CLINICAL LABORATORY TESTING:

BLOOD CHEMISTRY & CBC ANALYSIS

FROM A FUNCTIONAL MEDICINE PERSPECTIVE

Part 7 of 8

The 'Must Know' advanced laboratory tests for a successful treatment outcome

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EVEXIA DIAGNOSTICS™

8 PART SERIES

Integrative and Functional Medicine Stool Analysis

D: Digestive
I: Inflammation/immune system
G: Gastrointestinal microbiome

GI-MAP ™ DNA Stool Analysis

Patient: Jane Doe
Collected: 07/24/2017
DOB: 12/19/1971

Accession: 20170724-0102
Received: 07/24/2017
Completed: 07/31/2017

Ordered by: Diane Farhi, MD

Pathogens			
Bacterial Pathogens	Result		Expected
Campylobacter	<dl		<dl
C. difficile Toxin A	<dl		<dl
C. difficile Toxin B	<dl		<dl
Enterohemorrhagic *E. coli*	<dl		<dl
E. coli O157	<dl		<dl
Enteroinvasive *E. coli/Shigella*	<dl		<dl
Enteropathogenic *E. coli*	<dl		<dl
Enterotoxigenic *E. coli* LT/ST	<dl		<dl
Shiga-like Toxin *E. coli* stx1	<dl		<dl
Shiga-like Toxin *E. coli* stx2	<dl		<dl
Salmonella	6.4 e2	Low	<dl
Vibrio cholerae	<dl		<dl
Yersinia enterocolitica	<dl		<dl

Some Diseases Associated with GI Dysfunction

- Gastroesophageal reflux (GERD)
- Irritable bowel syndrome
- Inflammatory bowel disease
- Non-alcoholic steatohepatitis
- Colorectal cancer
- Allergy and asthma
- Autism
- Autoimmune disorders: type 1 diabetes, and
- Hashimoto's thyroiditis

Clinical Microbiology: Bacteriology, Parasitology, Virology via PCR testing	• Bacterial Pathogens • Parasitic Pathogens • Viral Pathogens
H. pylori	• H. pylori and Virulence Factor
Normal Bacteria Flora	• Bacteroides fragilis • Biffidobacterium species • Enterococcus species • Lactobaccillus species • Clostridium species • Enterbacter species
Phyla Microbiotia	• Bacteroidetes • Firmicutese • Firmicutes:Bacteroidetes Ratio
Opportunistic Bacteria (dysbiosis/overgrowth)	• Bacillus species • Enterococcus faecalis • Enterococcus faecium • Morganella species • Pseudomonas species • Pseudomonas aeruginosa • Staphylococcus species • Staphylococcus aureus • Streptococcus species

Opportunistic Bacteria **Potential Autoimmune Triggers**	• Citrobacter species • Citerbacter freudii • Klebseilla pneumoniae • M. avium subsp. paratuberculosis • Prevotella copri • Proteus species • Proteus mirabilis
Fungi/Yeast	• Candida species • Candida albicans • Geotrichum species • Microsporidium species • Rodotoula speccies
Viruses	• Cytomegalovirus • Epstein Barr Virus
Parasites	• Protozoa • Worms

Gut Immunology/Inflammation Markers	• Calprotectin • Secretory IgA • Anti-gliadin IgA
Digestion and GI Markers	• Occult Blood –Fecal Immunochemical Test • Beta-Glucuronidase • Elastase-1 • Steatocrit

Clinical Microbiology: Bacteriology and Mycology

Beneficial Bacteria: Health promoting bacteria - Controls potentially pathogenic organism and opportunistic organisms, synthesize vitamins, aids in digestion of protein and carbohydrates, removal of toxins, stimulates the intestinal immune system and produces of short chain fatty acids (e.g. butyrate – fuel for the colonocytes and reduces DNA damage).

Dysbiotic Bacteria: Known pathogenic bacteria and/or overgrowth of certain commensal bacteria.

Commensal/Imbalanced Bacteria: Bacteria that are part of the normal flora (co-evolved). Imbalances (e.g. overgrowth) can occur when there are insufficient levels of beneficial bacteria, resulting in dysbiosis and opportunistic infection.

***Yeast (Mycology)*:** Yeast is normally found in small numbers as a part of the colonic flora. Over growth of yeast can infect virtually every organ system, leading to an extensive array of clinical manifestations.

Parasitology

- Traditionally, a one-sample stool is collected for examination of parasites.
- Most integrative and functional medicine labs use three stool samples generally collected on consecutive days.
- Laboratory techniques used for identifying parasites and ova can vary among labs.
- It is generally recognized that stained fecal films are a productive means of stool examination for intestinal protozoa.
- **PCR testing and Antigen Detection Testing**

General Considerations for Abnormal GI Microbiology

- **Medical History**: antibiotic use; NSAIDs; antacids, acid-blocking medication

- **Associated Conditions**: hypochlorhydria; pancreatic insufficiency; Standard American Diet; exposures to pathogens (esp. water and food), inflammatory bowel disease, oxidative stress, emotional stress, depressed immune system (e.g. low secretory IgA)

Conditions	Potential Etiology
Low beneficial bacteria	• Antibiotic use • Poor diet
Abnormally high count of some beneficial bacteria	• Poor diet • Maldigestion • Malabsorption • Food intolerance
Presence of Potential Bacterial Pathogens (opportunistic) (Especially with high counts/growth)	• Low beneficial bacteria • Poor diet • Antibiotic use • Low gut immunity
Pathogenic bacteria	• Well-recognized pathogens of concern

Conditions	Potential Etiology
Yeast /Fungi **(Candida are normal inhabitants the GI tract when present in small numbers. They may become potential pathogens when the intestinal barrier is compromised and/or with overgrowth.)**	• **Antibiotic use** • Hypochlorhydria • Food allergies • Altered intestinal flora • Poor diet with high intake of carbohydrates and dairy • **Depressed immune system**

Conditions	Potential Etiology
Parasitic infection	**Suspicion of parasitic infection** • Skin irritation and itching • Anal or rectal itching • Low lactobacillus on stool analysis • Blood in stool • Unexplained anemia • Abdominal discomfort especially right lower quadrant • Low blood amino acid assay and low protein • Unexplained nutritional deficiencies (e.g. iron, zinc, selenium) • Continued GI symptoms after treatment for yeast and/or bacterial infection.

Digestion and Absorption Markers

Marker	Explanation
Pancreatic elastase	Digestive enzyme produced by the pancreas. Low levels suggest: • Pancreatic insufficiency • Gallstones or post-cholecystectomy • Chronic pancreatitis • Diabetes • Hypochlorhydria • Cystic fibrosis • Chronic inflammatory bowel disease If low, consider **digestive enzyme support** and treat the underlying cause

Marker	Explanation
Fecal fats - Steatocrit: Triglycerides, long chain fatty acids, cholesterol, phospholipids	Increased levels are associated with **fat malabsorption** • Pancreatic insufficiency • Cholestasis • **Celiac disease** • Short bowel syndrome • Post-cholecystectomy

Gastrointestinal Immunology and Inflammatory Markers

Marker	Explanation
Lactoferrin	Lactoferrin is an iron-binding glycoprotein that serves as a marker for **leukocytes activityIn the GI tract, it serves as a non-specific marker of inflammation.** Elevated levels as associated with: • Enteric infection • IBD • Colorectal cancer
Calprotectin	Calprotectin is a calcium-binding neutrophil derived protein. Elevated levels of calprotectin are associated with IBD.

Marker	Explanation
Secretory IgA	**sIgA is the first line of defense of the GI mucosa.** Elevated sIgA potential causes: • Normal immune response to pathogenic organism • Chronic elevations have been found in intractable (stubborn) GI infections, atopic dermatitis and colorectal cancer. Depressed sIgA potential causes: • Immunocompromised • Dysbiosis • Partial or primary selective IgA deficiency • Chronic stress

Marker	Explanation
Occult Blood **(Fecal Immunochemical Test)**	Hidden blood in the stool. • Colorectal cancer • Inflammatory bowel disease • Peptic ulcer • Polyps • Diverticulosis • Other cancers of the GI tract or accessory organs (Consider FIT test – Insure Test - and colonoscopy)
Beta-Glucuronidase	Beta-glucuronidase is an inducible **enzyme** elaborated by anaerobic intestinal bacteria. Increased activity of this enzyme has been implicated in **increased enterohepatic recirculation of toxins, steroids hormones, drugs and carcinogens.**

GI-MAP DIAGNOSTIC

(MULTIPLEX PCR)

HOW TO READ THE REPORT

GI-MAP quantifies bacteria, fungi, viruses, and parasites using qPCR. This is a leap forward from older methodologies that report only positive or negative. Results are reported as colony forming units per gram of stool (CFU/g). One CFU is roughly equivalent to one microorganism *(or one cell)*. Results are expressed in standard scientific notation. A reported result of 3.5e7 is equivalent to 3.5 x 10^7 CFU/g, which equals 35,000,000 CFU/g, or 35 million CFU per gram of stool.

GI-MAP INTERPRETIVE GUIDE

Pathogens			
Bacterial Pathogens	Result		Normal
Campylobacter	<dl		<1.00e3
C. difficile, Toxin A	1.21e5	High	<1.00e3

Figure 1. The normal reference range for *C. difficile*, Toxin A is 0–1,000 CFU/g. The patient's result is very high at 1.21 x 10^5, or 121,000 CFU/g.

Reference ranges were developed using known positive, diseased samples to construct cut off values that distinguish disease-causing amounts of pathogenic and opportunistic microbes. Reference ranges for the pathogens were correlated with an FDA cleared assay for GI pathogens. The GI-MAP is capable of detecting as low as 0.1 cell per gram of stool.

Table 1. Scientific notation; a basic reference table.

1.0e1	1 X 10^1	10	Ten
1.0e2	1 X 10^2	100	One hundred
1.0e3	1 X 10^3	1,000	One thousand
1.0e4	1 X 10^4	10,000	Ten thousand
1.0e5	1 X 10^5	100,000	
1.0e6	1 X 10^6	1,000,000	

GI-MAP

Pathogens		
Bacterial Pathogens	Result	Normal
Campylobacter	<dl	<1.00e3
C. difficile, Toxin A	<dl	<1.00e3
C. difficile, Toxin B	<dl	<1.00e3
Enterohemorrhagic E. coli	<dl	<1.00e3
E. coli O157	<dl	<1.00e3
Enteroinvasive E. coli/Shigella	<dl	<1.00e2
Enterotoxigenic E. coli LT/ST	<dl	<1.00e3
Shiga-like Toxin *E. coli* stx1	<dl	<1.00e3
Shiga-like Toxin *E. coli* stx2	<dl	<1.00e3
Salmonella	<dl	<1.00e4
Vibrio cholerae	<dl	<1.00e5
Yersinia enterocolitica	<dl	<1.00e5

GI-MAP

Parasitic Pathogens	Result	Normal
Cryptosporidium	**<dl**	<1.00e6
Entamoeba histolytica	**<dl**	<1.00e4
Giardia	**<dl**	<5.00e3

Viral Pathogens	Result	Normal
Adenovirus 40/41	**<dl**	<1.00e10
Norovirus GI/II	**<dl**	<1.00e7

GI-MAP

H. pylori		
	Result	Normal
Helicobacter pylori	**<dl**	<1.0e3
Virulence Factor, babA	**N/A**	Negative
Virulence Factor, cagA	**N/A**	Negative
Virulence Factor, dupA	**N/A**	Negative
Virulence Factor, iceA	**N/A**	Negative
Virulence Factor, oipA	**N/A**	Negative
Virulence Factor, vacA	**N/A**	Negative
Virulence Factor, virB	**N/A**	Negative
Virulence Factor, virD	**N/A**	Negative

GI-MAP

Normal Bacterial Flora			
	Result		Normal
Bacteroides fragilis	5.1e6	Low	1.60e9 - 2.50e11
Bifidobacterium spp.	1.4e8		>6.70e7
Enterococcus spp.	6.4e6		1.9e5 - 2.00e8
Escherichia spp.	8.4e5	Low	3.70e6 - 3.80e9
Lactobacillus spp.	1.5e6		8.6e5 - 6.20e8
Clostridium spp.	<dl		1.20e3 - 1.00e6
Enterobacter spp.	3.60e5	Low	1.00e6 - 5.00e7
Phyla Microbiota	Result		Normal
Bacteroidetes	1.48e9	Low	8.61e11 - 3.31e12
Firmicutes	1.35e11		5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	90.87	High	<1.00

GI-MAP

Opportunistic Bacteria			
Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	5.89e4		<1.50e5
Enterococcus faecalis	<dl		<1.00e4
Enterococcus faecium	2.70e2		<1.00e4
Morganella spp.	1.80e3	High	<1.00e3
Pseudomonas spp.	<dl		<1.00e4
Pseudomonas aeruginosa	1.86e3	High	<5.00e2
Staphylococcus spp.	2.09e3		<1.00e4
Staphylococcus aureus	2.80e2		<5.00e2
Streptococcus spp.	<dl		<1.00e3
Potential Autoimmune Triggers	Result		Normal
Citrobacter spp.	<dl		<5.00e6
Citrobacter freundii	<dl		<5.00e5
Klebsiella spp.	<dl		<5.00e3
Klebsiella pneumoniae	<dl		<5.00e4
M. avium subsp. paratuberculosis	<dl		<5.00e3
Prevotella copri	<dl		<1.00e7
Proteus spp.	<dl		<5.00e4
Proteus mirabilis	<dl		<1.00e3

GI-MAP

Fungi/Yeast			
	Result		Normal
Candida spp.	3.72e5	High	<5.00e3
Candida albicans	<dl		<5.00e2
Geotrichum spp.	<dl		<3.00e2
Microsporidium spp.	<dl		<5.00e3
Rodotorula spp.	<dl		<1.00e3

Viruses			
	Result		Normal
Cytomegalovirus	<dl		<1.00e5
Epstein Barr Virus	<dl		<1.00e7

GI-MAP

Parasites		
Protozoa	Result	Normal
Blastocystis hominis	**<dl**	<2.00e3
Chilomastix mesnili	**<dl**	<1.00e5
Cyclospora spp.	**<dl**	<5.00e4
Dientamoeba fragilis	**<dl**	<1.00e5
Endolimax nana	**<dl**	<1.00e4
Entamoeba coli	**<dl**	<5.00e6
Pentatrichomonas hominis	**<dl**	<1.00e2
Worms	Result	Normal
Ancylostoma duodenale	**Not Detected**	<Not Detected
Ascaris lumbricoides	**Not Detected**	<Not Detected
Necator americanus	**Not Detected**	<Not Detected
Trichuris trichiura	**Not Detected**	<Not Detected
Taenia spp.	**Not Detected**	<Not Detected

GI-MAP

Intestinal Health			
Digestion	Result		Normal
Elastase-1	**262**		>200 ug/g
Steatocrit	**<dl**		<15 %
GI Markers	Result		Normal
b-Glucuronidase	**136**		<2486 U/mL
Occult Blood - FIT	**0**		<10 ug/g
Immune Response	Result		Normal
Secretory IgA	**467**	Low	510 - 2010 ug/g
Anti-gliadin IgA	**19**		0 - 157 U/L
Inflammation	Result		Normal
Calprotectin	**12**		<173 ug/g

Antibiotic Resistance Genes, phenotypes					
Helicobacter		**Result**			**Expected Result**
Clarithromycin		**Negative**			Absent
A2142C	N/A	A2142G	N/A	A2143G	N/A
Fluoroquinolones		**Negative**			Absent
gyrA N87K	N/A	gyrA D91N	N/A	gyrA D91G	N/A
gyrB S479N	N/A	gyrB R484K	N/A		

EVEXIA DIAGNOSTICS™

NutrEval Test = Nutritional testing tool for **complex chronic illness** as well for those seeking to **improve health**

Targeted personalized nutrition (biochemical individuality) that provides the framework of core nutrients in 5 key areas:

1. Antioxidants
2. B-vitamins
3. Minerals
4. Essential Fatty Acids
5. Digestive support (pancreatic/need for probiotics)

EVEXIA DIAGNOSTICS™

Most Comprehensive

- ✓ NutrEval Plasma
- ✓ NutrEval FMV (first morning void)
  - both require urine and blood

Genomic testing can be added to both tests to assess for SNPs

Shorter version with no EFA testing

- ✓ ONE-FMV – urine only (Optimal Nutritional Evaluation)

Why use the NutrEval Profile?

NutrEval Profile is an advanced nutritional analysis designed to reveal nutritional imbalances or inadequacies.

Evaluates the functional need for antioxidants, B-vitamins, minerals, essential fatty acids, amino acids, digestive support, and other select nutrients.

Provides insight into nutrient status and allows you to provide targeted treatment (**i.e. personalized nutrition**) for the particular needs of each patient, often augmenting and speeding recovery of **complex chronic conditions**.

Effective for individuals experiencing the following conditions

- Mood disorders (e.g. depression, anxiety)
- Fatigue
- Digestive Complaints
- Chronic Pain/Inflammatory Conditions (e.g. migraine, musculoskeletal)
- Cardiovascular Risk
- Weight Issues
- Dietary Guidance
- General Health
- Sports Fitness Optimization

NutrEval FMV Profile

- Metabolic Analysis (urine organic acids)
- Urine Amino Acid Analysis (essential and non-essential amino acids, plus intermediary metabolites)
- Essential and Metabolic Fatty Acids (red blood cell essential and non-essential fatty acids, including Omega-3 and Omega-6 fatty acids)
- Oxidative Stress Analysis (blood and urine biomarkers indicative of oxidative stress)
- Elemental Markers (both nutrient and toxic elements)

NutrEval Plasma Profile

- Urine Amino Acid Analysis is **replaced with Plasma Amino Acid Analysis** (essential and non-essential amino acids, plus intermediary metabolites)

What's the difference between the two tests?

NutrEval **Plasma Profile**

A fasting plasma amino acid highlights the dynamic balance of the amino acid pool, independent of recent dietary intake. Plasma amino acid analysis is favored when the primary clinical consideration are conditions in which the supply of essential amino acid precursors is critical, such as in **mood and neurobehavioral disorders**.

NutrEval **FMV Profile**

Urine amino acid testing is valuable for assessing vitamin/mineral cofactors that affect amino acid metabolism and provide insight into **protein digestion**.

Select genomics biomarkers may be added to the profile for enhanced personalization of therapies such as MTHFR, COMT, TNF-alpha and APOE.

Biomarkers on the NutrEval Profile

- Metabolic Analysis Markers (urine organic acids)
  - Malabsorption and Dysbiosis Markers
    - Malabsorption Markers
    - Bacterial Dysbiosis Markers
    - Yeast/Fungal Dysbiosis Markers
  - Cellular Energy & Mitochondrial Metabolites
    - Carbohydrate Metabolism
    - Energy Metabolism
    - Fatty Acid Metabolism
  - Neurotransmitter Metabolites
  - Vitamin Markers
  - Toxin & Detoxification Markers
  - Tyrosine Metabolism

Biomarkers on the NutrEval Profile (continued)

- Urine Amino Acid Analysis **(FMV)**
  - Nutritionally Essential Amino Acids
  - Nonessential Protein Amino Acids
  - Intermediary Metabolites
  - Dietary Peptide Related Markers

- Plasma Amino Acid Analysis **(Plasma)**
  - Nutritionally Essential Amino Acids
  - Nonessential Protein Amino Acids
  - Intermediary Metabolites
  - Dietary Peptide Related Markers

Biomarkers on the NutrEval Profile (continuted)

- **Essential and Metabolic Fatty Acids**
  - Omega 3 Fatty Acids
  - Omega 6 Fatty Acids
  - Omega 9 Fatty Acids
  - Saturated Fatty Acids
  - Monounsaturated Fats
    - Omega 7 Fats
    - Trans Fat
  - Delta-6 Desaturase Activity
  - Cardiovascular Risk – featuring key ratios: Omega 6/Omega 3, AA/EPA, and the Omega 3 Index

J Clin Lipidol. 2014 Nov-Dec;8(6):612-7. doi: 10.1016/j.jacl.2014.08.001. Epub 2014 Aug 19.

Purified palmitoleic acid for the reduction of high-sensitivity C-reactive protein and serum lipids: a double-blinded, randomized, placebo controlled study.

Bernstein AM[1], Roizen MF[2], Martinez L[3].

⊕ Author information

Abstract

BACKGROUND: Purified palmitoleic acid (16-1; omega-7) has shown lipid-lowering and anti-inflammatory benefits in open label, epidemiologic, and animal studies.

OBJECTIVE: Our objective was to perform the first randomized controlled trial of purified palmitoleic acid supplementation in humans.

METHODS: Adults with dyslipidemia and evidence of mild systemic inflammation (high-sensitivity C-reactive protein [hs-CRP] between 2 and 5 mg/L) were randomly allocated to receive either 220.5 mg of cis-palmitoleic acid (n = 30) or an identical capsule with placebo (1000 mg of medium chain triglycerides, n = 30) once per day for 30 days. Participants were asked to maintain their current diet. Serum lipids and hs-CRP were drawn at baseline and study completion.

RESULTS: At 30 days, there were significant mean (95% confidence interval [CI]) reductions in CRP (-1.9 [-2.3 to -1.4] mg/L), triglyceride (-30.2 [-40.2 to -25.3] mg/dL), and low-density lipoprotein (LDL) (-8.9 [-12.0 to -5.8] mg/dL), and a significant increase in high-density lipoprotein (HDL) (2.4 [1.5, 3.3] mg/dL) in the intervention group compared with control. These changes equated to 44%, 15%, and 8% reductions in CRP, triglyceride, and LDL respectively, and a 5% increase in HDL compared with control.

CONCLUSIONS: Purified palmitoleic acid may be useful in the treatment of hypertriglyceridemia with the beneficial added effects of decreasing LDL and hs-CRP and raising HDL. Further study is needed to elucidate mechanisms and establish appropriate human doses.

Sources: Macadamia oil and sea buckthorn oil

Biomarkers on the NutrEval Profile (continuted)

Oxidative Stress Markers

- Glutathione (whole blood)
- Lipid Peroxides (urine)
- 8-OHdG (urine – 8-hydroxy-2-deoxyguanosine)
- Coenzyme Q10 (plasma)

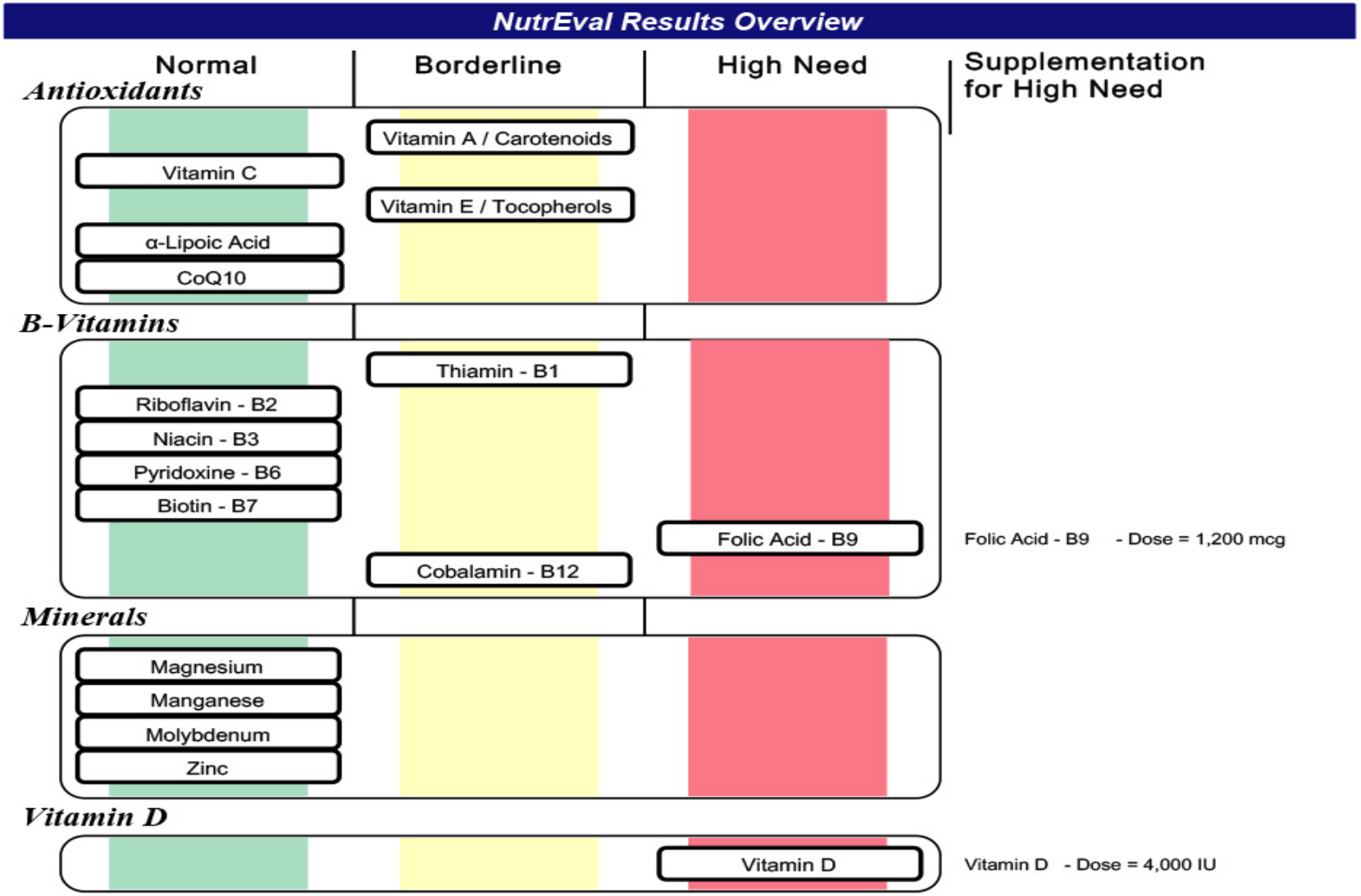
Elemental Markers

- Nutrient Elements
  - Copper
  - Magnesium
  - Manganese
  - Potassium
  - Selenium
  - Zinc
- Toxic Elements
  - Lead
  - Mercury
  - Antimony
  - Arsenic
  - Cadmium
  - Tin

Advantages of the NutrEval Tests

- Identification of imbalances that may **precede** abnormal findings on standard laboratory panels
- Comprehensive nutritional assessment indicating the **functional need** for specific nutrients, diet modification, antioxidant protection, detoxification and other therapies
- **Personalized nutrient** recommendations based on biochemical individuality

Applying the NutrEval In Clinical Practice



Applying the NutrEval In Clinical Practice

SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	2,333 IU	5,000 IU	
Vitamin C	75 mg	250 mg	
Vitamin E / Tocopherols	22 IU	200 IU	
α-Lipoic Acid		50 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.1 mg	25 mg	
Riboflavin - B2	1.1 mg	10 mg	
Niacin - B3	14 mg	20 mg	
Pyridoxine - B6	1.5 mg	10 mg	
Biotin - B7	30 mcg	100 mcg	
Folic Acid - B9	400 mcg	1,200 mcg	
Cobalamin - B12	2.4 mcg	500 mcg	
Minerals			
Magnesium	320 mg	400 mg	
Manganese	1.8 mg	3.0 mg	
Molybdenum	45 mcg	75 mcg	
Zinc	8 mg	10 mg	

Green = normal
Yellow = borderline
Red = high need

Applying the NutrEval In Clinical Process

Essential Fatty Acids		
Omega-3 Oils	500 mg	1,000 mg
Digestive Support		
Probiotics		50 billion CFU
Pancreatic Enzymes		10,000 IU
Other Vitamins		
Vitamin D	800 IU	4,000 IU

Amino Acid	mg/day	Amino Acid	mg/day
Arginine	0	Methionine	0
Asparagine	0	Phenylalanine	0
Cysteine	0	Serine	0
Glutamine	334	Taurine	0
Glycine	327	Threonine	0
Histidine	0	Tryptophan	0
Isoleucine	0	Tyrosine	0
Leucine	0	Valine	0
Lysine	0		

Recommendations for age and gender-specific supplementation are set by comparing levels of nutrient functional need to optimal levels as described in the peer-reviewed literature. They are provided as guidance for short-term support of nutritional deficiencies only.

The Suggested Supplemental Schedule is provided at the request of the ordering practitioner. Any application of it as a therapeutic intervention is to be determined by the ordering practitioner.

Key — Normal — Borderline — High Need

AUNT1.3

Applying the NutrEval In Clinical Practice

Nutritional Needs

Antioxidants

Vitamin A / Carotenoids

- Beta-carotene & other carotenoids are converted to vitamin A (retinol), involved in vision, antioxidant & immune function, gene expression & cell growth.
- Vitamin A deficiency may occur with chronic alcoholism, zinc deficiency, hypothyroidism, or oral contraceptives containing estrogen & progestin.
- Deficiency may result in night blindness, impaired immunity, healing & tissue regeneration, increased risk of infection, leukoplakia or keratosis.
- Food sources include cod liver oil, fortified cereals & milk, eggs, sweet potato, pumpkin, carrot, cantaloupe, mango, spinach, broccoli, kale & butternut squash.

Vitamin C

- Vitamin C is an antioxidant (also used in the regeneration of other antioxidants). It is involved in cholesterol metabolism, the production & function of WBCs and antibodies, and the synthesis of collagen, norepinephrine and carnitine.
- Deficiency may occur with oral contraceptives, aspirin, diuretics or NSAIDs.
- Deficiency can result in scurvy, swollen gingiva, periodontal destruction, loose teeth, sore mouth, soft tissue ulcerations, or increased risk of infection.
- Food sources include oranges, grapefruit, strawberries, tomato, sweet red pepper, broccoli and potato.

Vitamin E / Tocopherols

- Alpha-tocopherol (body's main form of vitamin E) functions as an antioxidant, regulates cell signaling, influences immune function and inhibits coagulation.
- Deficiency may occur with malabsorption, cholestyramine, colestipol, isoniazid, orlistat, olestra and certain anti-convulsants (e.g., phenobarbital, phenytoin).
- Deficiency may result in peripheral neuropathy, ataxia, muscle weakness, retinopathy, and increased risk of CVD, prostate cancer and cataracts.
- Food sources include oils (olive, soy, corn, canola, safflower, sunflower), eggs, nuts, seeds, spinach, carrots, avocado, dark leafy greens and wheat germ.

α-Lipoic Acid

- α-Lipoic acid plays an important role in energy production, antioxidant activity (including the regeneration of vitamin C and glutathione), insulin signaling, cell signaling and the catabolism of α-keto acids and amino acids.
- High biotin intake can compete with lipoic acid for cell membrane entry.
- Optimal levels of α-lipoic acid may improve glucose utilization and protect against diabetic neuropathy, vascular disease and age-related cognitive decline.
- Main food sources include organ meats, spinach and broccoli. Lesser sources include tomato, peas, Brussels sprouts and brewer's yeast.

Key

- Function
- Causes of Deficiency
- Complications of Deficiency
- Food Sources

Function

Cause of Deficiency

Complications of Deficiency

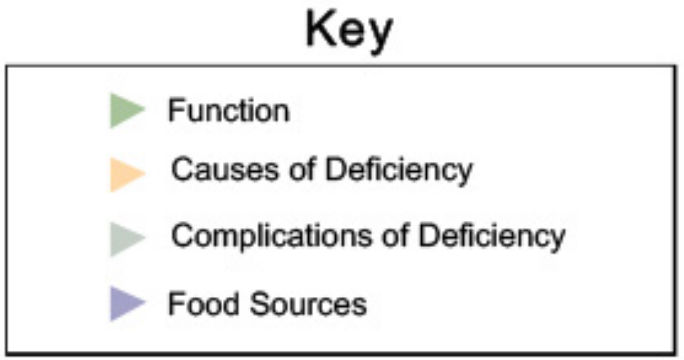
Food sources

Applying the NutrEval In Clinical Practice

- CoQ10 is a powerful antioxidant that is synthesized in the body and contained in cell membranes. CoQ10 is also essential for energy production & pH regulation.
- CoQ10 deficiency may occur with HMG-CoA reductase inhibitors (statins), several anti-diabetic medication classes (biguanides, sulfonylureas) or beta-blockers.
- Low levels may aggravate oxidative stress, diabetes, cancer, congestive heart failure, cardiac arrhythmias, gingivitis and neurologic diseases.
- Main food sources include meat, poultry, fish, soybean, canola oil, nuts and whole grains. Moderate sources include fruits, vegetables, eggs and dairy.

- Oxidative stress is the imbalance between the production of free radicals and the body's ability to readily detoxify these reactive species and/or repair the resulting damage with anti-oxidants.
- Oxidative stress can be endogenous (energy production and inflammation) or exogenous (exercise, exposure to environmental toxins).
- Oxidative stress has been implicated clinically in the development of neurodegenerative diseases, cardiovascular diseases and chronic fatigue syndrome.
- Antioxidants may be found in whole food sources (e.g., brightly colored fruits & vegetables, green tea, turmeric) as well as nutraceuticals (e.g., resveratrol, EGCG, lutein, lycopene, ginkgo, milk thistle, etc.).

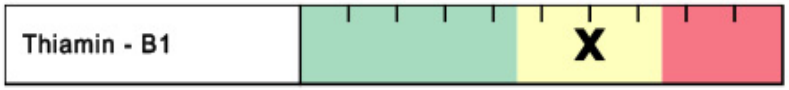
- Glutathione (GSH) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection, inflammation and toxic exposure.
- Deficiency may result in oxidative stress & damage, impaired detoxification, altered immunity, macular degeneration and increased risk of chronic illness.
- Food sources of GSH precursors include meats, poultry, fish, soy, corn, nuts, seeds, wheat germ, milk and cheese.



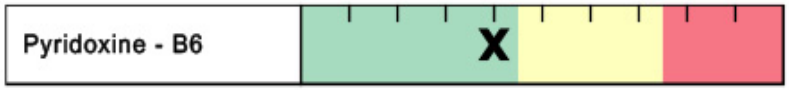
Applying the NutrEval In Clinical Practice

Nutritional Needs

B-Vitamins



- B1 is a required cofactor for enzymes involved in energy production from food, and for the synthesis of ATP, GTP, DNA, RNA and NADPH.
- Low B1 can result from chronic alcoholism, diuretics, digoxin, oral contraceptives and HRT, or large amounts of tea & coffee (contain anti-B1 factors).
- B1 deficiency may lead to dry beriberi (e.g., neuropathy, muscle weakness), wet beriberi (e.g., cardiac problems, edema), encephalopathy or dementia.
- Food sources include lentils, whole grains, wheat germ, Brazil nuts, peas, organ meats, brewer's yeast, blackstrap molasses, spinach, milk & eggs.



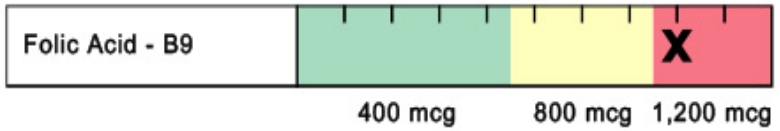
- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or digoxin.
- B6 deficiency may result in neurologic symptoms (e.g., irritability, depression, seizures), oral inflammation, impaired immunity or increased homocysteine.
- Food sources include poultry, beef, beef liver, fish, whole grains, wheat germ, soybean, lentils, nuts & seeds, potato, spinach and carrots.

- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.
- B2 deficiency may result in oxidative stress, mitochondrial dysfunction, low uric acid, low B3 or B6, high homocysteine, anemia or oral & throat inflammation.
- Food sources include milk, cheese, eggs, whole grains, beef, chicken, wheat germ, fish, broccoli, asparagus, spinach, mushrooms and almonds.

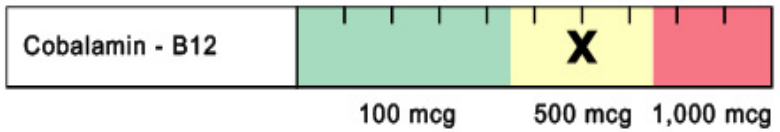
- Biotin is a cofactor for enzymes involved in functions such as fatty acid synthesis, mitochondrial FA oxidation, gluconeogenesis and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN, anticonvulsants, high-dose B5, sulfa drugs & other antibiotics.
- Low levels may result in neurologic symptoms (e.g., paresthesias, depression), hair loss, scaly rash on face or genitals or impaired immunity.
- Food sources include yeast, whole grains, wheat germ, eggs, cheese, liver, meats, fish, wheat, nuts & seeds, avocado, raspberries, sweet potato and cauliflower.

Applying the NutrEval In Clinical Practice

- B3 is used to form NAD and NADP, involved in energy production from food, fatty acid & cholesterol synthesis, cell signaling, DNA repair & cell differentiation.
- Low B3 may result from deficiencies of tryptophan (B3 precursor), B6, B2 or Fe (cofactors in B3 production), or from long-term isoniazid or oral contraceptive use.
- B3 deficiency may result in pellagra (dermatitis, diarrhea, dementia), neurologic symptoms (e.g., depression, memory loss), bright red tongue or fatigue.
- Food sources include poultry, beef, organ meats, fish, whole grains, peanuts, seeds, lentils, brewer's yeast and lima beans.



- Folic acid plays a key role in coenzymes involved in DNA and SAMe synthesis, methylation, nucleic acids & amino acid metabolism and RBC production.
- Low folate may result from alcoholism, high-dose NSAIDs, diabetic meds, H2 blockers, some diuretics and anti-convulsants, SSRIs, methotrexate, trimethoprim, pyrimethamine, triamterene, sulfasalazine or cholestyramine.
- Folate deficiency can result in anemia, fatigue, low methionine, increased homocysteine, impaired immunity, heart disease, birth defects and CA risk.
- Food sources include fortified grains, green vegetables, beans & legumes.



- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2 blockers, PPIs), vegan diets, diabetic meds, cholestyramine, chloramphenicol, neomycin or colchicine.
- B12 deficiency can lead to anemia, fatigue, neurologic symptoms (e.g., paresthesias, memory loss, depression, dementia), methylation defects or chromosome breaks.
- Food sources include shellfish, red meat poultry, fish, eggs, milk and cheese.

Applying the NutrEval In Clinical Practice

Nutritional Needs

Minerals

Manganese

- Manganese plays an important role in antioxidant function, gluconeogenesis, the urea cycle, cartilage & bone formation, energy production and digestion.
- Impaired absorption of Mn may occur with excess intake of Fe, Ca, Cu, folic acid, or phosphorous compounds, or use of long-term TPN, Mg-containing antacids or laxatives.
- Deficiency may result in impaired bone/connective tissue growth, glucose & lipid dysregulation, infertility, oxidative stress, inflammation or hyperammonemia.
- Food sources include whole grains, legumes, dried fruits, nuts, dark green leafy vegetables, liver, kidney and tea.

Magnesium

- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses of zinc.
- Low Mg may result in muscle weakness/spasm, constipation, depression, hypertension, arrhythmias, hypocalcemia, hypokalemia or personality changes.
- Food sources include dark leafy greens, oatmeal, buckwheat, unpolished grains, chocolate, milk, nuts & seeds, lima beans and molasses.

Molybdenum

- Molybdenum is a cofactor for enzymes that convert sulfites to sulfate, and nucleotides to uric acid, and that help metabolize aldehydes & other toxins.
- Low Mo levels may result from long-term TPN that does not include Mo.
- Mo deficiency may result in increased sulfite, decreased plasma uric acid (and antioxidant function), deficient sulfate, impaired sulfation (detoxification), neurologic disorders or brain damage (if severe deficiency).
- Food sources include buckwheat, beans, grains, nuts, beans, lentils, meats and vegetables (although Mo content of plants depends on soil content).

Zinc

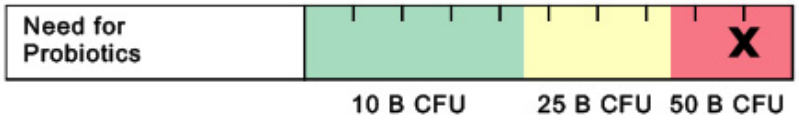
- Zinc plays a vital role in immunity, protein metabolism, heme synthesis, growth & development, reproduction, digestion and antioxidant function.
- Low levels may occur with malabsorption, alcoholism, chronic diarrhea, diabetes, excess Cu or Fe, diuretics, ACE inhibitors, H2 blockers or digoxin.
- Deficiency can result in hair loss and skin rashes, also impairments in growth & healing, immunity, sexual function, taste & smell and digestion.
- Food sources include oysters, organ meats, soybean, wheat germ, seeds, nuts, red meat, chicken, herring, milk, yeast, leafy and root vegetables.

Applying the NutrEval In Clinical Process

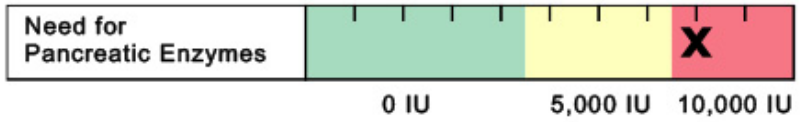
Essential Fatty Acids

- Omega-3 (O3) and Omega-6 (O6) fatty acids are polyunsaturated fatty acids that cannot be synthesized by the human body. They are classified as essential nutrients and must be obtained from dietary sources.
- The standard American diet is much higher in O6 than O3 fatty acids. Deficiency of EFAs may result from poor dietary intake and/or poor conversion from food sources.
- EFA deficiency is associated with decreased growth & development of infants and children, dry skin/rash, poor wound healing, and increased risk of infection, cardiovascular and inflammatory diseases.
- Dietary sources of the O6 Linoleic Acid (LA) include vegetable oils, nuts, seeds and some vegetables. Dietary sources of the O3 a-Linolenic Acid (ALA) include flaxseeds, walnuts, and their oils. Fish (mackerel, salmon, sardines) are the major dietary sources of the O3 fatty acids EPA and DHA.

Digestive Support



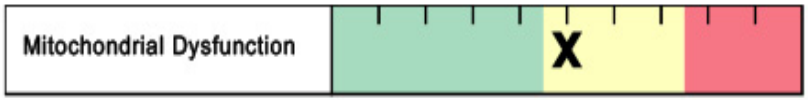
- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhance digestion & absorption; decrease severity of diarrheal illness; modulate of immune function & intestinal permeability.
- Alterations of gastrointestinal microflora may result from C-section delivery, antibiotic use, improved sanitation, decreased consumption of fermented foods and use of certain drugs.
- Some of the diseases associated with microflora imbalances include: IBS, IBD, fibromyalgia, chronic fatigue syndrome, obesity, atopic illness, colic and cancer.
- Food sources rich in probiotics are yogurt, kefir and fermented foods.



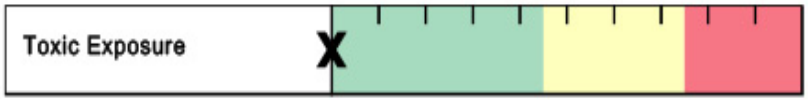
- Pancreatic enzymes are secreted by the exocrine glands of the pancreas and include protease/peptidase, lipase and amylase.
- Pancreatic exocrine insufficiency may be primary or secondary in nature. Any indication of insufficiency warrants further evaluation for underlying cause (i.e., celiac disease, small intestine villous atrophy, small bowel bacterial overgrowth).
- A high functional need for digestive enzymes suggests that there is an impairment related to digestive capacity.
- Determining the strength of the pancreatic enzyme support depends on the degree of functional impairment. Supplement potency is based on the lipase units present in both prescriptive and non-prescriptive agents.

Applying the NutrEval In Clinical Practice

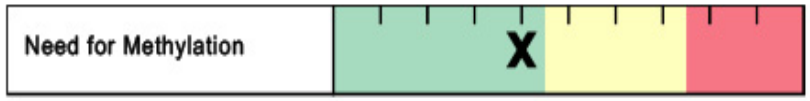
Functional Imbalances



- Mitochondria are a primary site of generation of reactive oxygen species. Oxidative damage is considered an important factor in decline of physiologic function that occurs with aging and stress.
- Mitochondrial defects have been identified in cardiovascular disease, fatigue syndromes, neurologic disorders such as Parkinson's and Alzheimer's disease, as well as a variety of genetic conditions. Common nutritional deficiencies can impair mitochondrial efficiency.

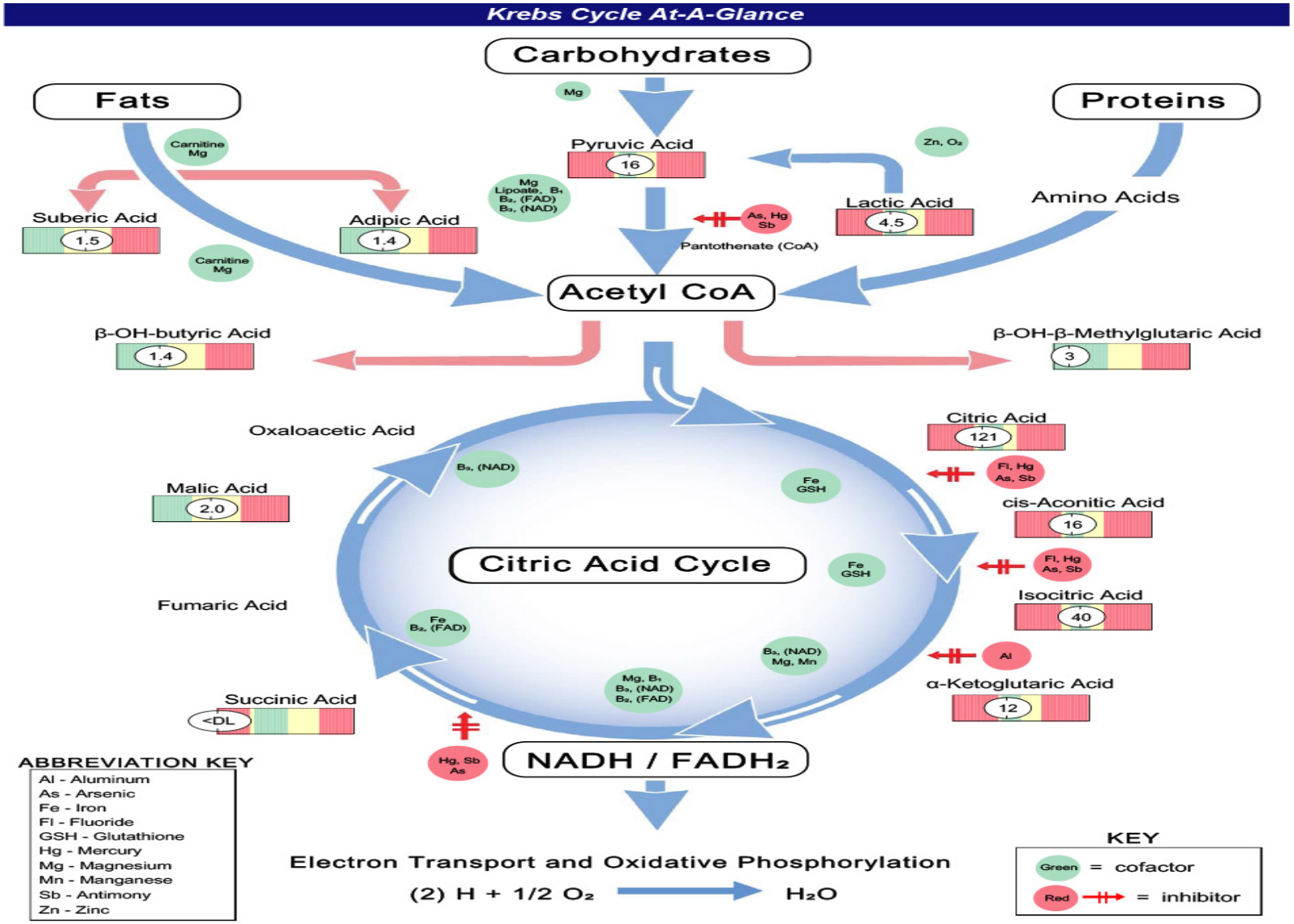


- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal studies suggest that drinking MTBE may cause gastrointestinal irritation, liver and kidney damage and nervous system effects.
- Styrene is classified by the US EPA as a "potential human carcinogen," and is found widely distributed in commercial products such as rubber, plastic, insulation, fiberglass, pipes, food containers and carpet backing.
- Levels of these toxic substances should be examined within the context of the body's functional capacity for methylation and need for glutathione.

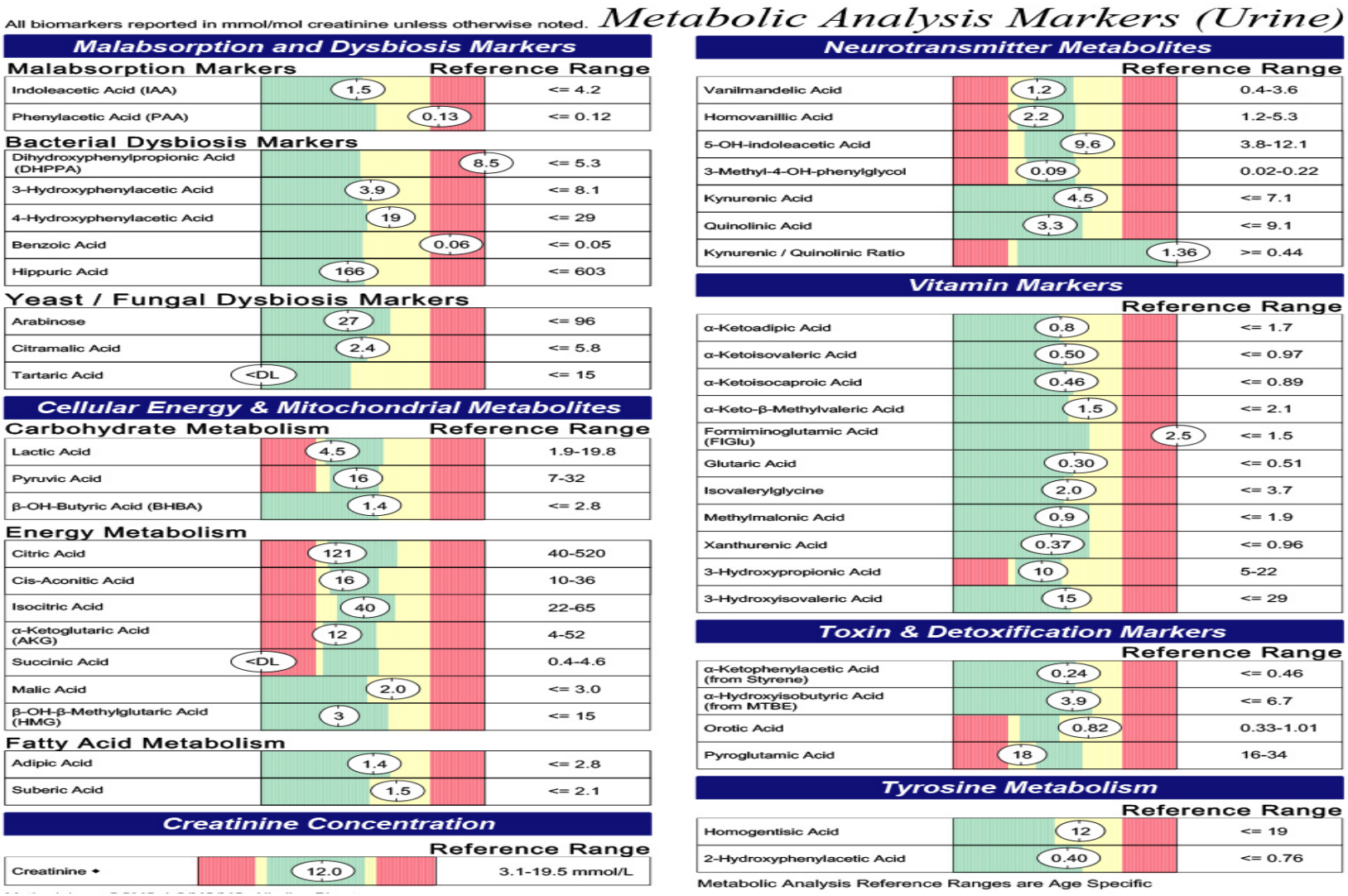


- Methylation is an enzymatic process that is critical for both synthesis and inactivation. DNA, estrogen and neurotransmitter metabolism are all dependent on appropriate methylation activity.
- B vitamins and other nutrients (methionine, magnesium, selenium) functionally support catechol-O-methyltransferase (COMT), the enzyme responsible for methylation.

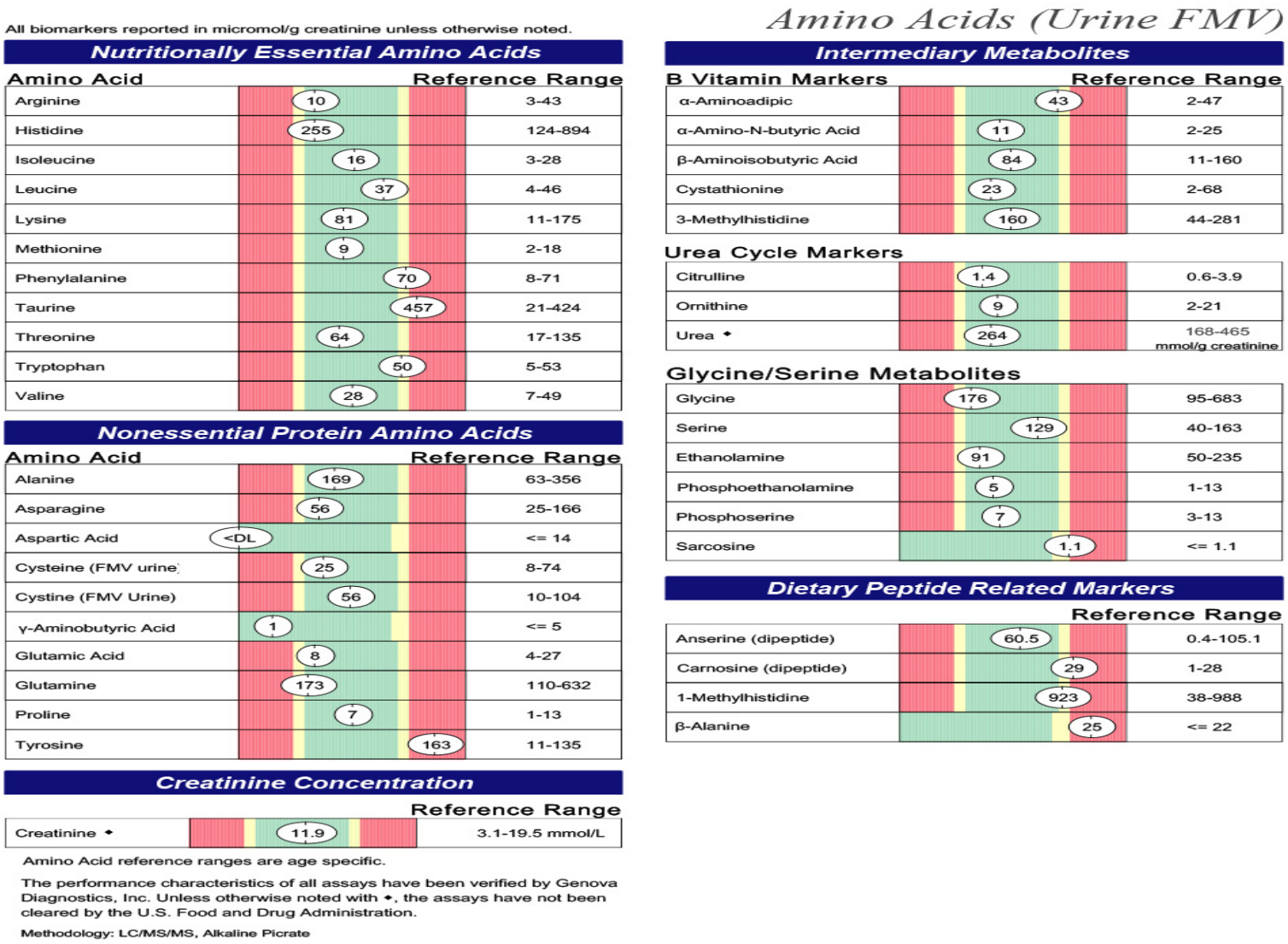
Applying the NutrEval In Clinical Practice



Applying the NutrEval In Clinical Practice



Applying the NutrEval In Clinical Practice



All biomarkers reported in micromol/g creatinine unless otherwise noted.

Amino Acids (Urine FMV)

Nutritionally Essential Amino Acids

Amino Acid	Reference Range
Arginine	3-43
Histidine	124-894
Isoleucine	3-28
Leucine	4-46
Lysine	11-175
Methionine	2-18
Phenylalanine	8-71
Taurine	21-424
Threonine	17-135
Tryptophan	5-53
Valine	7-49

Nonessential Protein Amino Acids

Amino Acid	Reference Range
Alanine	63-356
Asparagine	25-166
Aspartic Acid	<= 14
Cysteine (FMV urine)	8-74
Cystine (FMV Urine)	10-104
γ-Aminobutyric Acid	<= 5
Glutamic Acid	4-27
Glutamine	110-632
Proline	1-13
Tyrosine	11-135

Creatinine Concentration

	Reference Range
Creatinine ✦	3.1-19.5 mmol/L

Amino Acid reference ranges are age specific.

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ✦, the assays have not been cleared by the U.S. Food and Drug Administration.

Methodology: LC/MS/MS, Alkaline Picrate

Intermediary Metabolites

B Vitamin Markers

	Reference Range
α-Aminoadipic	2-47
α-Amino-N-butyric Acid	2-25
β-Aminoisobutyric Acid	11-160
Cystathionine	2-68
3-Methylhistidine	44-281

Urea Cycle Markers

Citrulline	0.6-3.9
Ornithine	2-21
Urea ✦	168-465 mmol/g creatinine

Glycine/Serine Metabolites

Glycine	95-683
Serine	40-163
Ethanolamine	50-235
Phosphoethanolamine	1-13
Phosphoserine	3-13
Sarcosine	<= 1.1

Dietary Peptide Related Markers

	Reference Range
Anserine (dipeptide)	0.4-105.1
Carnosine (dipeptide)	1-28
1-Methylhistidine	38-988
β-Alanine	<= 22

Applying the NutrEval In Clinical Practice

Essential and Metabolic Fatty Acids Markers (RBCs)

Omega 3 Fatty Acids

Analyte	(cold water fish, flax, walnut)	Reference Range
α-Linolenic (ALA) 18:3 n3	0.13	>= 0.09 wt %
Eicosapentaenoic (EPA) 20:5 n3	0.59	>= 0.16 wt %
Docosapentaenoic (DPA) 22:5 n3	1.79	>= 1.14 wt %
Docosahexaenoic (DHA) 22:6 n3	3.2	>= 2.1 wt %
% Omega 3s	5.8	>= 3.8

Omega 9 Fatty Acids

Analyte	(olive oil)	Reference Rang
Oleic 18:1 n9	11	10-13 wt %
Nervonic 24:1 n9	2.2	2.1-3.5 wt %
% Omega 9s	13.7	13.3-16.6

Saturated Fatty Acids

Analyte	(meat, dairy, coconuts, palm oils)	Reference Range
Palmitic C16:0	21	18-23 wt %
Stearic C18:0	20	14-17 wt %
Arachidic C20:0	0.28	0.22-0.35 wt %
Behenic C22:0	0.78	0.92-1.68 wt %
Tricosanoic C23:0	0.17	0.12-0.18 wt %
Lignoceric C24:0	2.5	2.1-3.8 wt %
Pentadecanoic C15:0	0.08	0.07-0.15 wt %
Margaric C17:0	0.28	0.22-0.37 wt %
% Saturated Fats	44.6	39.8-43.6

OMEGA 7

Omega 6 Fatty Acids

Analyte	(vegetable oil, grains, most meats, dairy)	Reference Range
Linoleic (LA) 18:2 n6	14.1	10.5-16.9 wt %
γ-Linolenic (GLA) 18:3 n6	0.07	0.03-0.13 wt %
Dihomo-γ-linolenic (DGLA) 20:3 n6	1.70	>= 1.19 wt %
Arachidonic (AA) 20:4 n6	16	15-21 wt %
Docosatetraenoic (DTA) 22:4 n6	2.60	1.50-4.20 wt %
Eicosadienoic 20:2 n6	0.32	<= 0.26 wt %
Omega 6s	34.4	30.5-39.7

Monounsaturated Fats

Omega 7 Fats		Reference Range
Palmitoleic 16:1 n7	0.30	<= 0.64 wt %
Vaccenic 18:1 n7	0.85	<= 1.13 wt %
Trans Fat		
Elaidic 18:1 n9t	0.38	<= 0.59 wt %

Delta - 6 Desaturase Activity

	Upregulated / Functional / Impaired	
Linoleic / DGLA 18:2 n6 / 20:3 n6	8.3	6.0-12.3

Cardiovascular Risk

Analyte		Reference Range
Omega 6s / Omega 3s	6.0	3.4-10.7
AA / EPA 20:4 n6 / 20:5 n3	26	12-125
Omega 3 Index	3.8	>= 4.0

Applying the NutrEval In Clinical Practice

Oxidative Stress Markers

Oxidative Stress Markers

	Reference Range
Methodology: Colorimetric, thiobarbituric acid reactive substances (TBARS), Alkaline Picrate, Hexokinase/G-6-PDH, LC/MS/MS, HPLC	
Glutathione (whole blood) — 1,241	>=669 micromol/L
Lipid Peroxides (urine) — 8.0	<=10.0 micromol/g Creat.
8-OHdG (urine) — 4	<=15 mcg/g Creat.
Coenzyme Q10, Ubiquinone (serum) — 1.29	0.43-1.49 mcg/mL

The Oxidative Stress reference ranges are based on an adult population.

The performance characteristics of the Oxidative Stress Markers have been verified by Genova Diagnostics, Inc. They have not been cleared by the U.S. Food and Drug Administration.

Vitamin D (Serum)

	Inside Range	Outside Range	Reference Range
Methodology: Chemiluminescent			
25 - OH Vitamin D ◆		25	50-100 ng/mL

Deficiency = < 20 ng/mL (< 50 nmol/L)
Insufficiency = 20-49 ng/mL (50-124 nmol/L)
Optimal = 50-100 ng/mL (125-250 nmol/L)
Excessive = > 100 ng/mL (> 250 nmol/L)

Elemental Markers

Nutrient Elements

Element	Reference Range	Reference Range
Copper *(plasma)* — 118.8		75.3-192.0 mcg/dL
Magnesium *(RBC)* — 60.9		30.1-56.5 mcg/g
Manganese *(whole blood)* — 8.3		3.0-16.5 mcg/L
Potassium *(RBC)* — 3,376		2,220-3,626 mcg/g
Selenium *(whole blood)* — 269		109-330 mcg/L
Zinc *(plasma)* — 134.3		64.3-159.4 mcg/dL

Toxic Elements*

Element	Reference Range	Reference Range
Lead — 1.05		<= 2.81 mcg/dL
Mercury — <DL		<= 4.35 mcg/L
Arsenic — 0.2		<= 13.7 mcg/L
Cadmium — <DL		<= 1.22 mcg/L
Tin — <DL		<= 0.39 mcg/L

* All toxic Elements are measured in whole blood.
Methodology: ICP-MS

EVEXIA DIAGNOSTICS™

ORGANIC ACID TEST

Indications & Clinical Interpretation

Organic Acids

- Family of compounds that are intermediates in a variety of metabolic pathways.
- Normally found in the urine of health individuals
- Increased levels of specific organic acids or elevations of combinations of specific organic acids are often seen in metabolic disorders in which there is a blockage or blockages in certain metabolic pathways.

Organic Acids

- Abnormal urinary organic acids, **organic aciduria**, is seen genetic disorders of amino acid metabolism, mitochondrial fatty acid beta-oxidation metabolism, and of mitochondrial oxidative phosphorylation metabolism.

- Inborn errors of metabolism such as **phenylketonuria** and **methylmalonic aciduria**

Key test in evaluation of individuals with suspected genetic disorders of organic acid metabolism.

Organic Acids

Genetic disorders detected by urinary acid analysis present at some time during infancy or childhood

Significant catabolic stresses such as illness with vomiting, diarrhea and/or fever or fasting.

Organic Acids

Most laboratories only test for genetic inborn errors of metabolism via urinary organic acid evaluation.

However, there are labs that analysis the urine for organic acid abnormalities from a **pathological/non-genetic perspective**.

Many of the blocked metabolic pathways can be <u>treated nutritionally</u> once they have been identified.

Common Clinical Laboratory and Patient Assessment Indications for Ordering a Urinary Organic Acid Test

Patient Assessment Indications

- Neonates and infants with unexplained life-threatening phenotype
- Infants, children and selected adults with unexplained cognitive or developmental regression
- Infants, children and selected adults with unexplained epilepsy
- Any age individual with unexplained encephalopathy
- Infants, children and selected adults with two or more unexplained CNS peoblems
- Infants, children and selected adults with unexplained growth retardation or failure to thrive
- Any age individual with unexplained fasting intolerance
- Any age individual with exercise intolerance

Common Clinical Laboratory and Patient Assessment Indications for Ordering a Urinary Organic Acid Test

Laboratory Indications

- Neonates with unexplained moderate or marked ketouria
- Neonates, infants, children and selected adults with unexplained anion gap acidosis.
- Neonates, infants, children and selected adults with unexplained hyperammonemia
- Neonates, infants, children and selected adults with unexplained hypoglycemia
- Neonates, infants, children and selected adults with unexplained lactic acidemia

Common Clinical Laboratory and Patient Assessment Indications for Ordering a Urinary Organic Acid Test

Non-Genetic Pathologic / Functional Conditions

- **Fatigue/Weakness** (decreased energy production – Krebs cycle, fatty acid metabolism, carbohydrate metabolism)
- **Fibromyalgia**/chronic fatigue
- **Chemical Sensitivity**: detoxification /dysfunction markers
- **Neurological Signs and Symptoms**: cognitive impairment, headaches, irritability and motor impairment. Assess for nutritional deficiencies esp. B-vitamins and neurotransmitter metabolism dysfunction
- **Candida/GI dysbiosis**: dysbiosis markers
- **Oxidative Stress**: Oxidative damage marker and antioxidant levels

Organic Acid Laboratory Interpretation

The information content of an organic acid profile is high, but the interpretation is **simplified** by keeping in mind that the results **supplies answers to a few clinically relevant questions**

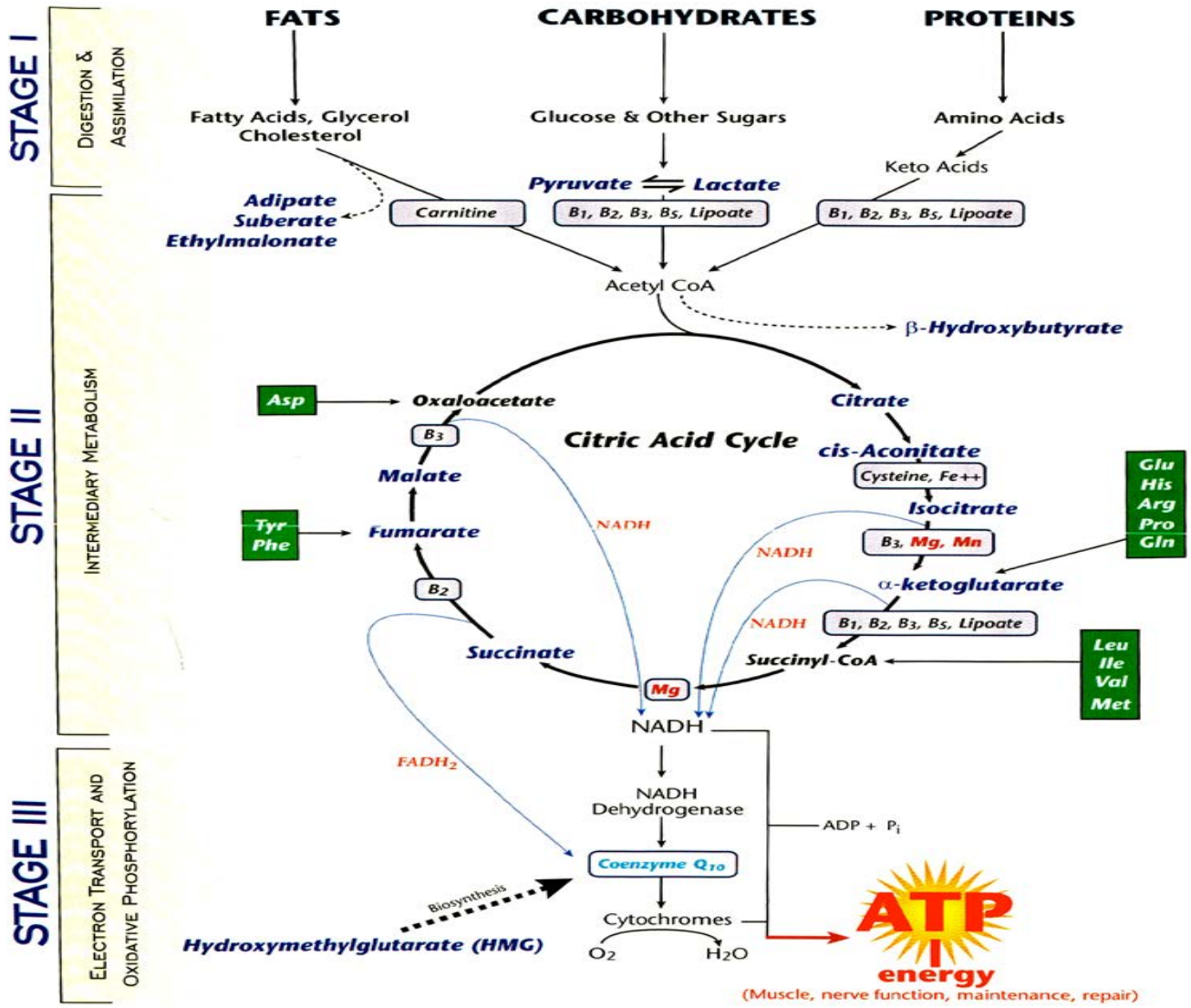
Clinically Relevant Questions (page 1 of 2)

- Are there signs of inborn errors of metabolism?
- Is mitochondrial energy production adversely affected? (Mitochondrial Function Assessment)
- Are functional nutrient deficiencies present? (B-complex Vitamin Markers)
- Does altered neurotransmitter turnover reveal symptom origins? (Neurotransmitter Metabolism Markers)

Clinically Relevant Questions (page 2 0f 2)

- Are antioxidants nutrients protecting against oxidative stress? (Oxidative Damage and Antioxidant Markers)
- Is there a high toxin load and is this adversely affecting detoxification capacity? (Detoxification Markers)
- Are symptoms related to excessive growth of bacteria and fungi in the gut? (Intestinal Dysbiosis Markers)

Mitochondrial Functional Assessment



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Sample Report

Ranges are for ages 13 and over	Results mcg/mg creatinine		Quintile Ranking (1st 2nd 3rd 4th 5th)	95% Reference Range
Nutrient Markers				
Fatty Acid Metabolism *(Carnitine & B2)*				
1. Adipate	6.3	H	6.2	<= 11.1
2. Suberate	0.7		2.1	<= 4.6
3. Ethylmalonate	0.9		3.6	<= 6.3
Carbohydrate Metabolism *(B1, B3, Cr, Lipoic Acid, CoQ10)*				
4. Pyruvate	2.4		3.9	<= 6.4
5. L-Lactate	2.6		12.6	1.6-57.1
6. ß-Hydroxybutyrate	<DL*		2.1	<= 9.9
Energy Production (Citric Acid Cycle) *(B comp., CoQ10, Amino acids, Mg)*				
7. Citrate	814	H	601	56-987
8. Cis-Aconitate	85	H	51	18-78
9. Isocitrate	214	H	98	39-143
10. a-Ketoglutarate	16.0		19.0	<= 35.0
11. Succinate	17.3	H	11.6	<= 20.9
12. Fumarate	0.68	H	0.59	<= 1.35
13. Malate	0.8		1.4	<= 3.1
14. Hydroxymethylglutarate	1.8		3.6	<= 5.1

Sample Report

Ranges are for ages 13 and over	Results mcg/mg creatinine		Quintile Ranking 1st 2nd 3rd 4th 5th	95% Reference Range
B-Complex Vitamin Markers *(B1, B2, B3, B5, B6, Biotin)*				
15. a-Ketoisovalerate	0.16		0.25	<= 0.49
16. a-Ketoisocaproate	0.12		0.34	<= 0.52
17. a-Keto-ß-methylvalerate	0.23		0.38	<= 1.10
18. Xanthurenate	0.21		0.34	<= 0.46
19. ß-Hydroxyisovalerate	6.0		7.6	<= 11.5
Methylation Cofactor Markers *(B12, Folate)*				
20. Methylmalonate	0.7		1.7	<= 2.3
21. Formiminoglutamate	0.1		1.2	<= 2.2
Cell Regulation Markers				
Neurotransmitter Metabolism Markers *(Tyrosine, Tryptophan, B6, antioxidants)*				
22. Vanilmandelate	4.2	H	1.6 – 3.9	1.2-5.3
23. Homovanillate	3.2		1.9 – 5.7	1.4-7.6
24. 5-Hydroxyindoleacetate	2.1		2.1 – 5.6	1.6-9.8
25. Kynurenate	0.9		1.0	<= 1.5
26. Quinolinate	1.8		4.0	<= 5.8
27. Picolinate	2.9		8.0	2.8-13.5
Oxidative Damage and Antioxidant Markers *(Vitamin C and other antioxidants)*				
28. p-Hydroxyphenyllactate	0.31		0.39	<= 0.66
29. 8-Hydroxy-2-deoxyguanosine	1.7		5.3	<= 7.6

(Units for 8-hydroxy-2-deoxyguanosine are ng/mg creatinine)

Sample Report

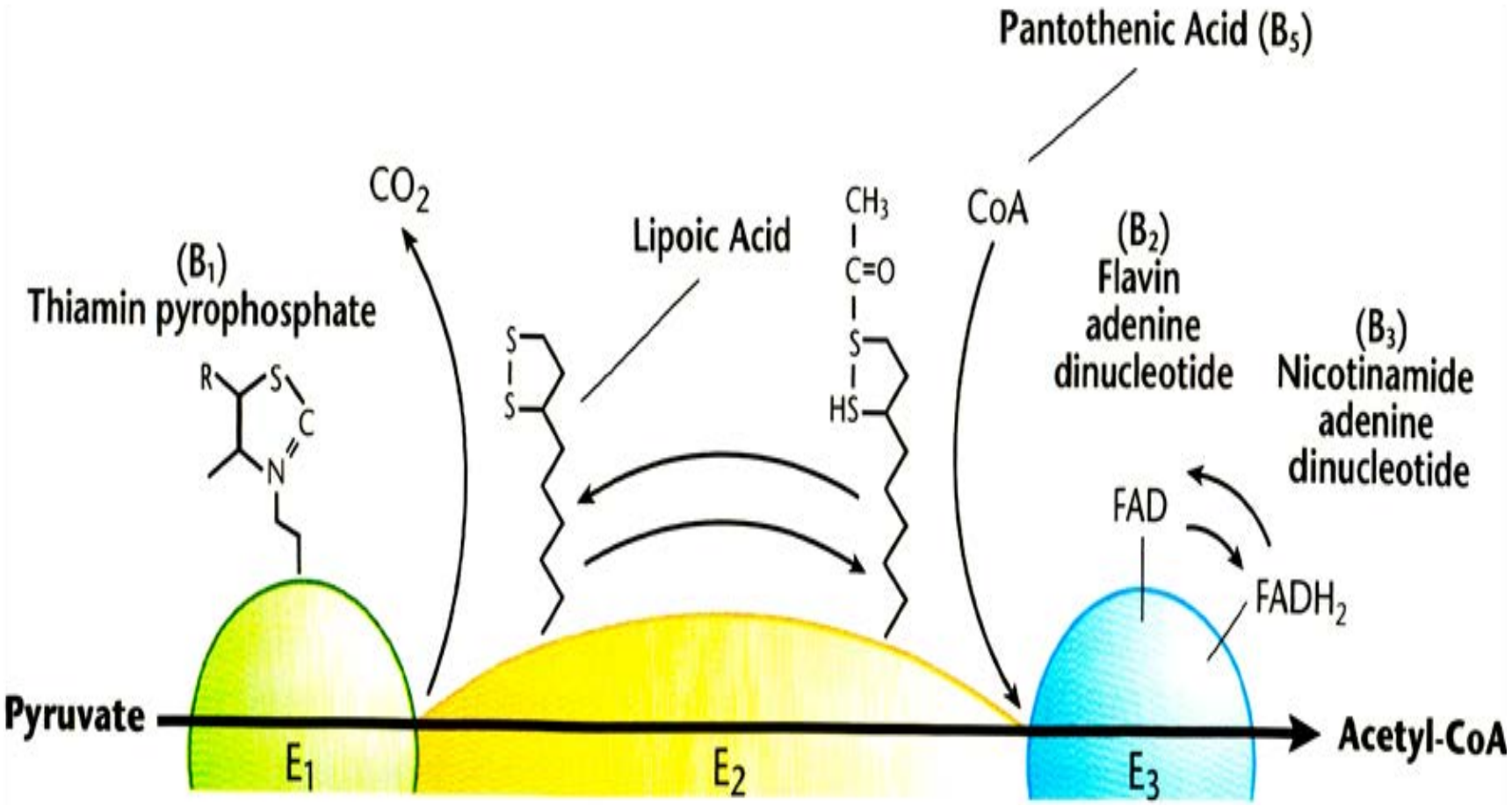
Ranges are for ages 13 and over	Results mcg/mg creatinine		Quintile Ranking 1st 2nd 3rd 4th 5th	95% Reference Range
Toxicants and Detoxification				
Detoxification Indicators				
(Arg, NAC, Met, Mg, antioxidants)				
30. 2-Methylhippurate	0.083		0.084	<= 0.192
31. Orotate	0.27		0.69	<= 1.01
32. Glucarate	10.1	H	6.3	<= 10.7
33. a-Hydroxybutyrate	0.35	H	0.3	<= 0.9
34. Pyroglutamate	115	H	59	28-88
35. Sulfate	958		958 2347	690-2988
Compounds of Bacterial or Yeast/Fungal Origin				
Bacterial - general				
36. Benzoate	<DL*		0.6	<= 9.3
37. Hippurate	164		548	<= 1070
38. Phenylacetate	<DL*		0.11	<= 0.18
39. Phenylpropionate	<DL*			<= 0.06
40. p-Hydroxybenzoate	<DL*		1.1	<= 1.8
41. p-Hydroxyphenylacetate	6		19	<= 34
42. Indican	29		64	<= 90
43. Tricarballylate	0.18		0.73	<= 1.41
L. acidophilus / general bacterial				
44. D-Lactate	0.5		1.9	<= 4.3
Clostridial species				
45. 3,4-Dihydroxyphenylpropionate	<DL*			<= 0.05
Yeast / Fungal				
46. D-Arabinitol	38	H	36	<= 73

Creatinine = 190 mg/dL

* <DL = less than detection limit

** >LIN = greater than linearity limit

Mitochondrial Functional Assessment



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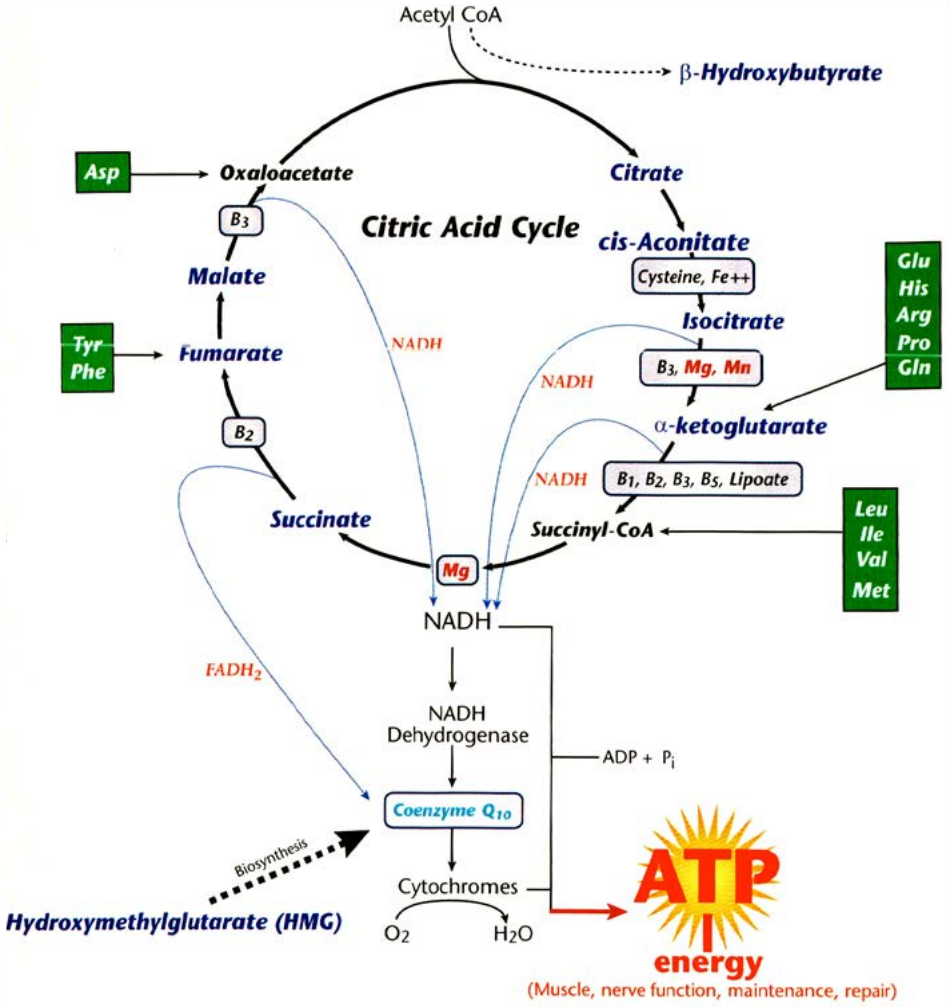
Mitochondrial Functional Assessment



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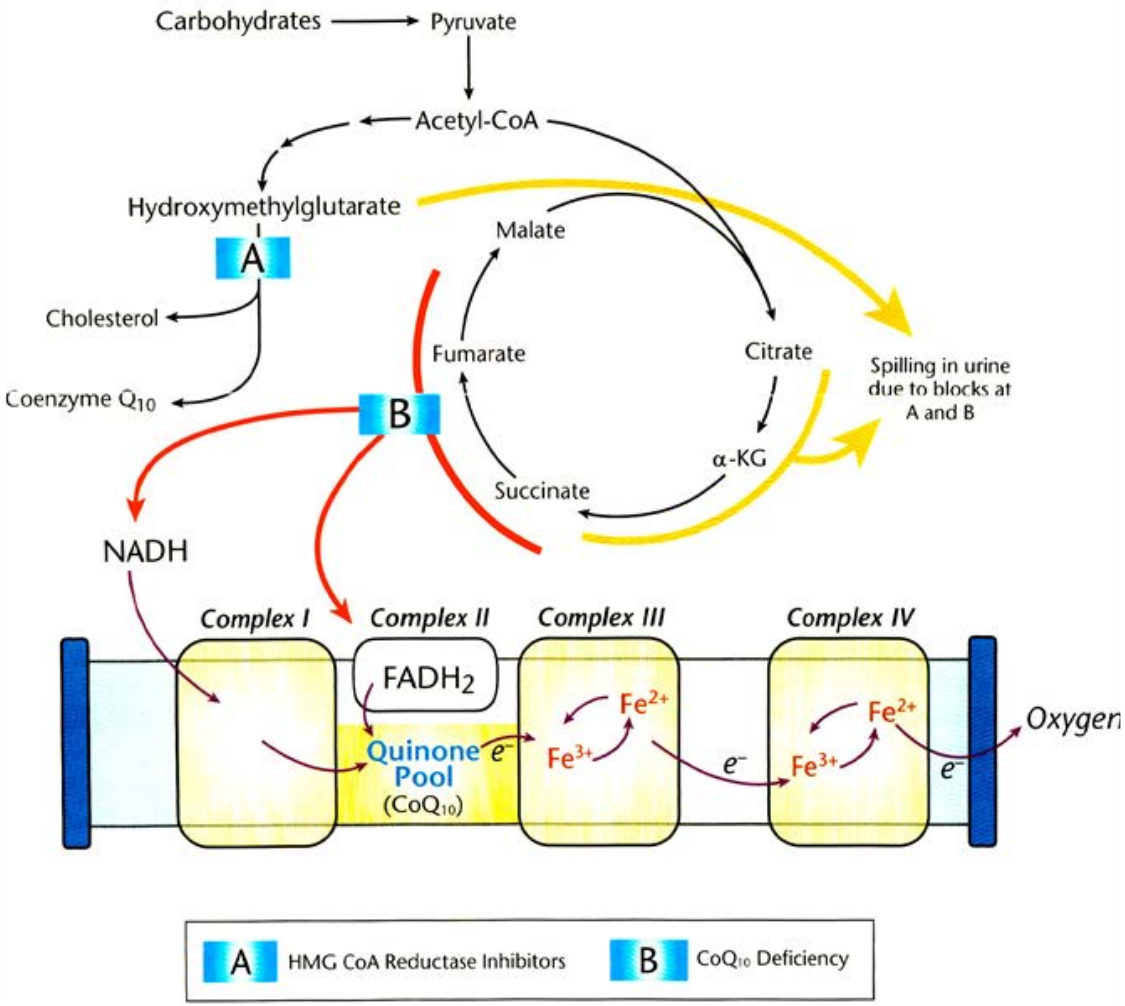
Mitochondrial Functional Assessment



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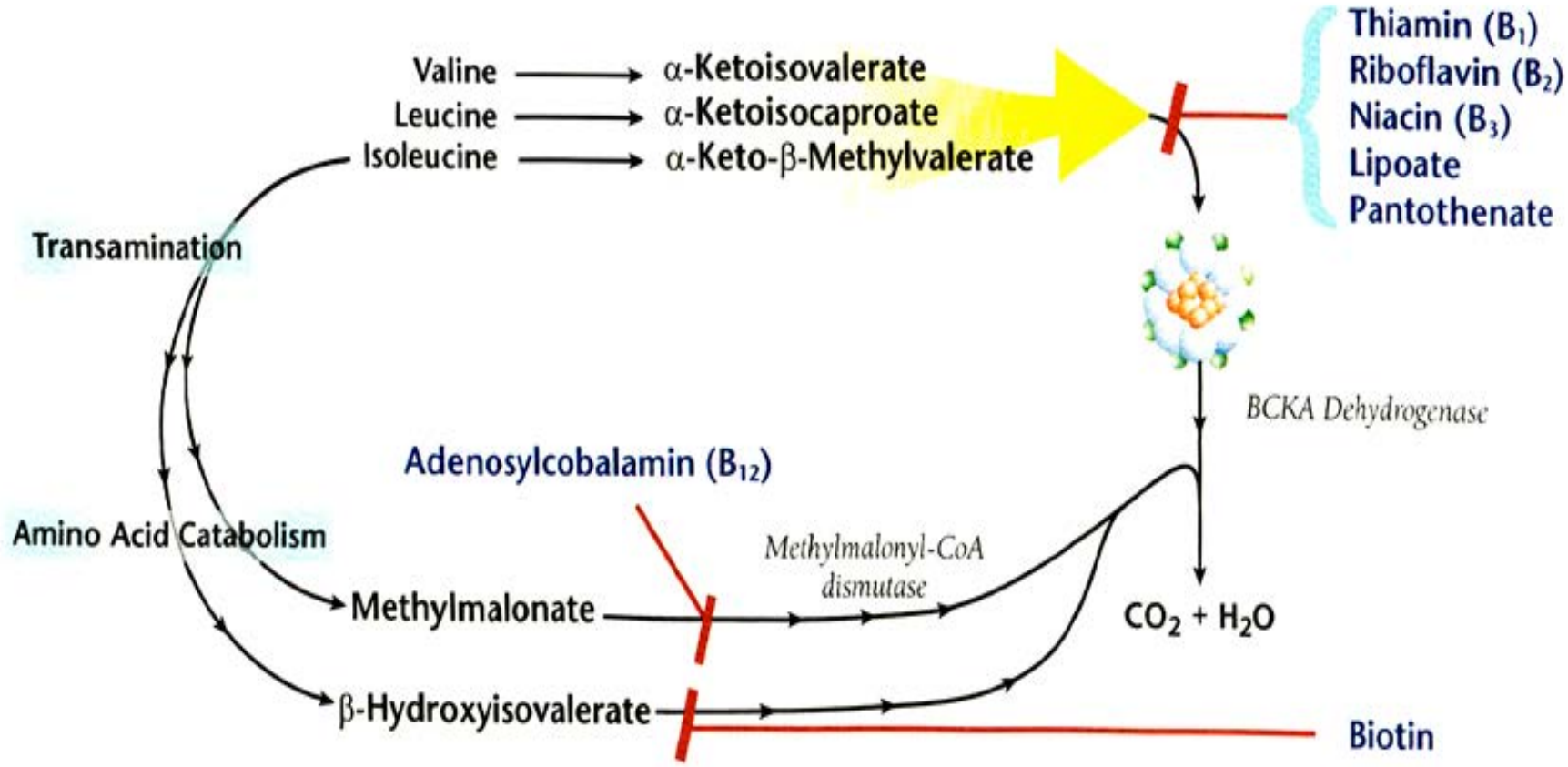
Nutritional Markers

- The degrading of amino acids requires many **vitamin cofactors**.
- During degradation intermediate acids are formed, which require these cofactors for continued catabolism.

Nutritional Markers



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Neurotransmitters Markers

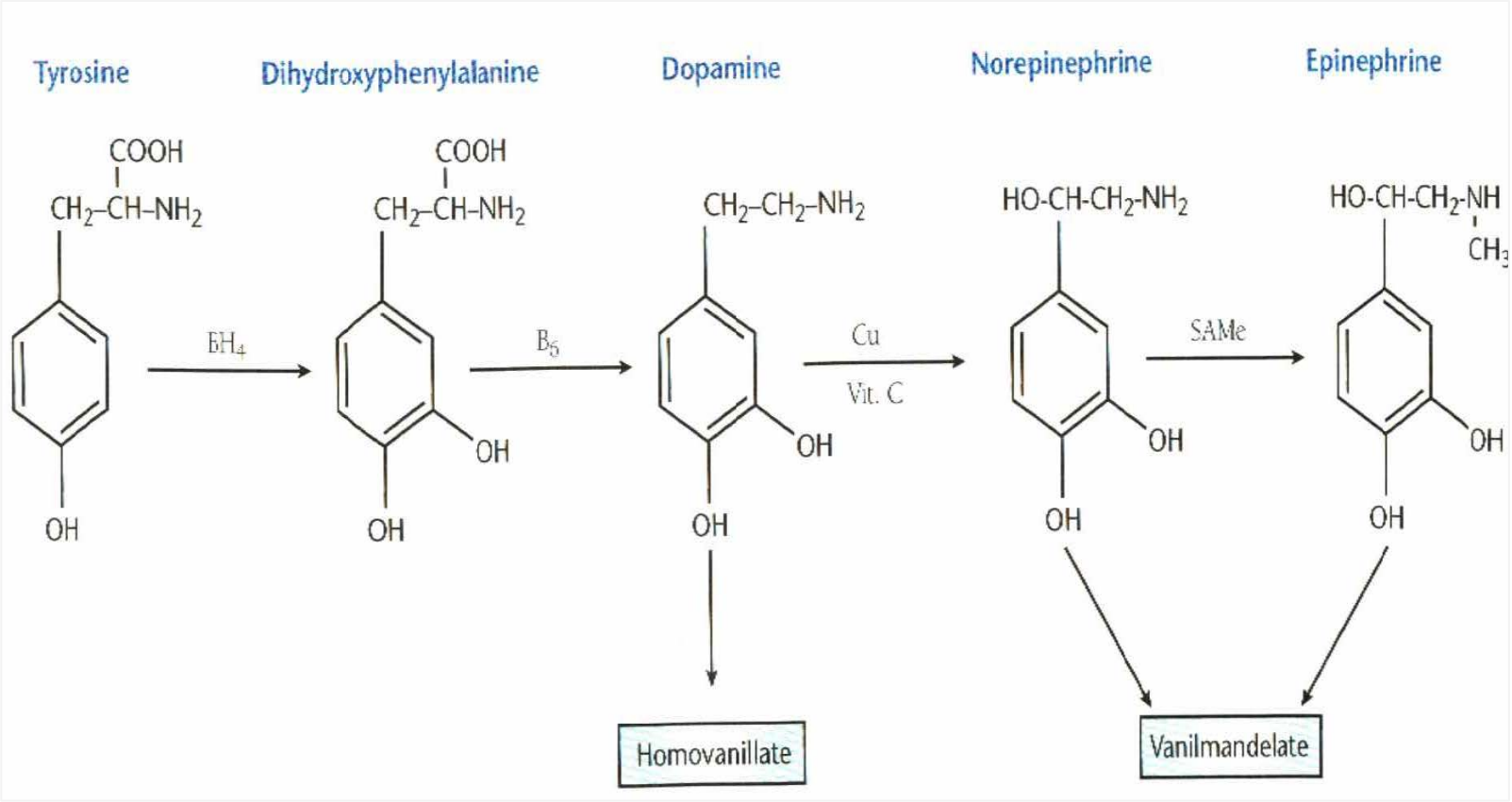
- Neurotransmitter Metabolism Markers (**Metabolites**)
- Neurotransmitters: include biogenic amines, amino acids, purines, and neuropeptides that are released from the neurons and change the electrical activity of other neurons and myocytes.
- Neurotransmitter disorders represent as enigmatic and enlarging group of neurometabolic conditions.

Inherited Neurotransmitter Disorders

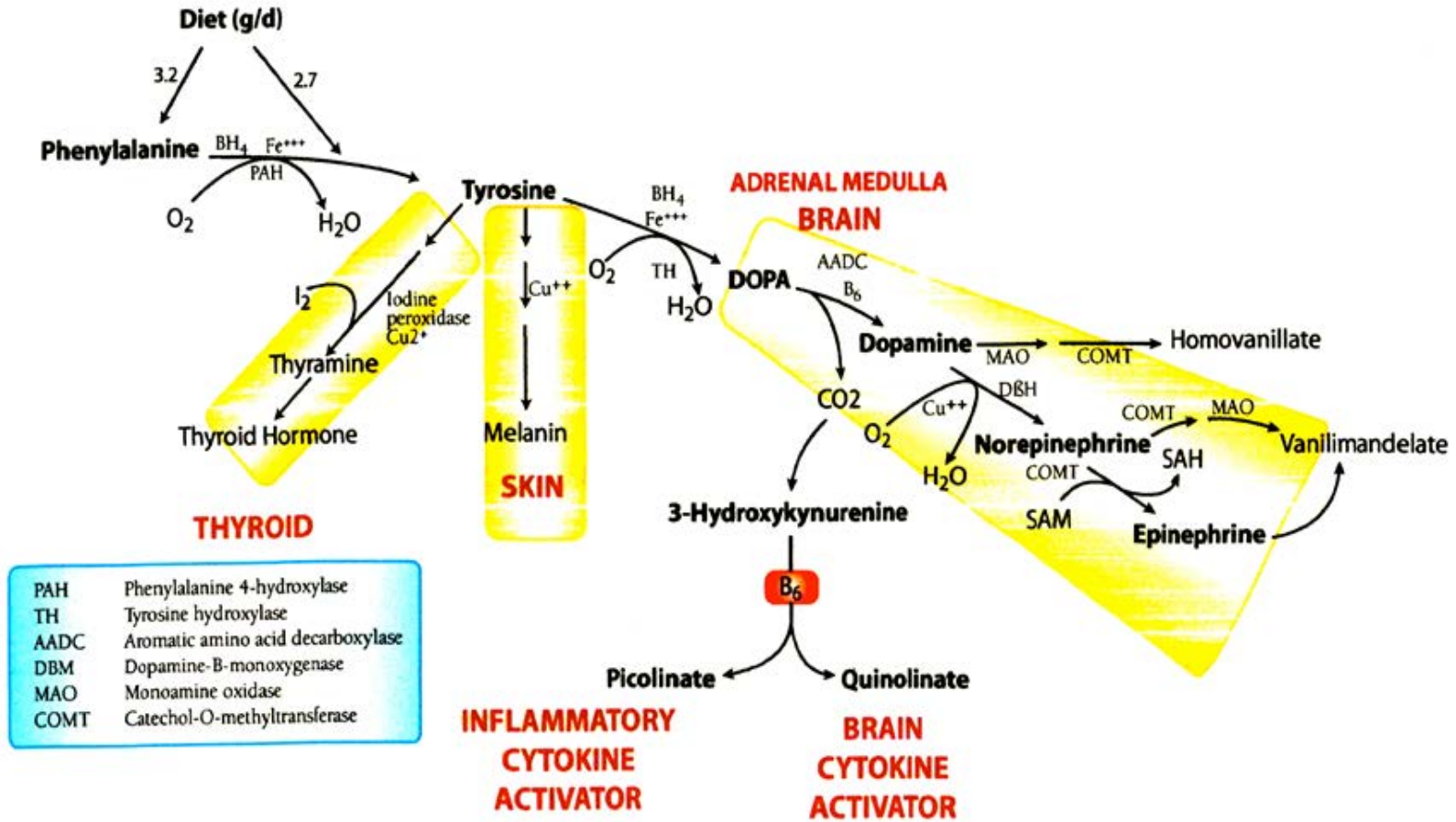
- **Primary defects of neurotransmitter metabolism and transport.**
- Include defects of catecholamine, serotonin, biopterin, glycine, pyridoxine and gamma amino butyric acid (GABA) metabolism.

- Defects of **catecholamine** (dopamine, epinephrine and norepinephrine) and **serotonin metabolism**, also called monoamine or biogenic amine metabolism, are the **most widely known** and investigated group of neurotransmitter disorders.

Neurotransmitter



Neurotransmitter



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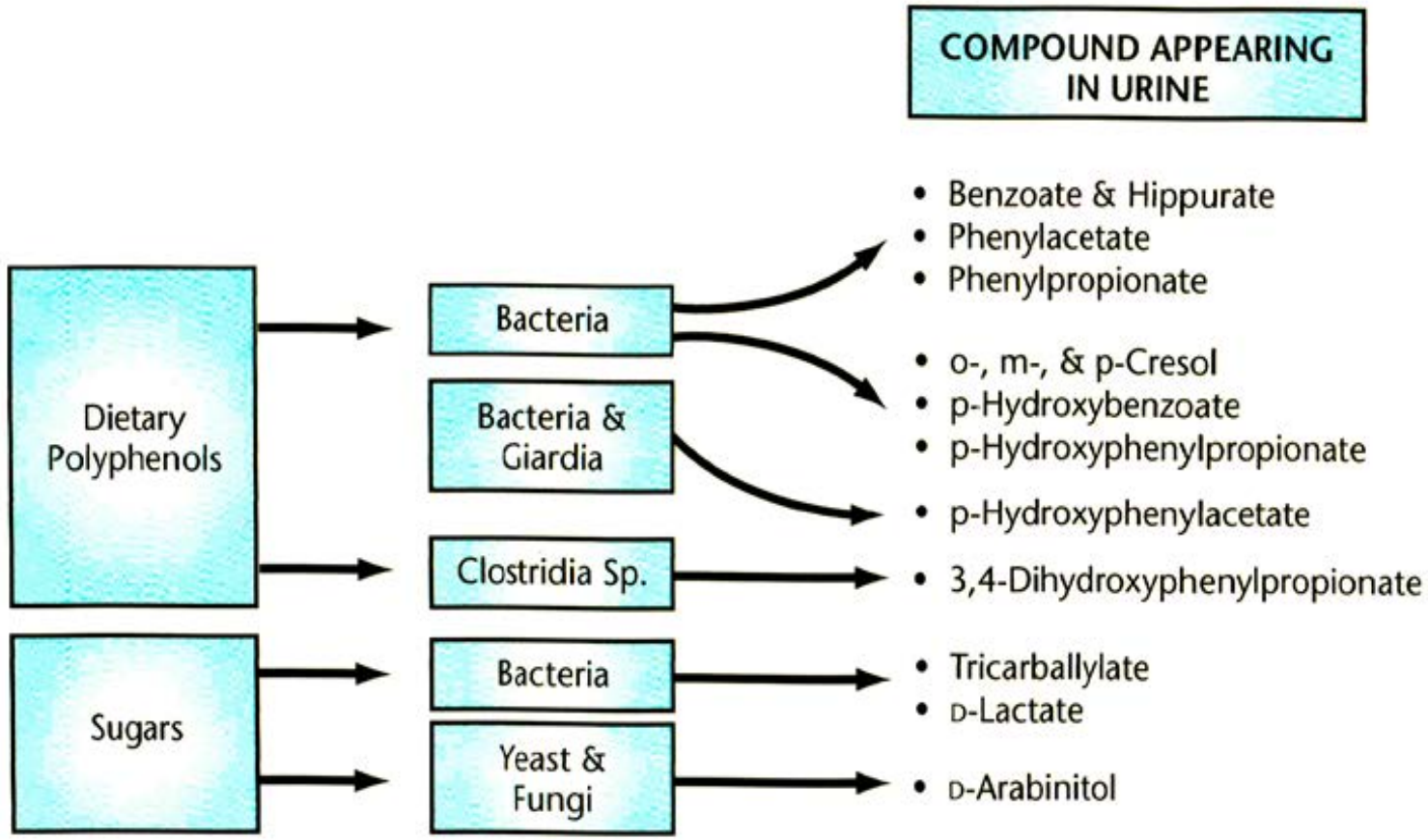
DNA Damage, Detoxification and Intestinal Dysbiosis Markers

- Urinary organic acid testing provides significant insight about DNA oxidative damage, detoxification, and gastrointestinal dysbiosis
- **8-hydroxy-2'-deoxyguanosine (8-OHdG)** **Marker of DNA Damage**
- Exogenous toxin accumulation and endogenous detoxification
- Metabolic products of bacterial and yeast infections

Intestinal Dysbiosis Markers



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Summary

- Organic acid testing provides valuable insight to the functioning of many biochemical processes in the body via spillage of **organic acid end products into the ur**ine.

- Aside from assessing for inborn errors of metabolism, organic acid testing at its very basic level **provides urinary markers of nutritional deficiencies of many pathways including central energy pathways.**

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DC, DABCI, DACBN, CFMP, CIHP, BCTN

Next lesson: Part 8 of 8

Laboratory Test Interpretation with Case Presetntations