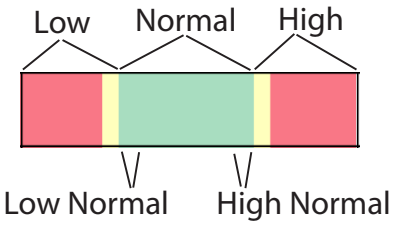
Nutreval Interpretation Guide

(a compilation of interpretations done by Rich Van Konynenburg)

The point of this test is to see what deficiencies, toxins or dysbiosis may be blocking your metabolism, in addition to seeing if you have a partial methylation block. Then to supplement, treat or do further testing based on this information.

General Notes

High-normal or low-normal results are just as significant as out-of-range high and low results since they show a tendency in the high or low direction.



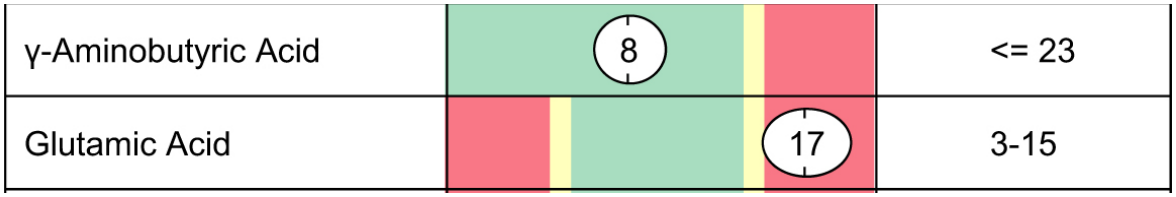
The various metabolites flow into each other in a cycle. We will often be comparing the relative values with each other to see if there are blocks in the cycle. We don't refer to the actual numbers because the metabolites all have different reference ranges. So seeing that one metabolite is high, while the next one is high-normal (a relatively lower value) and vice versa, is good enough.

If there is a drop in relative values from one metabolite to the next, (for example, the first metabolite is mid-normal, but the next one is low-normal), this indicates there is a block in the flow of the cycle. The flow can be inhibited either by vitamin deficiencies or by heavy metals. We can tell what to supplement or detox out based on this.

A drop in flow from Pyruvic Acid to Citric Acid.

As you go through your test results, you can use the worksheet at the end of this document to keep track of which deficiencies and toxins are present.

When two metabolites are compared in a ratio, it means is the first one higher or lower than the second one, For example, if glutamic acid is high, but γ-Aminobutyric acid is normal, then the ratio of glutamic acid to γ-Aminobutyric is high. If glutamic acid is low, but γ-Aminobutyric is normal, then the ratio is low.



The ratio of Glutamic Acid to γ-Aminobutyric Acid is high.

Greek letters are often used in the names of metabolites.
α = alpha
β = beta
γ = gamma

<dl = below detection limit

The European and USA versions are slightly different. I have indicated where this occurs.

1) Nutreval Results Overview
Skip over this section.

2) Interpretation At A Glance
Skip over this section.

3) Metabolic Analysis Markers

a) **Malabsorption and Dysbiosis Markers** – if any of the markers in this section are elevated, you have problems with your digestion and should get a comprehensive stool test done to see more specifically is going on and to help with selecting a treatment.

i) Malabsorption Markers - any elevated markers in this section means you have intestinal malabsorption

ii) Bacterial Dysbiosis Markers – any elevated markers in this section means you have bacterial dysbiosis

iii) Yeast/Fungal Dysbiosis Markers – any elevated markers in this section means you have yeast/fungal dysbiosis

b) Cellular Energy and Mitochondrial Metabolites

Refer to the Krebs Cycle At A Glance diagram to help with understanding how the metabolites flow through the cycle. In general, fats, carbohydrates and proteins flow into the citric acid cycle where energy is produced.

Note: Energy Metabolism = Citric Acid Cycle = Krebs Cycle. These all mean the same thing.

i) **Carbohydrate Metabolism** (Europe) or **Glycolysis Metabolism** (USA)

(1) If there is a drop in relative values from pyruvic acid to citric acid, the flow from the Carbohydrate Metabolism to the Energy Metabolism is inhibited, making it difficult to use carbohydrates as fuel in the mitochondria. This could be due to deficiencies of lipoic acid, B1, B2, B3 or magnesium. It could also be due to high mercury.

(2) A low value in lactic acid (and possibly also pyruvic acid?) indicates that this pathway is not running very fast. A low carb diet could be one possibility.

(3) Lactic acid – if this marker is high and citric acid is low, this suggests a deficiency in one of more B vitamins or lipoic acid, or mercury may be interfering with the flow of pyruvic acid into the Krebs cycle.

(4) β-OH-Butyric Acid (BHBA) - if this value is elevated, it means your body has moved into partial ketosis. This can be due to a block in the Carbohydrate Metabolism and/or a low carb diet.

ii) **Energy Metabolism** (Europe) or **Citric Acid Cycle Metabolites** (USA)

(1) A drop between citric acid and the next two Krebs metabolites is consistent with glutathione depletion. This also indicates the first part of the Krebs cycle is running slowly.

(2) α-ketoglutaric acid (AKG)– if this is high relative to the metabolites in the Krebs cycle before and after it, this suggests that it is being fed by glutamate, and that the flow from AKG to succinic acid is partially blocked. The latter could again be due to low magnesium or B vitamins, or to mercury toxicity. Check to see if glutamate

(NonEssential Protein Amino Acids/Glutamic Acid) is also high to verify.

(3) Succinic Acid – A low value indicates that you aren't burning amino acids as fuel at a normal rate. This is likely due to low B2, low B6, and/or low biotin.

(4) Low succinic and malic acids suggest low Coenzyme Q-10. This would be consistent with a partial methylation cycle block, because methylation is required to synthesize Co Q-10.

(5) If succinic acid and malic acid are low and the branched-chain amino acids (leucine, isoleucine and valine, Amino Acids/Nutritionally Essential Amino Acids) are high, the problem seems to be that they are not being fed into the Krebs cycle. The explanation would be a functional deficiency in B12, if methylmalonic acid is also high. The low succinic and malic acids will also contribute to low ATP production by the mitochondria, contributing to the fatigue.

iii) **Fatty Acid Metabolism** (Europe) or **Ketone and Fatty Acid Metabolites** (USA)

(1) Elevated adipic and suberic acid indicate that fatty acids are being mobilized, but deficiency in B2 or carnitine or both are impeding their use for fuel by the mitochondria, so they are being pushed into omega oxidation. Low carnitine would be consistent with a partial methylation cycle block, because carnitine requires methylation for its synthesis.

(2) β-OH-Butyric Acid (BHBA) - if this value is elevated, it means your body has moved into partial ketosis. This can be due to a block in the Carbohydrate Metabolism and/or a low carb diet.

iv) Neurotransmitter Metabolites

(1) If your neurotransmitter metabolites are low, it is probably due to low B2 or low B6 or both. Your tetrahydrobiopterin (BH4) and THF are probably low as well.

(2) If vanilmandelic acid is low relative to homovanillic acid, it suggests low copper or low vitamin C or both. Check the Elemental Markers (RBCs) page for copper in the red blood cells to verify if copper is actually low. Low vitamin C would be consistent with low glutathione, because glutathione recycles vitamin C.

(3) 5-OHindoleacetic acid (5-hydroxy indolacetic acid) (5-HIAA)– this is a breakdown product from tryptophan. A high value of 5-HIAA along with a low level tryptophan (Nutritionally Essential Amino Acids section) suggests low serotonin, melatonin, and sleep issues.

(4) Kyurenic Acid - an elevated marker suggests low B2.

v) Vitamin markers

(1) If the second, third and fourth vitamin markers are high, this indicates low B-complex vitamins or low lipoic acid, or both.

(2) Formiminoglutamic Acid (FIGlu) – If this is elevated, it indicates low tetrahydrofolate (THF). The low THF indicates that there is a partial block in methionine synthase, which links the folate metabolism with the methylation cycle, and that your folates have become depleted. FIGlu can be masked by low histidine, B2 and maybe B6. Check this against sarcosine (Amino Acids / Glycine/Serine Metabolites). A high value for sarcosine would be consistent with low THF. Elevated FIGlu is consistent with glutathione depletion.

(3) Methylmalonic Acid (MMA) – If this is elevated, it indicates a functional B12 deficiency. B complex deficiencies (B2, maybe B6 and biotin) can cause masking, making it look lower than it would be without them. Elevated MMA is consistent with glutathione depletion.

(4) If you have been treating for a partial methylation block, and FIGglu and MMA are still elevated, your B12 dosage is probably not high enough to overcome being hijacked by toxins.

(5) 2-hydroxyphenylacetic acid – if this is elevated it would likely be explained by bacterial dysbiosis, perhaps involving Proteus bacteria. A comprehensive stool test would be needed to identify the dysbiotic bacteria .

(6) α-ketoadipic acid (AKAA) – if this marker is high, it suggests a B6 deficiency.

(7) Glutaric Acid – An elevated marker could be caused by low vitamin B2.

(8) 3-hydroxyisovaleric acid – if this marker is high, it indicates low biotin.

(9) Orotic Acid - low orotic acid in the presence of high ammonia (Amino Acids / Intermediary Metabolites / Urea Cycle Markers) indicates magnesium deficiency.

(10) Pyroglutamic acid – A low marker indicates glutathione depletion in the kidneys and/or intestinal cells, which would be consistent with a partial methylation cycle block and with vitamin C deficiency.

vi) **Toxin and Detoxification Markers** (Europe)

(1) α-ketophenylacetic acid – if this marker is high, it indicate that you have been exposed to styrene (as from polystyrene cups, for example), and your detox system is not working well. The USA version does not include this marker.

(2) α-hyroxyisobutyric acid – if this marker is high it indicates that you have been exposed to MTBE (from gasoline fumes), and your detox system is not working well. The USA version does not include this marker.

(3) Orotic Acid - low orotic acid in the presence of high ammonia (Amino Acids / Intermediary Metabolites / Urea Cycle Markers) indicates magnesium deficiency.

(4) Pyroglutamic acid – A low marker indicates glutathione depletion in the kidneys and/or intestinal cells, which would be consistent with a partial methylation cycle block and with vitamin C deficiency.

ii) **Creatinine Concentration** - A low-normal value would be consistent with a partial methylation cycle block. since methylation is needed to make creatine, its precursor.

4) Amino Acids

a) Nutritionally Essential Amino Acids

i) If these are mostly low, but you have a high protein diet, and the rate of burning of amino acids is limited by B-vitamin deficiencies, this is probably due to intestinal maldigestion of protein or malabsorption of amino acids.

ii) If several of these are high, this is probably partly due succinic and malic acid not being fed into the Krebs cycle, partly due to low B6, and partly due to a slow rate of conversion of amino acids into neurotransmitters,

which could be due to low tetrahydrobiopterin (BH4), resulting from a methylation cycle/folate cycle block, or due to low iron.

iii) Histidine – a low marker is likely due to folate deficiency. This would be consistent with a partial methylation cycle block

iv) Lysine - a low marker suggests that carnitine may be low, as lysine is it's precursor.

v) Methionine – a low value is consistent with a partial methylation block.

vi) A high ratio of phenylalanine to tyrosine (Nonessential Protein Amino Acids) suggests low tetrahydrobiopterin (BH4), which would be consistent with low intracellular folates. This suggests a partial methylation block.

vii) Tryptophan – a precursor to serotonin. A low value suggests low serotonin and melatonin, causing sleep issues. A high value of tryptophan along with a low value of 5-HIAA (Neurotransmitter Metabolites section) indicates a neurotransmitter problem.

b) Dietary Peptide Related Markers (USA)

i) Elevated markers suggest that a high-meat diet.

ii) β-alanine – if this marker is high, it could be causing high wasting of taurine in the urine, since they compete for the same reabsorption transporters in the kidneys. High taurine levels (Nutritionally Essential Amino Acids) would verify this.

c) Nonessential Protein Amino Acids

i) If these are mostly low, it can be due to low essential amino acids and B vitamin deficiencies.

ii) If aspartic acid, citrulline, and to a lesser extent, arginine (Nutritionally Essential Amino Acids section), are on the low side, these results would be consistent with an elevated rate of consumption of amino acids for fuel. They are all involved in the urea cycle, which converts ammonia to urea. Ammonia is generated when amino acids are burned as fuel.

iii) Glutamic acid - if this is high, and glutamine/glutamate is low (Amino Acids/Markers for Urine Representativenes), it can be due a manganese deficiency. Check the Elemental Markers (RBCs) page for manganese in the red blood cells to verify.

Note: Glutamic Acid = Glutamate
γ-aminobutyric acid = GABA.

(1) If ratio of glutamic acid to γ-aminobutyric acid is high, this will make you feel anxious and wired. (Glutamic acid is stimulating; γ-aminobutyric acid is calming). The low γ-aminobutyric acid relative to glutamic acid would be consistent with excitoxicity, which would contribute to sleep problems. It can also cause anxiety, a "wired" feeling, and hypersensitivity of the senses. The low γ-aminobutyric acid could be due to low B6 functional availability as P5P, owing to low B2.

iv) Proline – if this is high, it suggests that your body has difficulty making collagen. Low vitamin C can cause that.

v) Tyrosine - Low tyrosine relative to phenylalanine suggests that tetrahydrobiopterin (BH4) might be low, which would be consistent with folate depletion.

d) **Intermediary Metabolites** (The European version breaks this section into several subsections. In the USA version, it's one big section.)

e) **B Vitamin Markers** (Europe)

i) α-Aminoadipic Acid – if this is high, it's likely due to a B6 deficiency. B6 is needed by the transaminase enzymes, which convert one amino acid to another, and thus facililitate feeding them into the Krebs cycle.

ii) α-Amino-N-butyric Acid (ANBA) – if this is low it is likely due to low glutamine (Non Essential Protein Amino Acids). An elevated marker indicates alcoholism.

iii) β-aminoisobutyric acid – if this is elevated, it suggests that thymine is being broken down at a higher than normal rate. Thymine is a component of DNA, so this suggests rapid cell turnover or excess production of thymine from uracil.

iv) Cystathionine – if this is low, it is likely due to low B2 and maybe also B6. This will limit flow into the transsulfuration pathway, which could limit glutathione synthesis, but see below. The low cystathionine would be consistent with low methionine and could also be caused by low magnesium or low B6 availability as P5P, the latter of which could be caused by low B2.

v) 3-Methylhistidine – an elevated marker means you're burning protein (amino acids) at a higher rate than average. This rate can be limited by deficiencies in B2 and maybe B6. If these deficiencies show up elsewhere on this test, then even though protein is burning at a rate, the Krebs cycle is operating at a lower rate than normal. This is consistent with fatigue and low body temperature.

f) **Urea Cycle Markers** (Europe)

i) Ammonia – if this marker is high, it suggests that you're burning protein for fuel at a higher than normal rate. This can be due to the problems in feeding both carbs and fats into the Krebs cycle.

ii) Urea - if this marker is high, it suggests that you're burning protein for fuel at a higher than normal rate. This can be due to the problems in feeding both carbs and fats into the Krebs cycle.

iii) Urea – if this is low, together with low orotic acid (Toxin and Detoxification Markers (Europe), Vitamin Markers (USA)), it suggests your cells are not burning protein for fuel at a very high rate. This is consistent with elevated branched-chain amino acids (leucine, isoleucine and valine, Amino Acids/Nutritionally Essential Amino Acids). It also means that you do not have gut bacteria that are producing a lot of ammonia. Check the bacterial dysbiosis markers to see if they're consistent.

g) **Glycine/Serine Metabolites** (Europe)

i) Glycine - if this is low, it will limit the production of glutathione.

ii) If the ethanoloamine to phosphoethanolamine ratio is low it suggests that your magnesium status is good, which is unusual in ME/CFS.

iii) If phosphoethanolamine is low relative to ethanolamine suggests low intracellular magnesium. This is consistent with glutathione depletion.

iv) Sarcosine – if this is elevated, it's consistent with low THF (folates), and a partial methylation cycle block.

h) Dietary Peptide Related Markers

i) 1-methylhistidine – if this is high it suggests that you eat a lot of poultry and/or fish, and perhaps that you have intestinal permeability (leaky gut), especially if you also have food sensitivities.

5) Essential and Metabolic Fatty Acids Markers (RBCs)
Refer to the Essential Fatty Acid Metabolism diagram to see how the conversions of essential fatty acids flow.

a) Omega 3 Fatty Acids

i) Normal to high markers, especially Eicosapentaenoic (EPA) and Docosapentaenoic (DHA), suggest you're consuming a lot of fish or fish oil.

ii) Low markers suggest you're consuming vegetable oil and not much flax or fish oil.

b) Omega 9 Fatty Acids

i) If the markers are low, it indicates you aren't getting much olive oil. High markers suggest high consumption of olive oil.

c) Saturated Fatty Acids

i) If some of these markers are high (such as stearic acid) it indicates you eat a high meat diet.

ii) Arachidic acid – a low marker suggests you don't eat many peanuts.

iii) Tricosanoic acid – if this is high, it's consistent with a biotin deficiency and/or a functional B12 deficiency.

d) Omega 6 Fatty Acids

i) A drop from γ-Linolenic Acid (GLA) to Dihomo-γ-Linolenic Acid (DGLA) means that the elongase reaction is not working well. This is likely because of deficiencies in one or more of the B-complex vitamins, including biotin. Note: The Essential Fatty Acid Metabolism diagram says (B3, B6, B5, Biotin and vit. C).

ii) A drop from Arachidonic Acid (AA) to Docosatetraenoic Acid (DTA) means that the elongase reaction is not working well. This is likely because of deficiencies in one or more of the B-complex vitamins, including biotin. Note: The Essential Fatty Acid Metabolism diagram Diagram says (B3, B6, B5, Biotin and vit. C).

iii) Arachidonic Acid (AA) – if this is elevated, it can cause proinflammatory prostaglandins to be produced.

b) **Monosaturated Fats** (Europe) or **Trans and Omega 7 Fatty Acids** (USA)

i) Low palmitoleic acid suggest you're not converting a lot of carbs to stored fats. If you're also not burning them, this suggests a low carb diet. See the lactic acid and BHBA markers in the Carbohydrate Metabolism (Europe) or Glycolysis Metabolism (USA) section to verify.

6) Oxidative Stress Markers

(1) Glutathione (whole blood) – if this marker is low, it indicates low glutathione. However, if it measures high, it doesn't necessarily mean that glutathione is high in the tissues. This is because it only measures the amount of glutathione in the blood, which doesn't reflect the level of reduced glutathione in the tissue cells. In this case, you should refer to the other indicators in this test to see if glutathione is low.

7) Elemental Markers (RBCs)

a) Nutrient Elements - If any of these markers are in the low range, you may be deficient.

8) Toxic Elements

a) If lead is somewhat elevated (at the high end of the yellow range) or elevated (red range), it suggests that you have had some exposure to lead (perhaps from old paint flaking off walls). If this exposure has gone on for a long time, you could have considerable lead in your bones, and if so, it takes years to get it out, because you have to wait for the bone to turn over. Getting glutathione back up should help, as it conjugates lead and carries it out of the body. Lead could also be due to solder in water pipes.

b) Mercury – if this is elevated, it suggests an ongoing exposure as mercury only stays in the blood for few weeks. This can be due to mecurcy amalgams or fish consumption.

c) Tin – if this is elevated along with mercury, it suggests an ongoing exposure from mercury amalgams. If elevated by itself, it could possibly be from corrosion of solder in water pipes.

d) Antimony – if this is elevated, it could be coming from drinking water from plastic bottles, or from solder in water pipes.

9) **Nutrient Elements** – if any of these markers are in the low range, you may be deficient.

a) If Copper, zinc, and manganese are low, all three of these are needed by superoxide dismutase enzymes, so the low levels could be contributing to oxidative stress, which would also be consistent with glutathione depletion, elevated lipid peroxides, perhaps low vitamin C, and low conzyme Q-10.
b) If zinc and B6 are low, manganese is somewhat low, and biotin could be low, I think it would be worthwhile to consider KPU. Dr. Klinghardt has reported finding a lot of this, and it would account for these deficiencies as well as inhibiting the methylation cycle. The Health Diagnostics and Research Institute in New Jersey offers a KPU test. I would recommend following Dr. Klinghardt's advice about sample collection and handling.

c) Selenium – this nutrient is important in utilizing glutathione to combat oxidative stress, as well as in the conversion of the thyroid hormones from T4 to T3. If selenium is low and if mercury is also elevated, it could be responsible for the low selenium. This is because mercury forms a very stable complex with selenium, and takes it out of biochemical availability.

d) Copper is needed for the conversion of dopamine to norepinephrine as well as in the antioxidant system.

Supplementation, Treatment and Further Testing Suggestions from Rich:

Gut problems are a basic issue for many people. Those who have the most success in treating them seem to be the ones who do repeated stool testing, and change the treatment with time to match what they are finding. It can take quite a while to get the gut back into good operation.

If the essential amino acids in general are on the low side, then I would suggest first checking the stomach acid using the baking soda burp test that has been described several times on the forum. If it is low, there are things that can be done to raise it, such as taking betaine-HCl or Allergy Research Group dilute hydrochloric acid. That can help protein digestion. If the pancreas is not putting out digestive enzymes well, proteolytic enzymes can also be taken.

If amino acids are to be supplemented, I would favor taking a combination supplement that includes all the essential amino acids, and then make sure the B-complex vitamins are high enough to carry out the transamination reactions needed to make the other amino acids in the body.

To raise glutathione in ME/CFS, I've found it best to treat to lift the partial methylation cycle block. We found that glutathione comes up automatically if this is done. (Rich developed the Simplified Methylation Protocol from Amy Yasko’s more complex and expensive protocol for this purpose.)

Rich's papers can be found here: http://phoenixrising.me/treating-cfs-chronic-fatigue-syndrome-me/treating-chronic-fatigue-syndrome-mecfs-glutathione-and-the-methylation-cycle

If you supplement with carnitine, the suggested form is carnitine fumarate.

If you have mercury toxicity, the methylation treatment alone may help. However, if the problem is severe enough you may have to address the mercury issue directly, using a chelation protocol. Andy Cutler's protocol seems to have helped quite a few people.

Further Testing:

Toxic Metals: Rich preferred a DMSA-challenged urine toxic and essential elements test, from Doctor's Data Lab. It's available through some doctors, or through www.directlabs.com without a doctor's order.

Dr. Shoemaker offers a visual contrast sensitivity test on his website www.chronicneurotoxins.com It isn't very expensive. He has found that this test is a good indicator for the presence of biotoxins in the brain. It is also sensitive to toxicity from some organic solvents and also heavy metals, which are also neurotoxins. He has shown that as neurotoxins are removed, the performance on this test improves.

KPU test – Health Diagnostics and Research Institute in New Jersey. http://www.hdri-usa.com/

Stool test - Metametrix G.I. Function Profile and/or Diagnos-Techs Expanded GI Panel.

Nutreval Worksheet

Deficiencies – Vitamins, etc.:																		**Notes**
Amino Acids																		
B vitamins																		
B1																		
B2																		
B3																		
B6 (P5P)																		
B12																		
Biotin																		
Carnitine																		
Co Q 10																		
Glutamine																		
Glutathione																		
Lipoic Acid																		
Melatonin																		
Serotonin																		
Tetrahydrobiopterin (BH4)																		
THF (folate)																		
Vitamin C																		
Deficiences - Minerals:																		
Copper																		
Iron																		
Magnesium																		
Manganese																		
Potassium																		
Selenium																		
Zinc																		
Toxins:																		
Antimony																		
Arsenic																		
Cadmium																		
Lead																		
Mercury																		
Tin																		
MTBE (Europe)																		
Styrene (Europe)																		
Other:																		
Partial Methylation Block																		
Malabsorption																		
Bacterial Dysbiosis																		
Yeast/Fungal Dysbiosis																		