

<b>Intervention Options</b>	<b>LOW</b>	<b>HIGH</b>
<b>Essential Amino Acids</b>		
Arginine (Arg)	Arg	Mn
Histidine (His)	Folate, His	
Isoleucine (Ile)	*	B6, Check for insulin insensitivity
Leucine (Leu)	*	B6, Check for insulin insensitivity
Lysine (Lys)	Carnitine	Vitamin C, Niacin, B6, Iron, $\alpha$ -KG
Methionine (Met)	*	B6, $\alpha$ -KG, Mg, SAM
Phenylalanine (Phe)	*	Iron, Vitamin C, Niacin, Low Phe diet
Threonine (Thr)	*	B6, Zn
Tryptophan (Trp)	Trp or 5-HTP	Niacin, B6
Valine (Val)	*	B6, Check for insulin insensitivity
<b>Essential Amino Acid Derivatives Neuroendocrine Metabolism</b>		
$\gamma$ -Aminobutyric Acid (GABA)		$\alpha$ -KG, B6
Glycine (Gly)	Gly	Folate, B6, B2, B5
Serine (Ser)	B6, Mn, Folate	*
Taurine (Tau)	Tau, B6	Vit. E, Vit. C, B-Carotene, CoQ10, Lipoate
Tyrosine (Tyr)	Iron, Tyr, Vitamin C, Niacin	Cu, Iron, Vitamin C, B6
<b>Ammonia/Energy Metabolism</b>		
$\alpha$ -Aminoadipic Acid		B6, $\alpha$ -KG
Asparagine (Asn)	Mg	
Aspartic Acid (Asp)	$\alpha$ -KG, B6	Mg, Zn
Citrulline (Cit)		Mg, Aspartic acid
Glutamic Acid (Glu)	B6, $\alpha$ -KG	Niacin, B6
Glutamine (Gln)		$\alpha$ -KG, B6
Ornithine (Orn)	Arg	Mg, $\alpha$ -KG, B6
<b>Sulfur Metabolism</b>		
Cystine (Cys)	NAC	B2
Cystathionine		B6
Homocystine (HCys)		B6, Folate, B12, Betaine
<b>Additional Metabolites</b>		
$\alpha$ -Amino-N-Butyric Acid	$\alpha$ -KG, B6	B6, $\alpha$ -KG
Alanine (Ala)	*	B6
Anserine		Zn
$\beta$ -Alanine		Lactobacillus and Bifidobacteria, B6
$\beta$ -Aminoisobutyric Acid		B6
Carnosine		Zn
Ethanolamine		Mg
Hydroxylysine (HLys)		Vitamin C, Iron, $\alpha$ -KG
Hydroxyproline (HPro)		Vitamin C, Iron, $\alpha$ -KG
1-Methylhistidine		Vitamin E, B12, Folate
3-Methylhistidine		BCAAs, Vit. E, Vit. C, $\beta$ -Carotene, CoQ10, Lipoate
Phosphoethanolamine (PE)		SAM, B12, Folate, Betaine
Phosphoserine		Mg
Proline (Pro)	$\alpha$ -KG	Vitamin C, Niacin
Sarcosine		B2

\* Use balanced or custom mixtures of essential amino acids

## Essential Amino Acids

### Arginine

**Low** - often reflects a diet poor in high quality protein, causing arginine to be poorly absorbed. Because arginine is required for nitric oxide production, deficiencies have wide-ranging effects on cardiovascular and other systems. **High** - may indicate a functional block in the urea cycle. Manganese activates an arginase enzyme, so supplementing with manganese may help.

### Histidine

**Low** - check dietary protein, or malabsorption if other essential AAs are low. Low histidine is associated with rheumatoid arthritis, folate deficiency, and/or salicylate/steroid use. **High** - may indicate excessive protein intake. If high 3-Methylhistidine, muscle protein breakdown is indicated.

### Isoleucine

**Low** - a chronic deficiency of this AA can cause hypoglycemia and related problems and loss of muscle mass or inability to build muscle. **High** - large intake of this AA or incomplete metabolism of it. If other BCAAs are high, add vitamin B<sub>6</sub> to aid metabolism.

### Leucine

**Low** - potential catabolism of skeletal muscle. Check 3-Methylhistidine to confirm this. **High** - large intake of this AA or incomplete metabolism of it. If other BCAAs are high, add vitamin B<sub>6</sub> to aid metabolism.

### Lysine

**Low** - either poor dietary intake or too high intake of arginine. Low levels can inhibit transamination of AA collagen synthesis. If concurrent weakness or high triglycerides, add carnitine. **High** - impaired metabolism of lysine. Add vitamin C, niacin, vitamin B<sub>6</sub>,  $\alpha$ -ketoglutarate and iron to enhance utilization of lysine.

### Methionine

**Low** - possible poor-quality protein diet. Adverse effects on sulfur metabolism. Improve dietary methionine intake or supplement. **High** - excessive intake of methionine-

rich protein or inefficient metabolism. If other sulfur-containing AAs are low, then enhance methionine utilization by adding the necessary cofactors, magnesium and vitamin B<sub>6</sub>.

### Phenylalanine

**Low** - can result in altered thyroid function and catecholamine deficits including symptoms of depression, cognitive disorders, memory loss, fatigue, and autonomic dysfunction. Reduce lifestyle stressors and supplement phenylalanine. **High** - high protein intake or a block in the conversion of phenylalanine to tyrosine. Iron, vitamin C, and niacin are necessary for this enzymatic step. Check tyrosine level and, if low, supplement tyrosine and iron.

### Threonine

**Low** - can result in hypoglycemic symptoms, particularly if glycine or serine is also low. Supplement threonine/BCAAs. **High** - excessive dietary intake or possible insufficient metabolism of threonine. The initial step here requires (vitamin B<sub>6</sub>) and zinc is needed to phosphorylate vitamin B<sub>6</sub> to its active coenzyme form, so supplementation with vitamin B<sub>6</sub> and zinc can be helpful.

### Tryptophan

**Low** - commonly correlated with depression, insomnia, and schizophrenia. Supplementation with 5-Hydroxytryptophan (5-HTP) may help. 5-HTP is one enzymatic step away from serotonin. **High** - possibly inadequate metabolism of tryptophan. Required nutrients for this process include niacin and vitamin B<sub>6</sub>.

### Valine

**Low** - deficiency in this or other BCAAs indicates potential muscle loss. If several essential AAs are low, check for adequate stomach acid. Supplement the BCAAs. **High** - excessive intake or vitamin B<sub>6</sub> functional deficit. If other BCAAs are high, vitamin B<sub>6</sub> should be given.

## Essential Amino Acid

### Derivatives Neuroendocrine Metabolism

**(GABA) Gamma-aminobutyric acid**  
**High** - may reflect decreased ability to

convert to succinate for use in the Krebs (citric acid) cycle for energy generation. Cofactors here are  $\alpha$ -KG and vitamin B<sub>6</sub>.

### Glycine

**Low** - possible generalized tissue loss, glycine being part of the nitrogen pool and important in gluconeogenesis. Supplement glycine. **High** - supplement vitamin B<sub>5</sub>, folic acid, and vitamins B<sub>6</sub>, and B<sub>2</sub> for the efficient metabolism of glycine to pyruvic acid for oxidation and for glutathione synthesis or gluconeogenesis.

### Serine

**Low** - can lead to disordered methionine metabolism and deficits in acetylcholine synthesis. If simultaneous high threonine or phosphoserine, then need for vitamin B<sub>6</sub>, folate, and manganese is indicated. **High** - when accompanied by low threonine, indicates glucogenic compensation and catabolism. Supplement threonine and BCAAs.

### Taurine

**Low** - may increase risk for oxidative stress, fat maldigestion, high cholesterol, atherosclerosis, angina, arrhythmias, and seizure disorders. Supplement taurine or cysteine and vitamin B<sub>6</sub>, even if fresh fish or lean meat is eaten. Females do not synthesize taurine as easily as males. **High** - may be due to excessive inflammation in the body or to supplementation of other amino acids.

### Tyrosine

**Low** - implicated in depression, hypothyroidism, and blood pressure disorders. If phenylalanine is normal or high (barring PKU), iron, vitamin C, and niacin supplementation might be indicated to help convert phenylalanine to tyrosine. **High** - inadequate utilization of tyrosine. Supplement the cofactors needed here including iron, copper, vitamin B<sub>6</sub>, and ascorbate.

## Ammonia/Energy Metabolism

### $\alpha$ -Aminoadipic acid

**High** - possible inhibition of lysine metabolism and lowered amine group transfer in the tissues. Supplement vitamin B<sub>6</sub> and  $\alpha$ -KG to facilitate the

transamination conversion of  $\alpha$ -aminoacidipic to  $\alpha$ -ketoacidipic acid.

## Asparagine

**Low** - can reflect functional need for magnesium in the conversion from aspartic acid.

**High** - Can indicate problems with purine (therefore protein) synthesis.

## Aspartic Acid

**Low** - inhibits ammonia detoxification in the urea cycle. Can be converted to oxaloacetate using B<sub>6</sub> and  $\alpha$ -KG and thus enter the Krebs cycle. Low levels can reflect decreased cellular energy generation, seen as fatigue. Citric and aspartic acids can drive the Krebs (citric acid) cycle, when combined with B<sub>6</sub> and  $\alpha$ -KG.

**High** - sometimes seen in epilepsy and stroke. Magnesium and zinc may counteract high aspartic acid levels.

## Citrulline

**High** - can indicate a functional enzyme block in the urea cycle, leading to an ammonia buildup. Supplement magnesium and aspartic acid to drive the cycle. Lower protein intake is suggested in ammonia toxicities.

## Glutamic Acid

**Low** - can suggest mild hyperammonemia, especially if high glutamine. Low protein, high complex carbohydrate and B<sub>6</sub>,  $\alpha$ -KG and BCAA's suggested to correct ammonia toxicity.

**High** - possible underconversion to  $\alpha$ -KG in liver for use in citric acid cycle. Supplement niacin and B<sub>6</sub>.

## Glutamine

**Low** - deficient intake or absorption of essential amino acids (glutamine is derived from histidine). Check overall amino acid level of diet.

**High** - marker of vitamin B<sub>6</sub> deficiency. Ammonia accumulation suspected, if low or low normal glutamic acid. Extra  $\alpha$ -KG needed to combine with ammonia and to make up for energy deficit caused by overutilization of  $\alpha$ -KG to deal with toxic ammonia levels.

## Ornithine

**Low** - possibly due to low arginine, as it is synthesized from arginine. As a source of regulatory polyamines, a low can affect cellular metabolism.

**High** - a possible metabolic block in urea cycle, causing excess ammonia burden. Confirm by checking for high glutamine, low glutamic acid.

## Sulfur Metabolism

### Cystine

**Low** - possible dietary deficiency of methionine and/or cystine. Low cystine can impair taurine synthesis.

**High** - excessive dietary intake or impaired cystine metabolism. Converted to cysteine (reduced cystine) via a B<sub>2</sub> and copper-dependent step. Cystine is a major component of tissue antioxidant mechanisms.

### Cystathionine

**High** - possible B<sub>6</sub> functional deficit as B<sub>6</sub> or P-5-P is required for the conversion of cystathionine to cysteine. Hence low cysteine can result.

### Homocystine

**High** - increased risk for atherosclerosis and abnormalities in the ocular, neurological and musculo-skeletal systems. The enzyme that converts homocysteine (reduced homocystine) to cystathionine is B<sub>6</sub> dependent; remethylation of homocysteine to methionine requires B<sub>12</sub>, folate and betaine. Supplementation of these nutrients plus magnesium is effective for the proper metabolism of homocystine.

## Additional Metabolites

### $\alpha$ -Amino-N-butyric acid

**Low** - possible increased need for the nutrients which aid in threonine metabolism from which this AA is derived. These include  $\alpha$ -KG and B<sub>6</sub>.

**High** - inadequate utilization of this AA for cellular energy generation. Alpha-ABA is converted to succinyl Co-A for use in the citric acid cycle via mechanisms requiring biotin and B<sub>12</sub>.

### Alanine

**Low** - may point to hypoglycemic conditions because of its role in gluconeogenesis. Supplement with alanine and the branched chain amino acids leucine, isoleucine and valine.

**High** - possible inadequate cellular energy substrates. Check for hypoglycemia or for exercise prior to blood draw. Chronic use of alanine

for energy can lead to muscle wasting. Supplement the branched-chain amino acids.

### Anserine

**High** - high dietary intake of poultry can contribute to elevated anserine. Zinc is required for the normal conversion to  $\beta$ -alanine plus 1-methylhistidine

### $\beta$ -Alanine

**High** - possible bowel toxicity due to  $\beta$ -alanine production by intestinal bacteria and/or *Candida albicans*. Possible cause for food sensitivity reactions when combined with low taurine and high 3-methylhistidine, carnosine and/or anserine, due to impaired renal tubular resorption. Supplement B<sub>6</sub> (to facilitate amine group transfer). Bowel detox or high potency *Lactobacillus acidophilus* and *Bifidobacteria* can help with gut dysbiosis.

### $\beta$ -Aminoisobutyric acid

**High** - indicates lack of a transaminase enzyme needed to metabolize this substance in the presence of  $\alpha$ -KG, an apparently benign phenomenon, seen in kwashiorkor (chronic protein deficiency).

### Carnosine

**High** - deficiency of enzyme carnosinase or its cofactor, zinc. This analyte is a  $\beta$ -alanyl dipeptide of histidine. Inherited carnosinase enzyme deficits lead to neurological development problems and sensory polyneuropathy.

### Ethanolamine

**High** - sluggish conversion of this serine derivative to phosphoethanolamine, possibly reducing acetylcholine synthesis. Supplement magnesium, a main cofactor for this conversion.

### Hydroxylysine

**High** - indicative of connective and bone tissue breakdown. Collagen synthesis requires iron,  $\alpha$ -KG and vitamin C. Supplementation of these plus chondroitin sulfate and manganese are extremely helpful.

### Hydroxyproline

**High** - another indicator of bone resorption via collagen breakdown. Supplement as in the case of high hydroxylysine above.

## 1-Methylhistidine

**High** - can mean impaired methionine metabolism. Supplement B12, folate or DMG. Can also inhibit carnosinase; give zinc.

## 3-Methylhistidine

**High** - indicates active catabolism of muscle protein which may be due to poor antioxidant nutrition.

## Phosphoethanolamine

**High** - possible inhibition of choline and acetylcholine synthesis due to impaired methionine metabolism involving methylation by S-adenosyl-methionine (SAM). Supplement B12, folate and betaine or SAM.

## Phosphoserine

**High** - functional magnesium deficiency causing incomplete conversion to serine.

## Proline

**Low** - tissue levels probably low. As proline is a major component of collagen, low plasma level can mean defective connective tissue synthesis. Proline metabolized to  $\alpha$ -KG. Check intake of high quality protein.

**High** - can demonstrate poor utilization. Add vitamin C to aid collagen synthesis if symptoms present. Niacin (cofactor precursor) helps oxidize proline to glutamate.

## Sarcosine

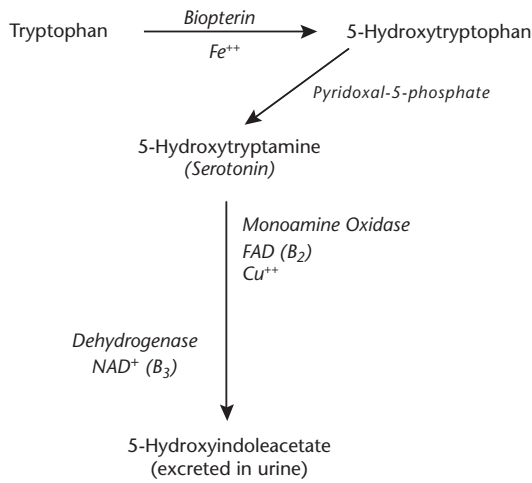
**High** - Metabolism requires B2. May indicate functional B2 deficiency.

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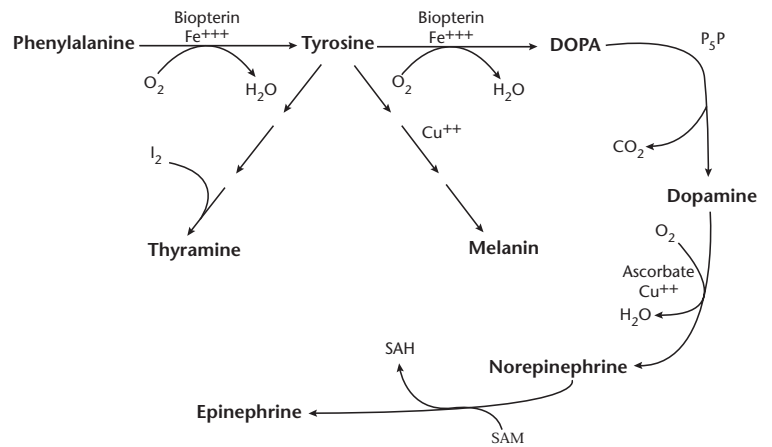
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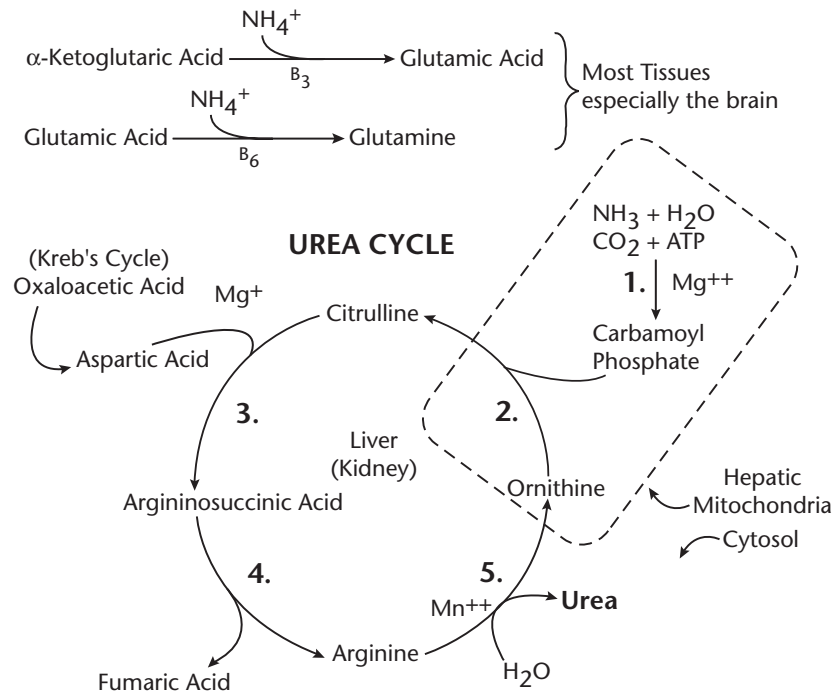
## Metabolism of Tryptophan



## Neurotransmitters from Amino Acids



## Relevant Ammonia Metabolism Pathways



### HYPERAMMONEMIA AND:

1. Low Urinary Orotate
2. Oroticaciduria
3. Citrullinemia
4. Argininosuccinic Aciduria
5. Hyperargininemia

### FAULTY ENZYME:

- Carbamoyl Phosphate Synthetase
- Ornithine Carbamoyl Transferase
- Argininosuccinate Synthetase
- Argininosuccinate Arginine Lyase
- Arginase

