

Test Items

Glycolysis

A series of enzyme-catalyzed steps to convert glucose into pyruvate, in which part of the energy of glucose is released. Other simple sugars, like fructose, can be incorporated into the pathway for energy utilization.

• Pyruvate

The anaerobic breakdown product of glucose. Its further conversion to acetyl-CoA feeding the Citric Acid Cycle (CAC) requires an enzyme complex which in turn requires cofactors derived from thiamin, riboflavin, niacin, pantothenic acid and lipoic acid. Its elevation may reflect the failure of the enzyme due to insufficient functional supply of cofactors mentioned above and alcohol consumption prior to specimen collection.

• Lactate

A principal product of anaerobic glucose oxidation in skeletal muscle. It accumulates when there is a block in the final stage of energy production. Its elevation is a sign of potential coenzyme Q10 and cofactors insufficiency. Moreover, increased lactate level is a common condition that can be caused by a variety of metabolic problems, such as alcohol intake, high fat diet, dieting abuse and even uncontrolled diabetes.

Citric Acid Cycle (CAC)

The central cyclic pathway of energy release and interchanges intermediates with other catabolic and anabolic pathways to maintain body functions and repair tissues.

• Citrate, Cis-Aconitate & Isocitrate

Their elevations are markers of arginine deficiency. Low levels of them suggest the possibility of multiple reactions which utilize CAC intermediates for biosynthesis.

• Alpha-Ketoglutarate

Low level of α -Ketoglutarate can be a marker for stimulated fatty acid synthesis, increased free fatty acid and serum triacylglycerol. High level of α -KG is the marker for vitamin B1, B2, B3, B5 & lipoic acid sufficiency.

• Succinate

Elevated succinate level in urine is a marker for deficiency of CoQ10 and riboflavin. Low level of succinate may indicate the inadequate supply of leucine, isoleucine and vitamin B12.

• Fumarate & Malate

High levels of fumarate & malate act as additional markers for the CoQ10 and riboflavin deficiency.

Elevated malate can also be the result of up-regulated fatty acid synthesis. On the other hand, low fumarate and malate concentrations in urine reveal CAC insufficiency.

Cofactors' Need

Cofactors include a group of nutrients, such as vitamin B complex, lipoic acid and minerals, which are essential for proper body functions. They are not made inside your body and must be consumed in the diet.

• Hydroxymethylglutarate (HMG)

Abnormal levels of HMG can reflect inadequate synthesis and deficiency of CoQ10.

• Alpha-Ketoisovalerate, Alpha-Ketoisocaproate & Alpha-Keto-Beta-methylvalerate (α -K- β -MV)

High levels of them all together serve as marker for the deficiency of vitamin B1, B2, B3, B5 and lipoic acid.

• Beta-Hydroxyisovalerate

Level of β -Hydroxyisovalerate serves as a fast marker for the biotin sufficiency. Its elevated level marks the biotin deficiency.

- ☐ • Methylmalonyate

Level of methylmalonate serves as a marker for the vitamin B12 sufficiency. Its elevated level marks the vitamin B12 deficiency.

- ☐ • Kynurenate

Abnormal levels of kynurenate suggest vitamin B3 and B6 deficiency. It is also a well-known neuroprotective agent.

Fatty Acid Oxidation

A collective term of different pathways of fat burning for energy. In human beings, the normal major pathway to burn fat is beta-oxidation. The final product, acetyl-CoA, then enters the Citric Acid Cycle to release energy. When β -oxidation is compromised, an alternative pathway, omega-oxidation, kicks in. ω -oxidation is much less efficient than its counterpart and produces different products, suberate and adipate, which cannot enter CAC.

- ☐ • Adipate & Suberate

A product of incomplete oxidation in the ω -oxidation pathway. High level indicates the normally dominant β -oxidation and general fatty acid oxidation are compromised, probably by a range of reasons, like carnitine deficiency.

- ☐ • Methylsuccinate & Ethylmalonate

A product of short- and medium- chain fatty acid oxidation that stack up when beta-oxidation is compromised. High level indicates an inadequate utilization of fatty acids as an energy source due to failure of any steps of the beta-oxidation cascade or ketone body pathway.

Ketone Bodies

The fuel molecules produced by the fatty acid metabolism for the use of our central nervous system when the glucose is not enough in situations like low carbohydrate diet or fasting. It will also build up in someone with insulin resistance.

- ☐ • Alpha-Hydroxybutyrate

Formed in the glutathione production under the apart from a ketone body. Elevated level may reflect the heavy oxidative stress stimulating the need and hence production of glutathione.

- ☐ • Beta-Hydroxybutyrate

The primary ketone bodies. Its elevation may indicate inefficient utilization of glucose and even insulin resistance, a risk factor of diabetes.

Neurotransmitter metabolism

A urine sample can also be used to gauge neurotransmitter levels. Metabolites of neurotransmitters are present in the urine. Research confirms that levels of urinary metabolites mirror levels of central nervous system production. Organic acid testing can be used to evaluate serotonin, epinephrine, norepinephrine, dopamine and NMDA antagonists and agonists.

- ☐ • 5 Hydroxyindoleacetate (5-HIA)

Catabolic breakdown of serotonin leads to excretion of 5-hydroxyindoleacetate.

Serotonin is required for control for gut mobility as it activates smooth muscle activity. Inadequate production of serotonin leads to constipation. Low levels of serotonin have also been associated with

depression, fatigue, insomnia and behavioral problem. A very high 5-HIA result calls attention to potential deficiency of tryptophan.

☐● Homovanillate (HVA)

The main metabolite of dopamine that appears in urine, often elevated due to stress increasing catecholamine output. Low urinary levels of VMA and HVA have been associated with low CNS levels of these neurotransmitters. Symptoms associated with this are depression, sleep disturbances, anxiety and fatigue. Elevated levels of VMA and HVA signals an increased rate of synthesis and degradation in normal tissue or abnormal production by tumor tissue.

☐● Quinolate (QUIN)

QUIN production is a link between the immune system and the brain, thus there is reason to suspect that QUIN elevation may indicate both inflammatory bowel conditions and neuronal degeneration. Its production may be a key feature in the progression of events that lead to chronic fatigue syndrome.

☐● Vanilmandelate (VMA)

The main metabolite of the catecholamines, epinephrine, and norepinephrine, often elevated due to stress increasing catecholamine output. Low urinary levels of VMA and HVA have been associated with low CNS levels of these neurotransmitters. Symptoms associated with this are depression, sleep disturbances, anxiety and fatigue. Elevated levels of VMA and HVA signals an increased rate of synthesis and degradation in normal tissue or abnormal production by tumor tissue.

Bacterial Metabolism

Appropriate balance of flora is associated with a healthy digestive process, by measuring compounds in the urine made by microbes judgment can be made as to how much the local growth of bacteria in the gut is causing systemic effect. Toxic by-products that are absorbed can only be measured in urine. Additionally, many species that cause dysbiosis are anaerobic. Urine specimen is preferred over stool specimen as the bacteria only grow in oxygen free environment. The exposure in oxygen environment results inability to culture them for analysis.

☐● 2-hydroxyphenylacetate (HPA)

Elevated in a wide variety of conditions involving direct intestinal pathology or digestive organ failure, which are obvious candidates for dysbiosis.

☐● 3-indoleacetate

The product of tryptophan metabolism, relates to the presence and the overgrowth of a typical putrefactive bacterial genus. It has been blamed for the cause of magnesium deficiency.

☐● Para-hydroxyphenylacetate

Not a product of normal human metabolism, but is produced by bacteria and protozoa that can populate the gut. It has been found useful in detecting small bowel disease associated with *Giardia lamblia* infestation, and other disease of the small intestine associated with anaerobic bacterial overgrowth. Use of antibiotics can encourage the growth of protozoa and anaerobic bacteria that then produce greater amounts of this.

☐● Para-Hydroxybenzoate

This compound is not a product of normal human metabolism, but is produced by bacteria and protozoa that can populate the gut. Strains of *Escherichia coli* can produce para-hydroxybenzoate from glucose. Use of antibiotics that act primarily against aerobic bacteria can encourage the growth of protozoa and anaerobic bacteria that then produce greater amounts of this compound.

☐● Tricarballic acid

Produced by a strain of aerobic bacteria that quickly repopulates in the gut of germ-free animals. It is produced by aerobic bacteria, and considered a fermentative marker.

Detoxification

Byproducts of detoxification are measure in the urine as part of the organic acid profile. This gives clinical evidence of type of exposure as well as how well the liver is handling the exposure.

☐● Benzoate

Bacterial deamination of the amino acid phenylalanine produces benzoate, which is conjugated with glycine in the liver to form hippurate. Benzoate is a common food additive. Whether the source is dietary intake or jejunal bacterial metabolism, benzoate is usually converted to hippurate by conjugation with glycine in the liver. Glycine and pantothenic acid are the limiting factors in this process. Elevated benzoate is a marker of inadequate levels of these nutrients.

☐● Hippurate

Bacterial deamination of the amino acid phenylalanine produces benzoate, which is conjugated with glycine in the liver to form hippurate. Benzoic acid is also a common food component used as preservative in packaged foods such as pickles and luncheon meats, and occurred naturally in cranberries. This should be taken into account when interpreting elevated hippurate levels in urine. Whether the source is dietary intake or jejunal bacterial metabolism, benzoate is usually converted to hippurate by conjugation with glycine in the liver.

☐● Orotate

Increased orotate production is a sensitive indicator of arginine deficiency, associated with ammonia toxicity. Orotate requires magnesium for its metabolism. While a normal level in a urinary organic acid panel may not necessarily indicate magnesium sufficiency, high levels should alert one to a significant possibility of intracellular magnesium insufficiency.

☐● Para-hydroxyphenyllacetate (HPLA)

A metabolite of tyrosine. Elevated HPLA is associated with tumor growth and leukemia. Elevation also results in a dramatic decrease of ascorbic acid (vitamin C) concentration in the liver, adrenal glands, and blood. Due to its pro-oxidative character, high levels are associated with carcinogenesis.

☐● Pyroglutamate

A metabolite of glutathione. Glutathione serves as an antioxidant and also is conjugated to toxic compounds in the liver. Deficiency of glutathione can lead to elevation. Small amounts of pyroglutamate are always present in overnight urine as it is an intermediate in a cycle used in the active transport of amino acids in renal tubules. This process utilizes glutathione as a carrier.