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Medical Miracle or Just Good Medicine

“Test, Don’t Guess”

Chris D. Meletis, N.D.

The healthy journey of young A.G. is a story that starts and ends simply enough but takes a few interesting turns along the way.

A.G. first presented to my office six years ago at the age of four. Her mother reported the all too often symptoms of recurrent otitis media, excessive earwax, and year-round sinus congestion with post-nasal drip. As a nutritionally oriented physician the first step that I pursued was food sensitivity testing. A.G. though a mere four years old was a surprisingly willing participant, and had a standard venipuncture for a 96 General Food IgE and IgG Panel.

A.G.'s results revealed a high reaction to dairy, eggs, almonds, and peanuts. She also had numerous moderate reactions to lobster, asparagus, broccoli, and clams. Elimination of these foods from her diet was a prudent first step in her treatment, and I counseled A.G.'s mother on this fact. The only supplements I recommended at this time were a comprehensive children's multiple, a fish oil blend rich in EPA and DHA, and a child's probiotic formula. The latter two, to help re-establish gut tolerance.

Implementing the Elimination and Rotation Diet Plan for a four year old was no small feat. But, with patience I took A.G. and her mother on a field trip to our neighborhood natural foods market and introduced them to healthful alternatives that the mother could use in A.G.'s meals.

Food, one assumes provides nourishment; but “what is food to one man may be fierce poison to others” (Lucretius c. 99 B.C. - c. 55 B.C.). A concept that is so fundamentally true yet it never ceases to amaze me how overlooked a simple food sensitivity test is in general practice; an easy-to-do test that can steer treatment into the land of profound results.

At A.G.'s follow-up six week visit symptoms had resolved. I re-assessed A.G.'s diet plan and provided the mother with additional food choices for young A.G. At twelve weeks, A.G., now a glowing and vibrant little four year old, was in the peak of health. As a bonus, the mother had reported that A.G. had stopped wetting the bed.

Unfortunately, A.G.'s story doesn't end here at happily ever after. Three years later a more grown-up A.G. presented back to my office at the ripe old age of seven. At this time she was quite run-down; sinus congestion had returned with a vengeance, swollen cervical lymph nodes, otitis media with

excessive ear wax, erythematous and scaly ear canals, typical allergic shiners, and eczema on her arms and abdomen.

Apparently during A.G.'s hiatus from our office, her rhinitis had returned at the age of five and she was given a nasal steroidal spray and prescription oral anti-histamine to control the symptoms of hay fever, as diagnosed by her pediatrician. However, the anti-histamine had upset her stomach so much so that she was prescribed the acid blocker, cimetidine. With this, she could tolerate the medication routine which also included a steroidal ear drop for her itchy ears, a hydrocortisone cream for the eczema, and an antibiotic.

My course of action at this time was to “test, not guess”, so I ordered a follow-up 96 General Food IgE and IgG Panel, in addition to a full chemistry and CBC. Noteworthy was a remarkable eosinophilia which partly explained the classic atopic triad that presented in this little gal; eczema and hay fever – yes – but not yet asthma, by Joe! Also, her food antibody panel showed elevations for the same foods as before in addition to a few others. This was not the news I was looking for. Apparently, the mother had reported that A.G. had done so well on the Elimination and Rotation Diet Plan that she decided to reintroduce A.G.'s offending foods back into her diet. An error in judgment that I must take some responsibility for, as patient education can always go further.

The order of treatment was as before. She was doing well on this regimen, and was headed in the right direction. Very often, I find that children require very little intervention. They are resilient little creatures that only require a common sense approach to treatment with persistence being the key to success. Within six weeks, A.G. was doing much better, and under the supervision of her pediatrician, was gradually being weaned off of her prescription medications. Today, A.G. stands as a vibrant and rambunctious happy go-getter, whom I might add, at the age of ten, has taken an active role in preparing healthful school lunches with the careful guidance of her mother.

Note: Since treating A.G. US BioTek now offers an IgG finger stick test that does not require a venipuncture. This is a simple and effective way of getting the results of a 96 IgG Food Panel within 7-10 days.

Food Sensitivity Testing and Celiac Disease

Shalima Gordon, N.D.



What do birthday cake, vanilla wafers, pasta and hamburger buns have in common? Wheat flour.

To roughly 2.2 million Americans, wheat flour and other gluten-containing based foods from rye and barley; pose a serious health risk to those afflicted with celiac disease. Wheat proteins are collectively called gluten, and gluten is a mixture of individual proteins classified as prolamines and glutelins. The prolamine, gliadin, seems to be the injurious component of wheat for celiac patients while other prolamines; secalin, hordein, and avenin of rye, barley and oats respectively, pose a noxious threat as well, to varying degrees.

Other names for this condition including; idiopathic sprue, gluten intolerance, or gluten sensitive enteropathy (GSE), fall under the broad category of Food Sensitive Enteropathy. An alarming fact is that a majority of these affected individuals may not even know that they have the disease. Years of illness, unexplained weight loss, headaches, fatigue, abdominal pain, bloating, diarrhea and a host of other health problems may be misdiagnosed through lack of adequate patient follow-up and testing.

Celiac disease may be thought of as a non-IgE immune mediated food allergy. It is a complex disease process, associated with a variety of autoimmune disorders and carcinomas of the gastrointestinal tract. An immune hypersensitivity underlies this condition and involves both cellular and humoral immune responses, with T and B cell infiltration in the small intestine and antibody production namely; antigliadin antibodies (IgA, IgG), antiendomysial antibodies (IgA, IgG), and IgA antitransglutaminase antibodies.

There are many factors that contribute to disease progression. In over 95% of individuals affected, there is a defect at the level of gliadin



antigen presentation that is linked to a DQ2 gene that encodes MHC II molecules responsible for aberrant presentation of gliadin to T cells in the intestinal mucosa. Genetics aside, health experts agree that the number of affected individuals is disturbing, and on the rise.

Why?

Viral infections (adenovirus type 12), bacterial infections, prescription medications, highly processed foods, and a host of other insults and irritants to the gastrointestinal mucosa may abrogate oral tolerance to cereal grains causing inflammatory damage. In addition, wheat today is much different in its makeup to its ancestor. Today, wheat is more gluten-heavy from years of selective agriculture. This gluten-dense grain allows for lighter, fluffier, and puffier baked

products, but at the same time our average exposure to this protein is now higher than ever.

Chronic exposure to gluten-dense foods will promote IgG-specific antibody production in the susceptible individual, which may increase in concentration over time from continued dietary insult.

The gold standard in diagnosis of celiac disease is made from a biopsy of the small intestine showing abnormality, and clinical remission after a gluten-free diet as proven by a second biopsy. However, **serological tests may add considerable weight to the assessment of celiac disease** and may circumvent the need for such an invasive procedure. A rational screen for a suspect case of celiac disease may include a remarkable food antibody assay report showing multiple gluten-containing grain sensitivities in addition to elevated IgG antibodies to gliadin. Follow-up serology may include antiendomysial antibody (EMA) and/or tissue transglutaminase antibody (tTG), in addition to total serum IgA.

A unique feature of US BioTek's Food Antibody Assessment is the reporting of IgG-specific gliadin. Through US BioTek's proprietary sandwich ELISA methodology, gliadin and wheat gluten IgG- specific antibodies are assayed routinely as part of the Standard and Vegetarian Food Panels. The ELISA IgG antigliadin may serve as a sensitive screening test for jejunal biopsy in patients *with suspected celiac disease*. Once the disease has been clearly defined, the ELISA antigliadin IgG may aid follow-up in monitoring the success of diet therapy. Disappearance of IgG gliadin-specific antibodies, as exhibited by a quadrant shift over time, on the food sensitivity report, is demonstrated during a gluten-free diet.

Consumer information on gliadin and gluten-containing grain sources is included in the FOODStats Elimination Rotation Guide under Grass Family.

In addition to our IgG and IgE food-specific assays, US BioTek also offers the ALLER-Food Check test that assesses solely for IgG specific antibodies to foods, spices and herbs.



The ALLER-Food Check Personal Dietary Assessment is easy, quick and accurate, with a precision in reporting that is on par to that of liquid serum collection. All that is required is a finger stick to obtain the blood sample. A lancet is used on the finger for this procedure, and the blood sample is collected onto our micro collection strips. The strips are then air-dried and mailed to the lab. This process can easily be done in the convenience of the patient's home, or doctor's office.

Quality Assured

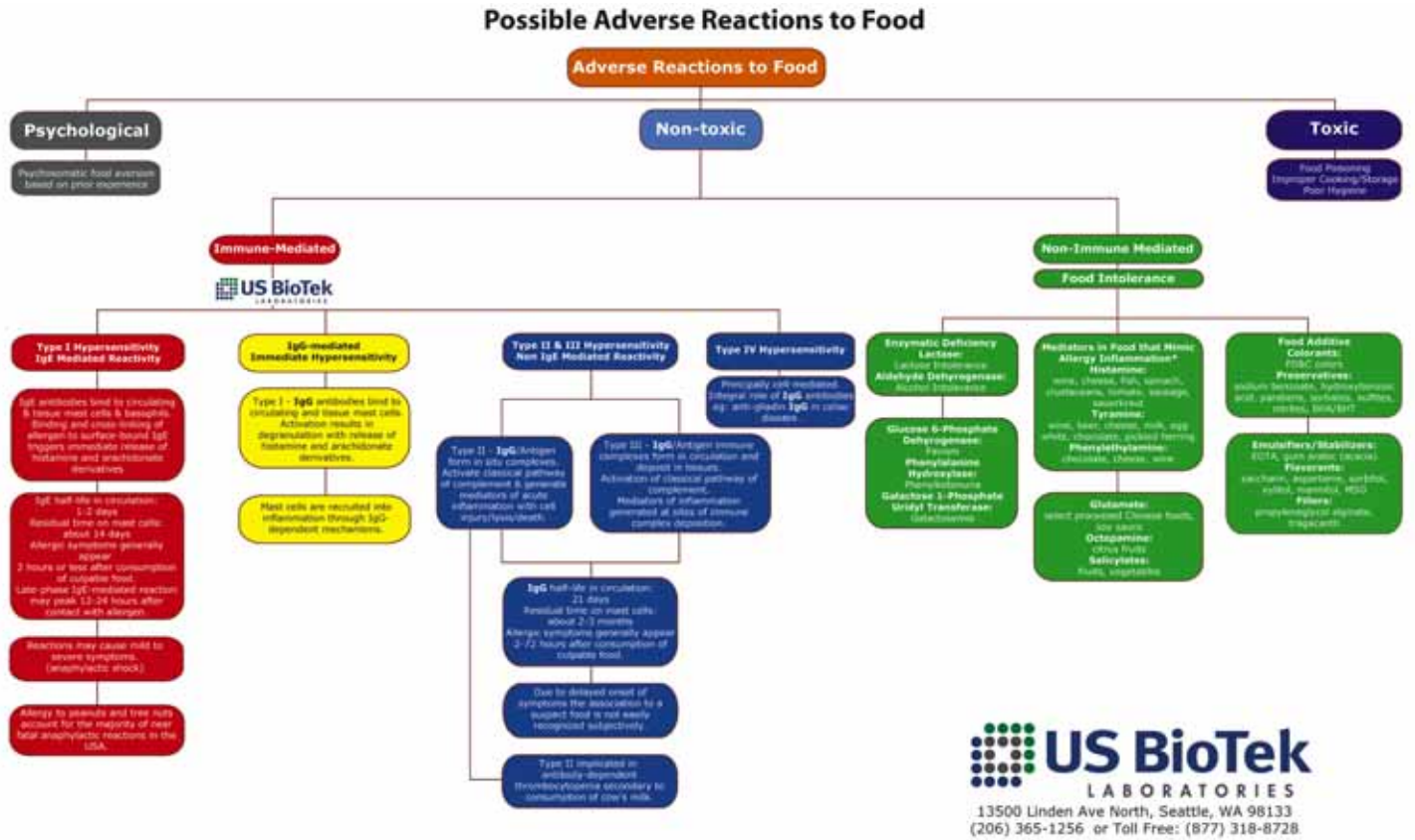
With US BioTek Food Antibody Testing, quality is assured. Every patient sample is done in complete duplicate. In other words, the results presented on the food antibody assay report have been confirmed by running each test twice to assure a reliable and accurate report.

US BioTek Laboratories subscribes to the College of American Pathologists (CAP) for periodic blinded testing, is certified and accredited under COLA (Commission of Laboratory

Accreditation), certified through CLIA (Clinical Laboratory Improvement Amendment) and is recognized as a Medical Test Site with the Washington State Department of Health.

We are proud to announce our recent Allergy and Total IgE proficiency test results for the last trimester from CAP (College of American Pathologists):

US BioTek scored 100%, on par with major allergy reagent manufacturers.



Any sign or symptom following the ingestion of a food is defined as an Adverse Reaction to Food. Adverse reactions to foods may be classified as psychological, non-toxic or toxic and encompass a wide clinical spectrum. *The greatest concern in foods may promote gut permeability with consequent sensitization to food allergens.

Any symptom following the ingestion of food is classified as an "adverse reaction to food", or ARF. Broadly speaking, ARF's are divided into psychological, non-toxic and toxic reactions, with non-toxic reactions further classified into immune and non-immune mediated. Immune-mediated reactions to foods, known as food allergies, can be further divided into IgE-mediated (Type I reactions) and non-IgE mediated reactions. The latter involving antibodies other than IgE, immune complexes and cell-mediated events. Once identified on USBioTek's Food Antibody Assay, the main aspects of dietary treatment for immune-mediated food reactions involves an elimination and rotation diet plan in addition to patient education on hidden food sources of his/her reactive foods, and pertinent food cross-reactivities.

DISCLAIMER

US BioTek has developed and determined the performance characteristics of its assays excluding the Adrenal Hormone Panel. These in-house assays have not been cleared or approved by the U.S. Food and Drug Administration ("FDA") and are considered for investigational and research purposes only. The FDA does not require these types of in-house testing to go through pre-market FDA review. Quantification of specific IgE antibodies to foods and inhalants is an FDA-accepted diagnostic procedure for the assessment of allergies. However, the assessment of human IgG antibodies specific for individual food antigens is not an FDA-approved diagnostic test. While still primarily a research and investigation tool, specific IgG quantification has been utilized in research settings to assess and investigate Type I and Type III allergies, respectively. The FDA considers IgG testing to be of an investigational or research nature and does not consider clinical data to be conclusive for the use of such testing in the diagnosis of food allergies. US BioTek makes no claims as to the diagnostic or therapeutic use of its tests or other informational materials. US BioTek is not responsible or liable for misuse or misinterpretation of the information provided, or any diagnoses or healthcare changes initiated by a patient or healthcare practitioner based on the content of US BioTek's informational materials.

Adrenal Hormone Analysis

The adrenal glands situated superior to the kidneys, coordinates the body's response to stress by releasing catecholamines and glucocorticoids into circulation. This function is key to coordinating the variety of bodily changes needed for stress adaptation. However, prolonged elevations of glucocorticoids, from chronic stress are detrimental to the health of the body. Elevated levels of glucocorticoids are well implicated in a number of pathologies including; coronary heart disease, hypertension, stroke, anxiety, depression, chronic fatigue, osteoporosis, in addition to learning and memory deficits. The latter of which are due to direct insult on the hippocampal formation of the brain; the area involved in learning and memory, and most sensitive to glucocorticoid damage. Exceptionally low levels of glucocorticoids, on the other hand, must also be considered in disease progression.

Low cortisol levels may promote sustained elevation of proinflammatory cytokines; TNF-alpha, IL-1, and IL-6, the three cardinal mediators of inflammation. Under acute stress, elevated cortisol levels act to suppress inflammatory mediator release and activity. However, under states of chronic stress,

as cortisol levels depreciate, its inhibitory activity on inflammatory cytokines, namely IL-6, is dampened. As a result levels of inflammatory cytokines go up with consequent production of acute phase proteins (C-reactive protein and fibrinogen) causing tissue inflammation and structural changes. Moreover, adrenal fatigue, with low cortisol levels, is correlated with an increase in inflammatory cytokine activity and chronic inflammatory states. This raises one's susceptibility to allergic reactions or any pathology where chronic inflammation plays an integral role; cardiovascular disease, chronic fatigue/pain syndrome, mental disease, and some cancers.

USBioTek's Adrenal Hormone Panel is a precise and non-invasive assay that measures the circadian rhythm of cortisol output X4, in relation to normal population variance. The ratio of cortisol to dehydroepiandrosterone, DHEA-S, is also expressed in comparison to normal range. Together, these values can assess the health status of an individual and screen for abnormality, which may warrant further investigation.

Urinary Metabolic Profile Organic Acid Testing

Understanding organic acid testing and its clinical use can provide the freedom you need for a well-tailored approach to the patient.



Organic acids are usually found in the urine, abnormal levels of which are functional markers for vitamin deficiencies, GI dysbiosis, toxic exposure, and neuroendocrine activity. Organic acid testing is used for customizing nutritional therapies for any disease condition; mood/behavior problems, chronic fatigue, fibromyalgia, depression, and metabolic toxicities.

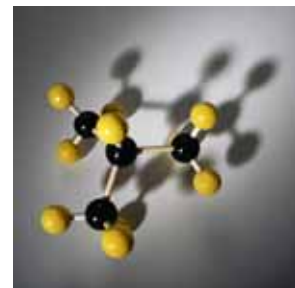
By the time your body begins to show signs of illness, changes have taken place within the cells, and many reactions required for healthy metabolism have already become compromised.

There are many factors that can contribute to this break down and symptoms of illness including; nutrient imbalances, stress, and poor lifestyle habits.

Through organic acid testing, we can visualize metabolism at the cellular level, how well the body is functioning, and how well the body is meeting its demands.

What are Organic Acids?

An organic acid is also called a carboxylic acid; an acid compound containing a carbonyl group of one carbon atom, two oxygen atoms and one hydrogen atom. Common examples of carboxylic acids are found in vinegar (acetic acid) and citrus fruits (citric acid). Examples of organic acids found in the body include the intermediate products of dietary carbohydrate, fat and protein breakdown.



Ideally, these intermediate products are metabolized fully through the central energy pathways in the mitochondria to yield cellular energy, ATP, for biosynthetic reactions. These pathways in the cell are catalyzed by enzymes, of which require vitamin or mineral cofactors. As such, an abnormal level of any one organic acid in the urine may indicate a functional deficit of the nutrients required by a key enzyme to drive utilization of that organic acid.

Other organic acids that may be found in a urine sample include intermediate metabolites of catecholamine metabolism and by-products of abnormal bacterial metabolism in the gut. Together, these markers can provide a useful indicator of cellular health. The latter, for example, is of prime clinical importance in any patient with a suspect case of gastrointestinal dysbiosis.

Among the factors that may promote such a state include; history of antibiotic use and other medications, poor lifestyle and dietary habits, compromised digestion, or an underlying disease such as celiac or Crohn's disease. Abnormal overgrowth of unfavorable microorganisms, covers a broad spectrum of signs and symptoms simply due to the release of their metabolic by-products or toxins into circulation. Elevated urinary acids from these organisms may suggest a relative need to treat an underlying state of dysbiosis, when taken into consideration with other signs and symptoms of the patient.








US BioTek's Urinary Metabolic Profile assays for 40 analytes involved in key cellular pathways including; mitochondrial energy production (glycolysis, Citric Acid Cycle, fatty acid oxidation, ketone formation), neurotransmitter metabolism, markers of vitamin deficiencies, and markers of detoxification and dysbiosis. A Quick Reference Guide is provided to the practitioner that lists key nutrients and clinical considerations of each of the analytes tested. Also, a metabolic pathway flow chart is included for patient education. In addition, each lab report is customized with a nutrient therapeutics guide that quantitates suggested nutrient interventions. A foods list is also provided for the patient for suggested natural vitamin/mineral sources.

Solutions for Serious Stability Issues of Urinary Organic Acids Analysis

Mark Newman, MS, Senior Chemist

For quite some time urinary organic acid analysis has been performed on newborns as a means of screening for Inborn Errors of Metabolism (IEM). From a functional medicine perspective, organic acid analysis is recognized as an essential test for the assessment of metabolic health in the general population. Organic acid testing offers a wealth of information for nutritional intervention in complex patient presentations assessing for:

-  Status of Mitochondrial Energy Production
-  Vitamin/Mineral Insufficiencies
-  Status of Cellular Detoxification

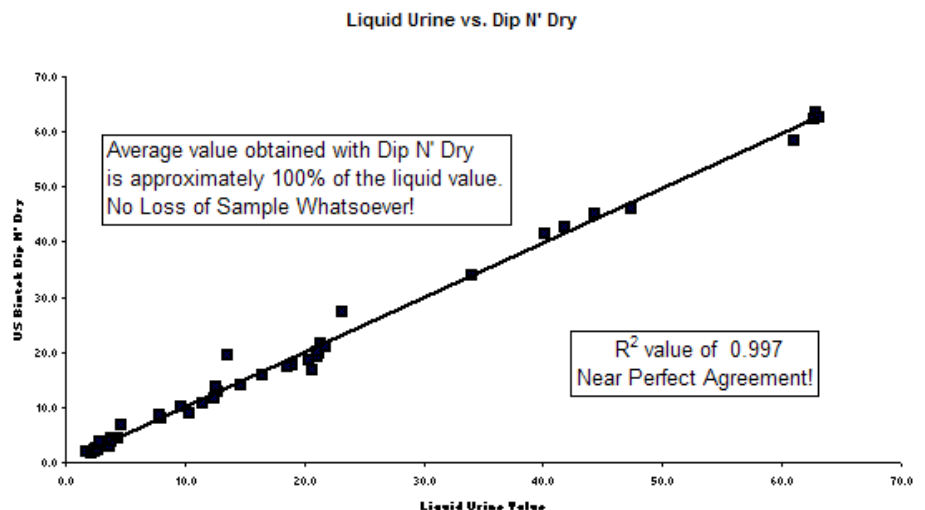
-  Neurotransmitter Metabolism
-  Bacterial Gut Dysbiosis

Using Gas Chromatography coupled to a Mass Spectrometer (GC-MS) this simple urine test allows for the measurement of a host of organic acids; by-products of cellular metabolic pathways. As such, this analysis can be an extremely cost-effective means of assessing a patient's overall cellular health. Unfortunately, there are a few major obstacles to this analysis, some of which can result in highly compromised test results, to be discussed.

Specimen Form – Liquid vs. Dry – A Methods Comparison

US BioTek has developed an innovative urine sample collection technique that is on par and exceeds sample stability compared to conventional liquid collection.


A thorough validation of US BioTek's proprietary Dip 'N Dry collection strips was performed by US BioTek. In comparing analyte values obtained from a fresh liquid urine sample to that of US BioTek's Dip 'N Dry collection method, incredible agreement was observed, as can be seen by the chart.



Organic acid analysis via GC-MS is a robust assay, obtaining results reproducibly and accurately. However, the problem lies in specimen stability prior to analysis. Some laboratories may use a preservative (typically Thymol or Ascorbic Acid) to ensure the stability of the analytes in the urine sample. Unfortunately, the preservative serves only one purpose – to

eliminate destructive effects from bacterial growth. This is a very critical issue since some organic acids, such as hippuric acid, can be destroyed through bacterial degradation. However, this does not, in any way, address instability due to chemical breakdown, which is independent of bacterial effects.

PYRUVATE & ALPHA-KETOACID INSTABILITY


 **Considerable degradation of these unstable organic acids is seen from a typical liquid urine analysis.**

 **Chemical breakdown in liquid samples can be irregular, unpredictable, and dramatic.**


US BioTek's in-house split studies have revealed considerable chemical instability of these organic acids. When spiked liquid samples were sent to two leading competitors, alarming results were obtained. Two urine samples were spiked with grossly

elevated levels of pyruvate and three alpha-ketoacids; alpha-ketoisovalerate, alpha-ketoisocaproate, and alpha-keto-beta-methylvalerate. The results obtained from these spiked samples showed a greater than 70% degradation for alpha-ketoisocaproate and complete degradation for alpha-ketoisovalerate in both of the samples! While in-house measurements confirmed the elevations of the analytes, both competing labs, measuring these markers using a liquid urine sample, failed to pick up these elevations due to sample degradation before analysis. Pyruvate and alpha-keto-beta-methylvalerate showed similar instabilities.

SUCCINATE INSTABILITY

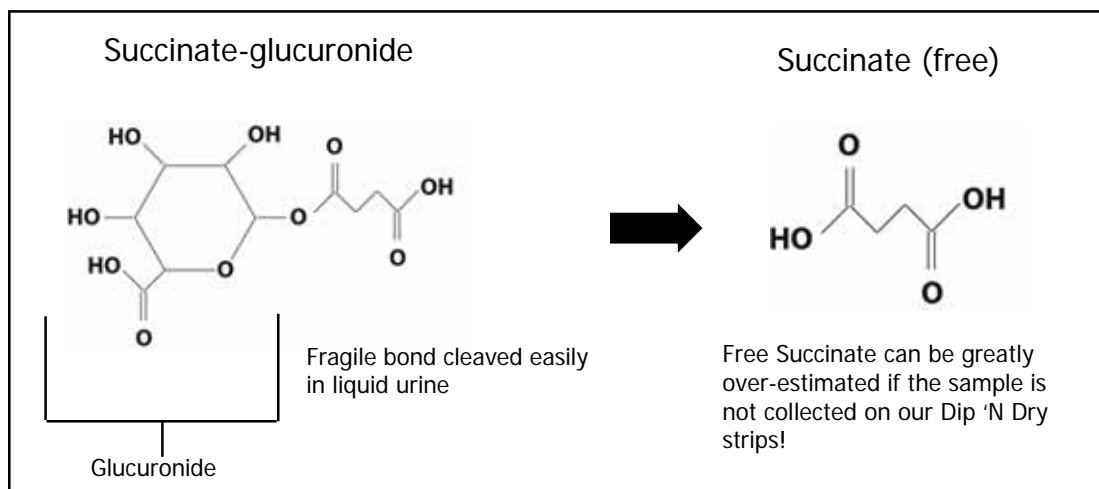
 **Approximately only 5% of succinate in urine is "free".**

 **Most succinate exists in urine as a glucuronide conjugate.**

 **The succinate-glucuronide bond is easily broken and may cause falsely elevated results.**





Like pyruvate and the alpha-ketoacids, once collected, urinary levels of succinate are be unstable. If the urine sample remains at room temperature for an extended period of time, or is refrigerated for more than a few hours, succinate values

will increase significantly. US BioTek's research has shown why. Only about 5% of succinate exists in the urine in its free form (the target of organic acid analysis). A reserve of the succinate-glucuronide conjugate is also present in the urine. Unfortunately, the succinate-glucuronide bond is incredibly fragile and may therefore result in a falsely elevated succinate value on the test report. The only way to keep this bond from breaking, in liquid urine, is to freeze the sample (and keep it completely frozen until analysis). Ironically though, the freeze/thaw cycle contributes to the problem by increasing free succinate by as much as 20-40%.



Clearly, liquid urine samples have significant chemical instability issues rendering the test results suspect and clinical use ambiguous, at best.

THE SOLUTION - US BioTek's Dip 'N Dry





-  **US BioTek's Dip 'N Dry collection strips provide accurate and reproducible results**
-  **Organic acids are stable for weeks once dried and "locked in" on the Dip 'N Dry collection strips**
-  **Succinate values remain stable and are not falsely elevated**
-  **Organic acids are not lost from evaporation or bacterial degradation**

In a typical urine collection, a patient collects a first morning urine, and the sample is either frozen or sent immediately to the chosen lab. Within hours of the sample collection, the concentration of vital acids can change due to chemical instability and degradation. If it were possible to get a 'snapshot' of the fresh sample, the results would be far more reliable. Fortunately, there now exists a means of doing just that. US BioTek's revolutionary urine collection strips, the Dip 'N Dry, are quick and easy to use. These absorbent strips are dipped in the urine, air-dried and sent via US Postal in specially designed mailing kits to ensure sample integrity.

In order for analytes in a urine samples to degrade, a medium is required in which to do so – a liquid medium. By eliminating

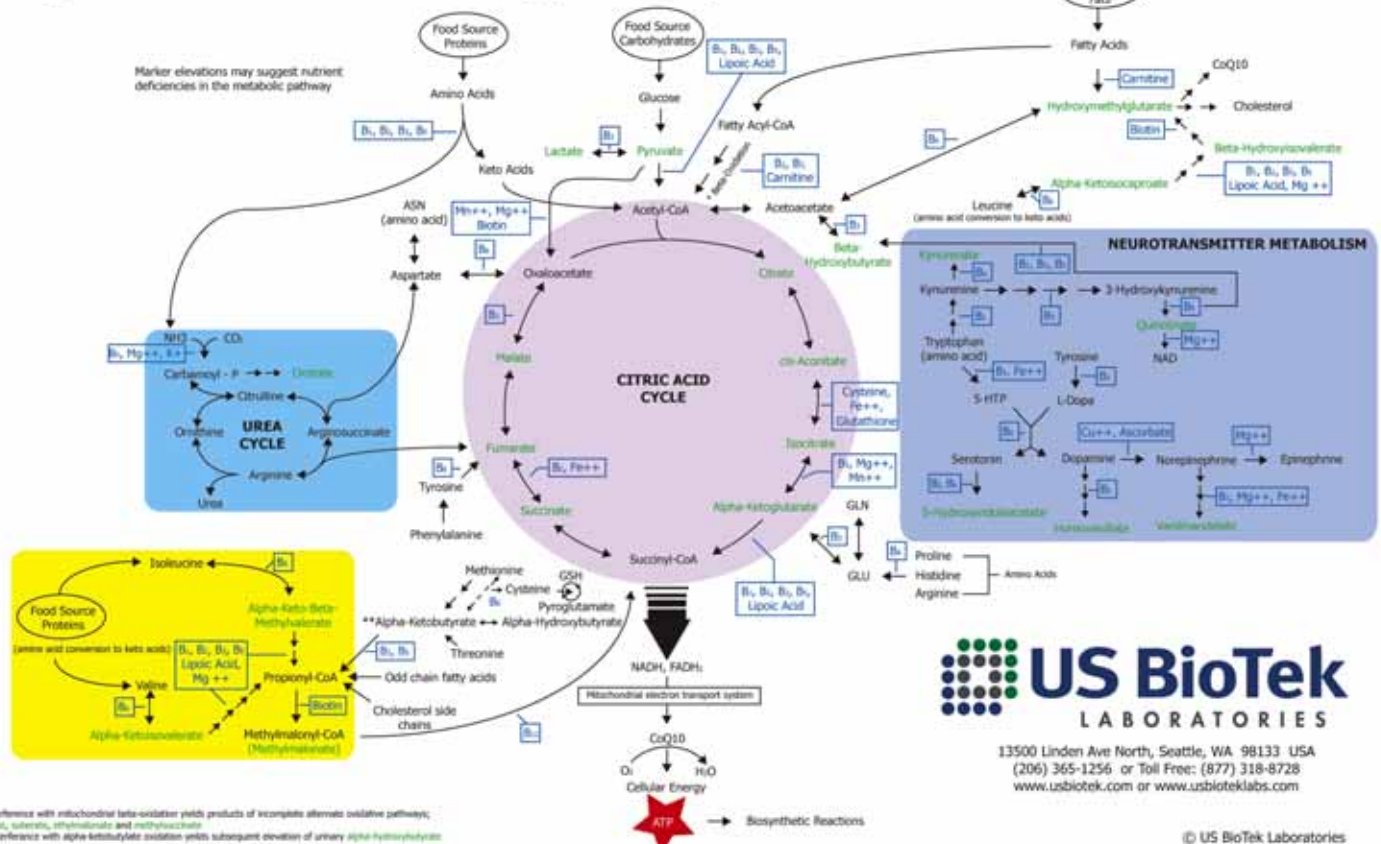
this medium through dehydration, the analytes may remain incredibly stable for weeks at a time without degradation. The successful use of urine collection strips for organic acid analysis has been well documented by various research groups, and US BioTek's research has proven stability & reproducibility on par and exceeding that of liquid urine collection. These strips ensure analyte stability of over two weeks for ALL organic acids represented on the US BioTek Urinary Metabolic Profile. Bacterial effects and chemical instability are eliminated by completely drying the urine sample onto US BioTek's innovative collection strips. This provides for a quick, easy and accurate test.

The advantages are clear:

-  Increased analyte stability with the use of the Dip 'N Dry collection strip
-  Easy processing and shipment via a standard envelope
-  No freezing of sample or express shipping required
-  A convenient, cost-effective and clinically useful test!

References available upon request.

Organic Acids In Central Energy Pathways



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NEW TEST ANNOUNCEMENT

Urinary Metabolic (Organic Acid) Profile

For the Assessment of Cellular Health

Urinary Organic Acids derived from the metabolic conversion of dietary proteins, fats, and carbohydrates, in addition to compounds of bacterial origin, provide a unique chemical profile into the patient's cellular health. Key metabolic markers of cellular physiology are quantified through GC/MS analysis to assess for compromised energy production, neurotransmitter metabolism, nutrient deficiencies, and intestinal dysbiosis. Clinically, these markers offer valuable information into possible causative factors of dysfunctional cellular physiology; affecting one's physical and mental performance, and overall health status. The profile provides data for 40 key intermediary cellular metabolites serving as markers for the categories of:

- ◆ Cellular Energy
- ◆ Cofactor Need
- ◆ Detoxification
- ◆ Dysbiosis

Sample Requirement: Collect first morning urine. Use our **Dip 'N Dry collection strip***. Send strip by regular mail to our laboratory.

* Our proprietary **Dip 'N Dry collection strip** ensures stability of analytes and provides convenient sample shipment by mail.

The Most Cost Effective

Urinary Organic Acid Profile

(40 Analytes)

Turnaround Time: 5-10 days
Free Submittal Kits

NEW USBT's Environmental Pollutants Panel to assess, via GC/MS, exposure to key environmental chemicals.

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