess the patient's diet and environment in determining his or her total load of biochemical disease-initiating stressors.[70] Glycine and pantothenic acid are limiting factors, so they are important to supplement.[71]

Other bowel indicators, such as indican, are more specific. When bacteria in the upper bowel convert tryptophan to an indole, which the liver then sulfates, indoxyl sulfate or indican results.[72] It becomes a marker for upper bowel bacterial overgrowth, which has severe consequences for pancreatic function. Results can be complicated by, for example, impaired protein digestion, which increases the available tryptophan for conversion. This is just one more example of how the history of the individual combined with other laboratory tests, such as amino acid testing, further clarifies the picture, which is certainly needed when as much as 30% of the elderly population has some sort of malabsorption.[73]

Many drugs, even non-prescription drugs, can foster intestinal dysbiosis, which often is unsuspected. The OTC H2-acid inhibitors also can trigger the overgrowth of *Clostridum difficile* and other unwanted organisms that disturb gut health.[74,75] There are other organics related to intestinal dysbiosis. Failure to diagnose and correct this leads to intestinal hyperpermeability, which can go on to cause auto-immune disease, multiple chemical sensitivities, chronic fatigue, and fibromyalgia.[48,76]

HIDDEN B VITAMIN DEFICIENCIES

Biotin is a forgotten B vitamin that is not directly assayed, but organic acid analysis may be helpful in this area. First, it can be deficient for a variety of reasons, including the biotin-poor diet of devitalized processed foods. Additionally, common supplements such as lipoic acid (thioctic acid) can lower biotin.[77] When this happens, compromised glucose-induced insulin secretion and increased insulin resistance can occur, which can contribute to the hidden epidemics of obesity, metabolic syndrome, chronic fatigue, hypoglycemia, and diabetes as well as the sequelae of accelerated arteriosclerosis.[78] In animals, these parameters improve with biotin treatment, and in humans there is improvement in glucose tolerance tests as well as diabetic neuropathy.[79-81] An elevated beta-hydroxyisovalerate is a specific and sensitive metabolic marker for functional biotin deficiency and drops to normal as biotin is replet-

ed.[82] Biotin is a cornerstone for carboxylation reactions, which can leave the patient with anything from poor hair health and hair loss to a weakened immune system, *Candida* resistance, or muscle weakness. Many medications, including anticonvulsants—and even pregnancy—can deplete biotin.[83] How would clinicians adequately diagnose and treat stalled energy or glucose metabolism without this test for biotin repleteness?

Vitamin B6

Vitamin B6, pyridoxine, is crucial for amino acid conversions for neurotransmitters of happy mood, homocysteine, and energy synthesis, and B6 deficiency plays a role in carpal tunnel syndrome, depression, and arteriosclerosis.[84] Xanthurenic acid spills over into the urine when the process is stalled for lack of B6.[85] Dietary tryptophan is normally metabolized into serotonin, 95% of which is made in the gut (if it is healthy), while the rest forms one of the "happy hormones" or neurotransmitters of the brain as well as nicotinic acid for nicotinamide adenine dinucleotide (NAD) energy reactions. Many drugs can inhibit or deplete trytophan, as can hormone replacement therapy.[86]

Fatty Acids

Organic acid testing can be used to measure fatty acids and determine whether they need to be supplemented. Some practitioners recommend giving them without the benefit of assay, but the most prevalent xenobiotic in the human body, phthalates, can poison carnitine synthesis so that regardless of how much fatty acid the practitioner gives, it cannot get inside the mitochondria to be turned into energy via beta-oxidation.[87] It can also impair docosahexaenoic acid (DHA) synthesis, which then goes on to repair 504 cancer genes. Organic acids testing can detect elevated adipate, suberate, and ethylmalonate, which indicates that carnitine needs to be supplemented, along with riboflavin (B2). The patient can get an erroneous abnormal result if he or she is taking aspirin or currently has the flu, as these can also inhibit beta-oxidation.[88]

BIOCHEMICAL MARKERS OF EXCESS FREE RADICALS

Lipoic Acid

Lipoic acid (thioctic acid) is an antioxidant made by the body that is easily consumed because it serves so many roles. First, it recycles many antioxidants, such as vitamins C and E as well as glutathione, returning them to a more useful state. It is also one of the few nutrients that have a role in reducing the fatal toxicity of mycotoxins,[89] which are becoming increasingly more ubiquitous. As little as 600 mg a day of lipoic acid played a unique role in improving insulin resistance—27% over placebo in type II diabetics in 1 month.[90]

In another study, diabetics taking 600 mg a day of lipoic acid, this time for 3 months, lowered their lipid peroxides 36%.[91] Lipoic acid protects the pancreas from inflammation and reduces complications associated with diabetes.[92,93] No medication has this power over lipid peroxidation, one of the main mechanisms responsible for the accelerated aging associated with diabetes. But how many diabetologists would think to raise the level of lipoic acid without telltale assay indicators like pyruvate and lactate? These metabolic products of carbohydrate breakdown can also indicate extra need for the B vitamins, thiamin (B1), niacin (B3), and pantothenic acid (B5, in addition to CoQ10 for the lactate). Not only is it needed for diabetes and its complications, but also for energy recovery in athletes, the obese, and cancer victims.[94,95]

Because lipoic acid is such a powerful antioxidant, it affects metabolic indicators other than just disordered carbohydrate metabolism. For example, if the 8-OhdG (8-hydroxy-2'-deoxyguanosine) marker for gene damage is elevated, this could indicate a variety of problems from excess phthalates or plasticizers, the number-one body pollutant that poisons peroxisomes, leading to abnormal fatty acid metabolism and faulty cell membranes, ion channels, and receptor sites to recurrence of a once-dormant cancer.[48] But with sufficient lipoic acid as well as vitamins C and E (which lipoic acid recycles) the elevated 8-OHdG will return to normal, correlating with symptom improvement.[96,97] If it does not normalize, the role of heavy metals and other nutrients should be pursued.[98,99] Lipoate is also recommended for attenuating the side effects of chemotherapy.[100] Combined with carnitine, it has actually reversed aging in the rat heart and brain.[101-104]

Another important indicator of the need for lipoic acid is elevated isocitrate and citrate, and isocitrate requires magnesium and manganese as well. Citrate elevation can also be a sign of ammonia accumulation due to arginine deficiency. If elevated citrate is accompanied by elevated cis-aconitate, alpha keto-glutarate, and orotate, this can be a sign of arginine deficiency, whereas cis-aconitate, pyruvate, and alpha keto-glutarate can signal lipoate deficiency. In other words, clinicians can be as sophisticated with organic acids as their knowledge allows. The increase in knowledge can be exponential as a clinician's biochemical knowledge and patient experience increase.

Vitamin C

Vitamin C is essential to keep free radicals controlled, and it is easily lost from the body. An excellent indicator of the need for additional ascorbate is an elevated p-hydroxyphenyllactate. And if there is elevation of the 8-OHdG—p-hydroxyphenyllactate, glucarate, and quinolinate—antioxidant control with the 8 forms of vitamin E, the 4 tocopherols, and 4 tocotrienols is indicated, along with ascorbate and lipoate, to stave off precancer changes.[105]

CoQ10

The millions of patients on the latest "blockbuster" drug category, statin cholesterol-lowering drugs, are at risk for developing symptoms of CoQ10 deficiency, from hypertension or congestive heart failure to chronic fatigue, encephalopathy, depression, or myopathy. An elevated lactate is a clue that could save a patient from a potentially lethal outcome, especially if he or she also has elevated hydroxymethylglutarate (HMG), as statins are HMG CoA reductase inhibitors. By poisoning the primary hepatic enzyme that makes cholesterol, they not only cause an increase in HMG

but also hamper the body's ability to make CoQ10.[106] which can lead to congestive heart failure.[107] The higher the levels of these 2 organics, the more likely it is that the patient is more uniquely vulnerable for the fatal rhabdomyolysis that can be caused by the drug. It may well be that supplementation of CoQ10 could protect against the adverse symptoms of statins. Likewise, succinate cannot proceed in the citric acid cycle for converting food to cellular energy without CoQ10. The addition of Riboflavin (B2) to CoQ10 has caused dramatic regression of neurologic impairment.[108] Fumarate and malate serve as additional markers of the need for CoQ10 or cytochrome oxidase defects.[109]

ORGANIC ACIDS AS MARKERS OF FAULTY DETOXIFICATION

Elevated alpha-hydroxybutyrate activity is a great indicator of myocardial infarction size and reperfusion effectiveness.[110] Alpha-hydroxybutyrate strongly inhibits mitochondrial energy synthesis in the heart, so assessing it in any cardiovascular disease is advised. Because it is restored by adequate n-acetylcysteine (NAC) and glutathione, it also is an important marker of intracellular detoxification. Elevated pyroglutamate also indicates a need for glutathione, which can improve a multitude of symptoms, depending on tissue target organ.[45] Combined with amino acids like taurine, the primary amino in the heart, brain and eye, but which is lost in the bile, it boosts detoxification while it spares magnesium and stabilizes the cell membrane, improving congestive heart failure, neurologic degenerative diseases, platelet aggregation and more.[111-113] Once you get clues about nutrients that facilitate pathways, the addition of targeted adjuncts can bring about the therapeutic magic that makes medicine so much fun. In more serious problems like cancer, glutathione reduces the toxicity of chemotherapy and improves quality of life.[114-116]

The Role of Glycine in Detoxification

Detoxification is pivotal in recovery from any disease. It is important to assess whether detoxification reserves are working overtime or have been dangerously depleted. A common environmental xenobiotic is xylene, which the body hooks onto glycine to make soluble and polar hippurate and thus easier to drag out through the liver sinusoids and into the bile and bowel for disposal. But overload of toxins in the home, travel, or office environment through new paint, carpets, furnishings, construction materials, or renovations can bring on symptoms that mimic anything from arthritis to toxic encephalopathy. This can stall healing until the practitioner can identify the weak link in detoxification and repair it.[117] Glycine is a detoxifier and inhibits cancers, improves memory, and helps fight *H pylori,* so it is helpful for people to know if they have sufficient glycine.[118-121] It works effectively only if there is enough left over from the daily neutralization of xenobiotics.[119-122] Wearing too much perfume or aftershave can compromise proper detoxification.[123]

Another source of the volatile organic hydrocarbons that deplete your glycine reserves is the parabens, antifungal preservatives that are in medication, toiletries, cosmetics, foods and other sources. They are absorbed from our deodorants and go into breast tissue; they are found on breast biopsy in greater amounts in women with breast cancer.[124-126]

The body absorbs toxins continually and stockpiles those that it does not have enough glycine and other detoxifiers with which to get rid of them.[116-127] But glycine's ability to prevent liver tumors caused by the ubiquitous plasticizers can occur only if it exists at sufficient levels.[122] Evidence of exhaustion or overuse of glycine from environmental contamination or bowel dysbiosis appears as 3-methylhippuric acid and hippurate.

SUMMARY

"Organic acids" refers to a broad class of compounds used in fundamental metabolic processes of the body. They provide valuable clues about functional nutrient deficiencies, mitochondrial energy production, intestinal dysbiosis, free radical overload, and more, including where to start when diagnosing a patient with complicated symptoms.

Organic acids present a whole new exciting world of therapeutic options. They are one of the tools that enable us to identify and correct the underlying causes of disease, and not merely temporarily suppress symptoms with pharmaceuticals. The sicker the patient, the more they need this intervention: half the patients in intensive care units were found to be nutrient-deficient in studies that look at only 1 or a few of the many nutrients.[24] Studies show that a patient's outcome is more dismal and his chances of dying are greater as undiagnosed nutrient deficiencies mount.[128,129] Furthermore, studies confirm that giving pennies' worth of antioxidants to patients in intensive care can cut the death rate in half.[130,131] What drug can accomplish this, much less for pennies a day? Doesn't it make more sense to individually determine the patients' deficiencies and correct them?

Combined with companion tests of intracellular minerals, toxic elements (heavy metals), fatty acids, vitamins, and amino acids, organic acids testing can clearly indicate health challenges the patient will face in the future. In many cases, they are correctable and curable.

This article explored only 5 categories of organic acids out of more than 9 and 29 organic acids out of more than 47. For physicians who want more information, there are several resources available.[76,99,132] This knowledge, along with biochemical knowledge and patient experience, can further empower physicians to help truly heal their patients.

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