INTEGRATIVE MEDICINE

URINE, SPOT

CITRIC ACID CYCLE Metabolites.

Citric Acid Cycle Metabolism

Citric Acid Cycle Metabolites serve both anabolic and catabolic functions. They are the final common pathway of energy release from catabolism of fats, proteins, and carbohydrates. They are the source of basic structural molecules that are drawn away from the cycle to support organ maintenance and neurological function—anabolic processes. Crossroads of food conversion and utilization. Spillage of Citric Acid Cycle intermediates into the urine may indicate mitochondrial inefficiencies in energy production. A block in any step may cause a build up of compounds that precede this step. Amino acids supply carbon skeletons for maintaining mitochondrial concentrations.

Citrate, cis-Aconitate and Isocitrate are the key organic acids in this biochemical pathway and are responsible for aerobic energy production

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Result</th>
<th>Range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyruvic Acid</td>
<td>5.78</td>
<td>0.60 - 6.61</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>Lactic Acid</td>
<td>2.70</td>
<td>0.00 - 1.58</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>Citric Acid</td>
<td>234.40</td>
<td>37.50 - 417.80</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>cis-Aconitic Acid</td>
<td>60.80</td>
<td>12.00 - 42.90</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>Isocitric Acid</td>
<td>34.30</td>
<td>7.80 - 45.90</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>a-Ketoglutaric Acid</td>
<td>36.02</td>
<td>10.40 - 168.30</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>Succinic Acid</td>
<td>2.33</td>
<td>1.80 - 13.30</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>Fumaric Acid</td>
<td>0.94</td>
<td>0.18 - 1.20</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>Malic Acid</td>
<td>1.07</td>
<td>0.30 - 1.45</td>
<td>ug/mgCR</td>
</tr>
</tbody>
</table>

KETONE/FATTY ACID Metabolites

Ketone/Fatty Acid Metabolism

Fatty Acid Metabolism is needed for energy production.

Key Supplements:
- Carnitine: a metabolic cofactor synthesized from L-Lysine and L-methionine (as SAMe)
- Conditionally essential nutrient
- Fatty acid transport carrier from cytosol into mitochondria for beta-oxidation
- Vitamin B2 (riboflavin): Aids oxidative metabolism of fats within the mitochondria

Key Organic Acids:
- Adipate (Adipic Acid) and Suberate (Suberic Acid)
  - Functional markers of carnitine insufficiency
  - Six and eight carbon dicarboxylic acids, respectively
  - Products of peroxisomal fatty acid oxidation
  - Increased when carnitine insufficiency limits long chain fatty acid entry into mitochondria

<table>
<thead>
<tr>
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<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adipic Acid</td>
<td>1.82</td>
<td>0.46 - 3.01</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>Suberic Acid</td>
<td>3.25</td>
<td>0.34 - 2.34</td>
<td>ug/mgCR</td>
</tr>
<tr>
<td>Ethylmalonic Acid</td>
<td>1.99</td>
<td>1.09 - 4.22</td>
<td>ug/mgCR</td>
</tr>
</tbody>
</table>

(*) Result outside normal reference range  (H) Result is above upper limit of reference range
Methyl-Succinic Acid 2.38 ug/mgCR 0.62 - 2.19
a-OH-Butyrate 0.46 ug/mgCR 0.16 - 2.76
b-OH-Butyrate 0.17 ug/mgCR 0.00 - 1.90

Cit Acid Cycle Metabs Comment
Pyruvate is the anaerobic breakdown product of glucose. Its further conversion to acetyl-CoA requires the pyruvate dehydrogenase enzyme complex. Pyruvate dehydrogenase requires cofactors derived from thiamin, riboflavin, niacin, lipoic acid, and pantothenic acid for optimal function.

Levels of pyruvate in the tissues are further controlled by the biotin-containing protein, pyruvate carboxylase, which controls the first step in the reformation of glucose from pyruvate. Multiple forms of pyruvate carboxylase deficiency, some of which are biotin responsive, have been reported.

Lactate Elevated:
This metabolic precursor to the Citric Acid Cycle, may indicate a block in the production of energy. Can also be indicative of an on-going infectious state, use of some recreational and/or pharmaceutical drugs, alcohol over consumption, poor blood sugar control (especially with diabetics), and a number of inborn errors of metabolism.

SUPPLEMENTATION RECOMMENDATIONS:
CoQ10, thiamin (Vit B1), riboflavin, niacin, lipoic acid, and pantothenic acid.

cis-Aconitate Elevated:
An intermediate of the citric acid cycle, an elevated level of this organic acid may be an indication of poor supplies or metabolism of amino acids. A clinical sign is fatigue.

If elevated with orotate, isocitrate and citrate, suspect hyperammonia.

SUPPLEMENTATION RECOMMENDATIONS:
alpha Lipoic Acid, Vitamin B Complex, Cysteine, Iron, Magnesium, Manganese.

Malate Comment:
A high level of this organic acid may be indicative of a need for certain nutrients such as niacin (B3) and Coenzyme Q10.

A low level of this organic acid may be indicative of the need for aspartic acid.

Ketone/FA Metabolites Comment
Suberate Elevated:
Adipate and suberate are short chain dicarboxylic fatty acids. Low levels of carnitine cause inadequate transfer of fatty acids into the cell's energy production processes in the mitochondria, producing excess amounts of adipate, suberate, and ethylmalonate. A deficiency of B2 (riboflavin) and to a lesser extent B5 (pantothenic acid) may also be found with elevations of Suberate.

SUPPLEMENTATION RECOMMENDATIONS:
B complex (B2, B5), CoQ10, L-Carnitine (may be contraindicated in patients on thyroid medications), L-Lysine (precursor to L-Carnitine), Other nutrients involved in Carnitine synthesis (Mg, SAMe, Vit B6, ascorbic acid, iron, niacin.

Creatinine, Urine Spot. 10.2 mmol/L 5.0 - 13.0

Tests ordered: CACM, KFAM, CACMF, KFAMF
(*) Result outside normal reference range (H) Result is above upper limit of reference range