The Great Plains Laboratory
GPL Academy
Practitioner Workshops

BEYOND THE BASICS:

ADVANCED ORGANIC ACIDS TESTING STRATEGIES

KURT WOELLER, DO

Organic Acids Test (OAT) Introduction and Overview of its Sections and Common Markers

The Great Plains Laboratory
GPL Academy
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BEYOND THE BASICS:

ADVANCED ORGANIC ACIDS TESTING STRATEGIES

I, Kurt N. Woeller, DO, have the following commercial relationships to disclose:

- Founder of Integrative Medicine Academy
- Consultant for Great Plains Laboratory

Disclaimer

- The material contained within this presentation is not intended to replace the services and/or medical advice of your personal licensed health care professional.
- This material is for educational purposes only
- This information is not meant to encourage diagnosis and treatment of disease.
- Any application of suggestions set forth in the following portions of this presentation is at the reader’s discretion.
- Implementation and/or experimentation with any supplements, herbs, dietary changes, medications, and/or lifestyle changes, etc., is done so at your sole risk and responsibility.

The Organic Acids Test

- The organic acids test (OAT) is a compilation of chemical metabolites that are representative of various endogenous biochemical pathways linked to cellular metabolic imbalances which can be linked to various diseases or disorders:
  - *Elevated succinic acid is linked to mitochondria dysfunction often caused by environmental chemical exposure.*
- Certain OAT markers (those found on page 1) are representative of intestinal colonization or overgrowth of opportunistic organisms.
  - *Tartaric acid is linked to aspergillus mold exposure and colonization*
- The OAT is separated into various sections each representative of individual metabolic pathways or nutrient status.

The Organic Acids Test

- It is important to understand that certain sections on the OAT, and their associated markers, may influence other sections on the test:
    - *Elevated tartaric, linked to aspergillus mold exposure, can cause a high oxalic acid which can be associated with mitochondrial dysfunction.*
- Pattern recognition within the organic acids test is an ongoing area of study. In many situations it is not just one marker being elevated that is clinically significant (although it can be), but what that elevated marker means to the clinical picture of your patient and its potential relationship to other markers on the OAT:
    - *High succinic acid can be associated with environmental chemical exposure causing mitochondria problems. There may be an elevated citric acid too linked to oxidative stress. This often occurs when pyroglutamic acid is elevated indicating a glutathione deficiency.*

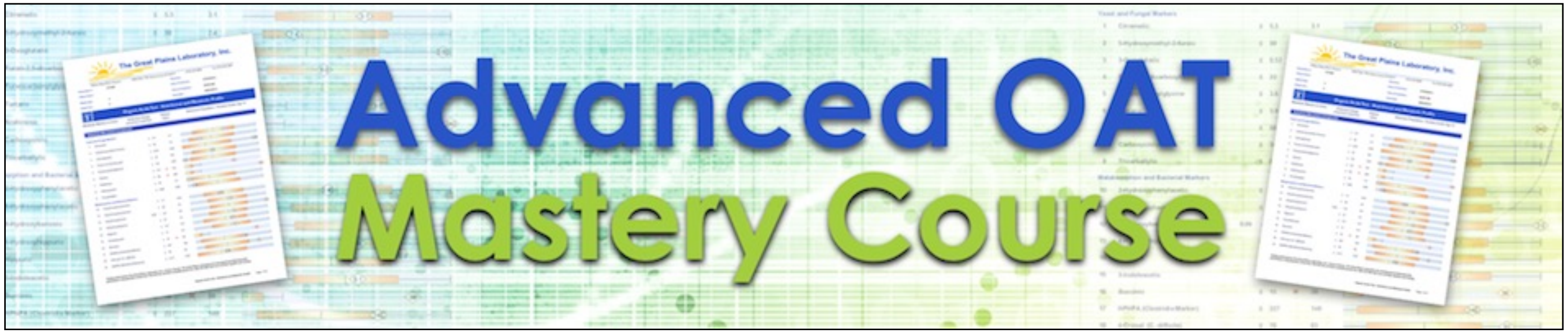
OAT Seminar Goals

- To provide an overview of various sections on the Organic Acids Test (OAT) from Great Plains Laboratory and how they relate to one another.
- To provide information about specific markers from the OAT and what they can indicate clinically for an individual:
  - *This seminar focuses on what is seen most common in practice with regards to the OAT.*
- To show how specific markers from the OAT can relate to other tests from Great Plains Laboratory.

OAT Seminar Goals

- To provide clinical insight regarding various OAT examples based on practice experience:
  - *Many OATs (approximately 80%) that you will see from a variety of patients (regardless of their diagnosis) <u>will often</u> have similar markers.*
- To provide various intervention options certain problems, e.g., candida, clostridia, high oxalate.
- To provide a framework for quickly interpreting the OAT and inspire a desire for further learning.

AdvancedOATMasteryCourse.com



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Key Point

Each OAT needs to be applied clinically to your patient and treatments not just implemented based on test markers.

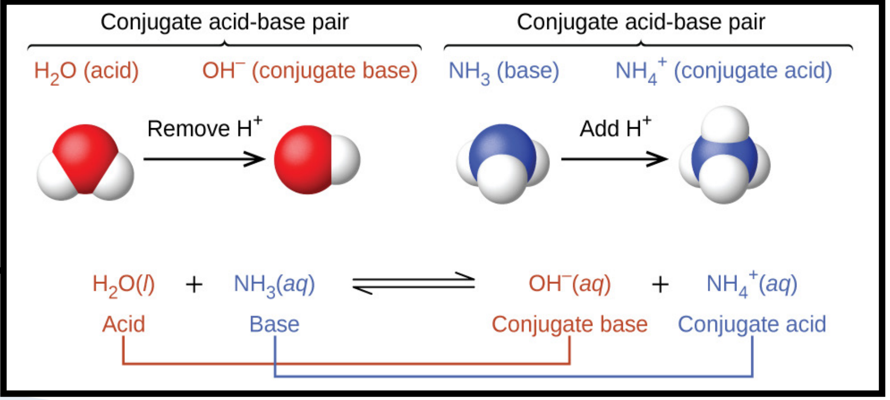
Who is the OAT beneficial for?

- Autism-spectrum disorders
- ADD/ADHD
- Autoimmune
- Chronic fatigue
- Digestive problems
- Metabolic disorders
- Mental health disorders
- Neurological disorders

Any individual with a chronic health condition where you suspect that metabolic imbalances and/or toxins may be a causative or contributing factor.

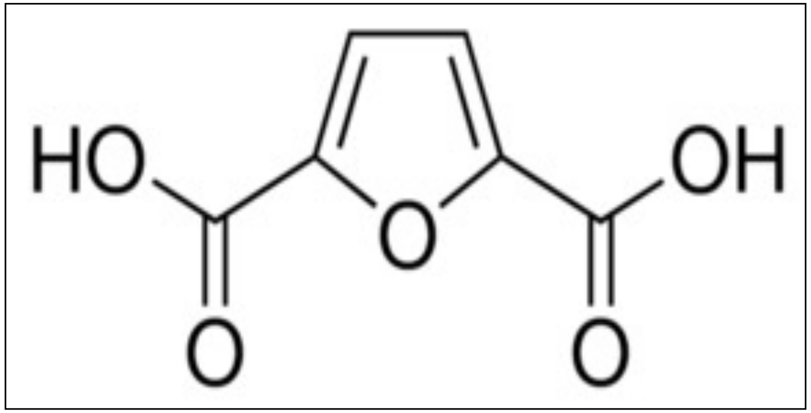
What are Organic Acids (OA)?

- Organic acids are chemical compounds excreted in the urine of mammals that are products of metabolism:
  - *Often present at 100X their concentration compared to blood*
- Organic acids are organic compounds that are acidic:
  - *Lactic acid (the conjugate base is lactate)*
- Organic acids are substances in which carbon and hydrogen are always present, but may also contain the elements of oxygen, nitrogen, sulfur and phosphorus:
  - *Carboxyl (-COOH)*
  - *Alcohol (-OH)*
  - *Thiol (-SH)*

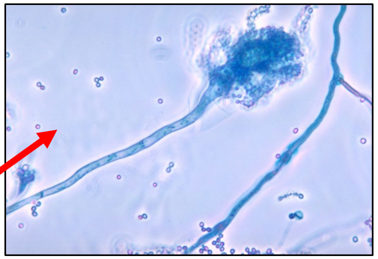


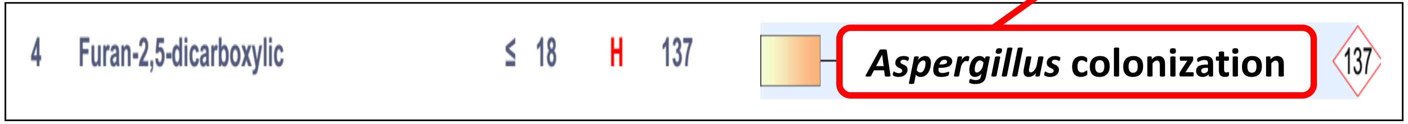
Source: *https://chem.libretexts.org*

Organic Acid Example – *2,5-Furandicarboxylic Acid*



Marker #4 on the Organic Acids Test from Great Plains Laboratory





4	Furan-2,5-dicarboxylic	≤ 18	H	137	*Aspergillus* colonization	137

Case Reports > Integr Med (Encinitas). 2020 Aug;19(4):20-27.

Case Study: Rapid Complete Recovery From An Autism Spectrum Disorder After Treatment of Aspergillus With The Antifungal Drugs Itraconazole And Sporanox

Sidney Baker [1], William Shaw [2]

Abstract

Context: A child with symptoms placing him within the autism spectrum and with urine biochemical markers consistent with fungal (*Aspergillus*) colonization of the gastrointestinal tract was first treated with the antifungal probiotic *Saccharomyces boulardii.* A dramatic Herxheimer reaction provided strong clinical indications that mold colonization might be a factor in causing autism in this child.

Objective: The child's physician (Baker) wished to try a more potent antifungal therapy, itraconazole, in an attempt to reverse the child's autism since itraconazole is an especially effective agent against *Aspergillus* species.

Setting: The child was treated as an outpatient b

with an autism spectrum disorder.

Participant: A child with an autism spectrum disorder.

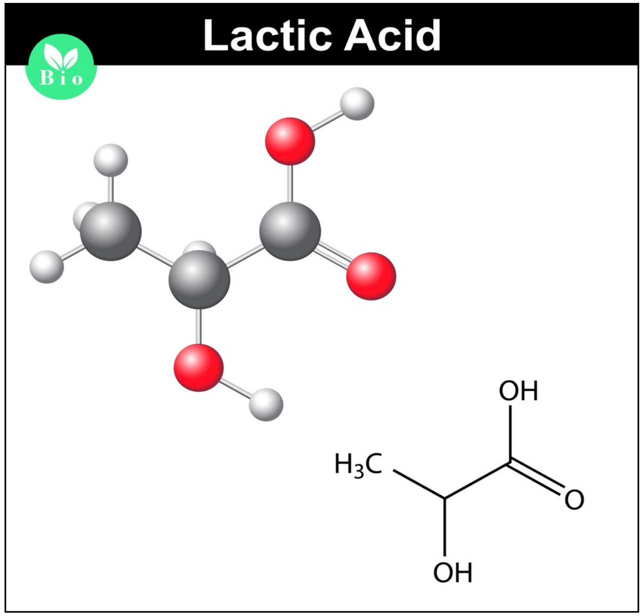
Intervention: The major intervention was increasing doses of the antifungal drug itraconazole. However, the Sporanox® brand of itraconazole gave the best results. The child was monitored twice weekly with liver function tests which remained normal throughout the therapy.

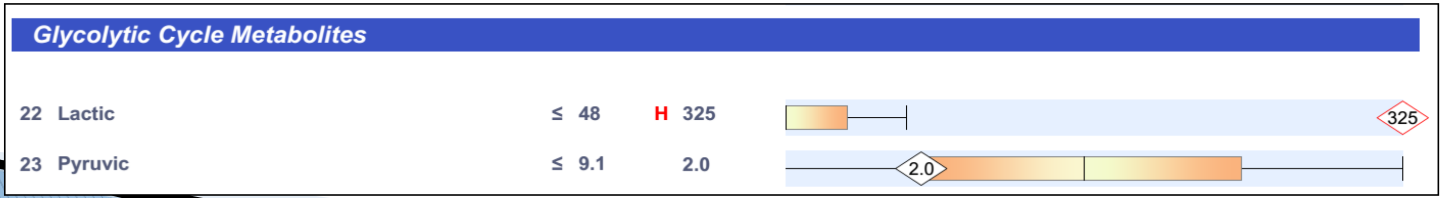
Results: The child had a complete recovery from all the symptoms of autism and in addition developed excellent academic, athletic, and musical skills. The recovery coincided with a marked reduction of urine markers of *Aspergillus* colonization.

Conclusions: Escalation of the dose of itraconazole resulted in a complete loss of all symptoms of autism over the course of three months. This rapid complete reversal of autism is consistent with several articles proposing mold in general and *Aspergillus* specifically as a potential major cause of autism.

Organic Acid Example - *Lactic Acid*

- **Lactic *(acid)*** – an organic acid that is the byproduct of glucose metabolism.
- Derived from pyruvic acid.




Glycolytic Cycle Metabolites

22	Lactic	≤ 48	H	325
23	Pyruvic	≤ 9.1		2.0

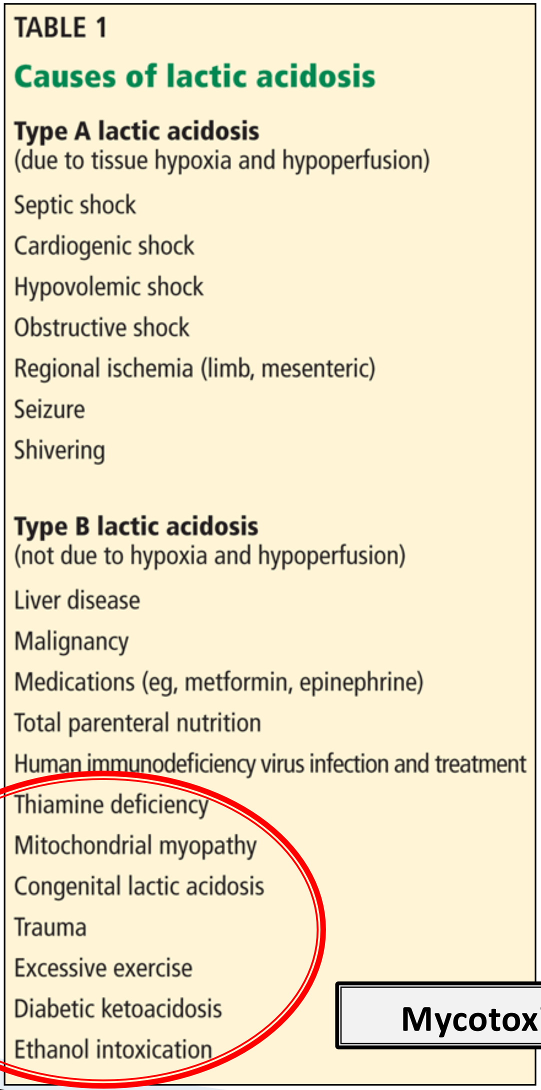


TABLE 1

Causes of lactic acidosis

Type A lactic acidosis
(due to tissue hypoxia and hypoperfusion)

Septic shock
Cardiogenic shock
Hypovolemic shock
Obstructive shock
Regional ischemia (limb, mesenteric)
Seizure
Shivering

Type B lactic acidosis
(not due to hypoxia and hypoperfusion)

Liver disease
Malignancy
Medications (eg, metformin, epinephrine)
Total parenteral nutrition
Human immunodeficiency virus infection and treatment
Thiamine deficiency
Mitochondrial myopathy
Congenital lactic acidosis
Trauma
Excessive exercise
Diabetic ketoacidosis
Ethanol intoxication

Mycotoxins

Lactic Acidosis

- Lactic acidosis is a high anion gap metabolic acidosis due to elevated lactic acid.
- This can occur from overproduction of lactic acid, decreased metabolism of lactic acid or both.
- There are two main types of lactic acidosis:
    - *Type A*
    - *Type B*
- D-lactic acidosis

Type A

- Most serious form of lactic acidosis
- Caused by lactic acid over-production in ischemic tissue via anaerobic generation of ATP from oxygen deprivation.
- Linked to hypoperfusion in hypovolemic, cardiac insufficiency and septic shock.
- Local tissue hypoxia, e.g., seizures, intense shivering
- Made worse by poor liver perfusion due to lack of clearance of lactic acid.
- Can occur from various hemoglobinopathies and lung diseases.

Type B

- Less serious form of lactic acidosis
- Local tissue hypoxia, e.g., vigorous exercise, seizures, intense shivering.
- Various medications such biguanide phenformins (e.g., metformin, glyburide, glipizide), liver insufficiency.
- Cancer
- Thiamine deficiency
- Mold exposure, i.e., producing mycotoxins

OAT Seminar Lectures

- Introduction to the Organic Acids Test *(lecture #1)*
- The role of the OAT in candida assessment *(lecture #2)*
- The role of the OAT in clostridia assessment *(lecture #3)*
- The role of the OAT in oxalate assessment *(lecture #4)*
- Indicators of other problems: *nutrient imbalances, fatty acid metabolites, etc*. *(lecture #1).*
- Neurotransmitter imbalances *(lecture #3 and #5)* and mitochondrial dysfunction assessment.

Mitochondria

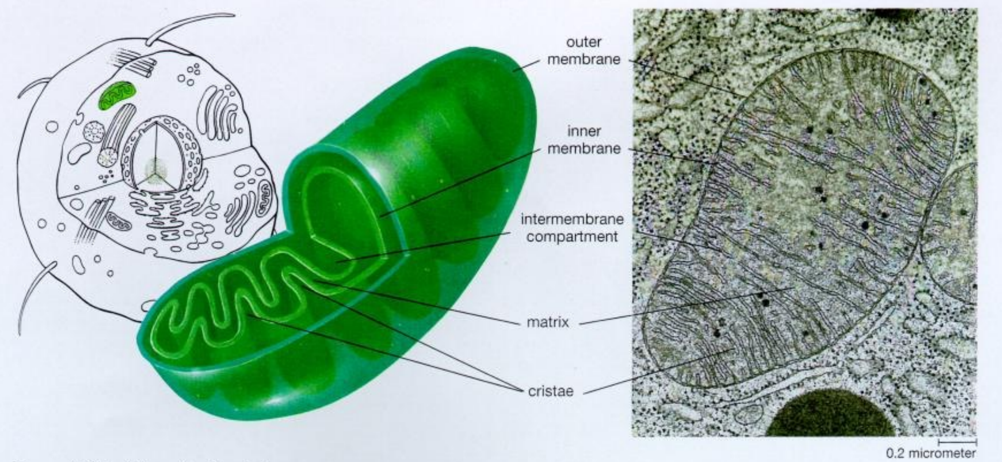
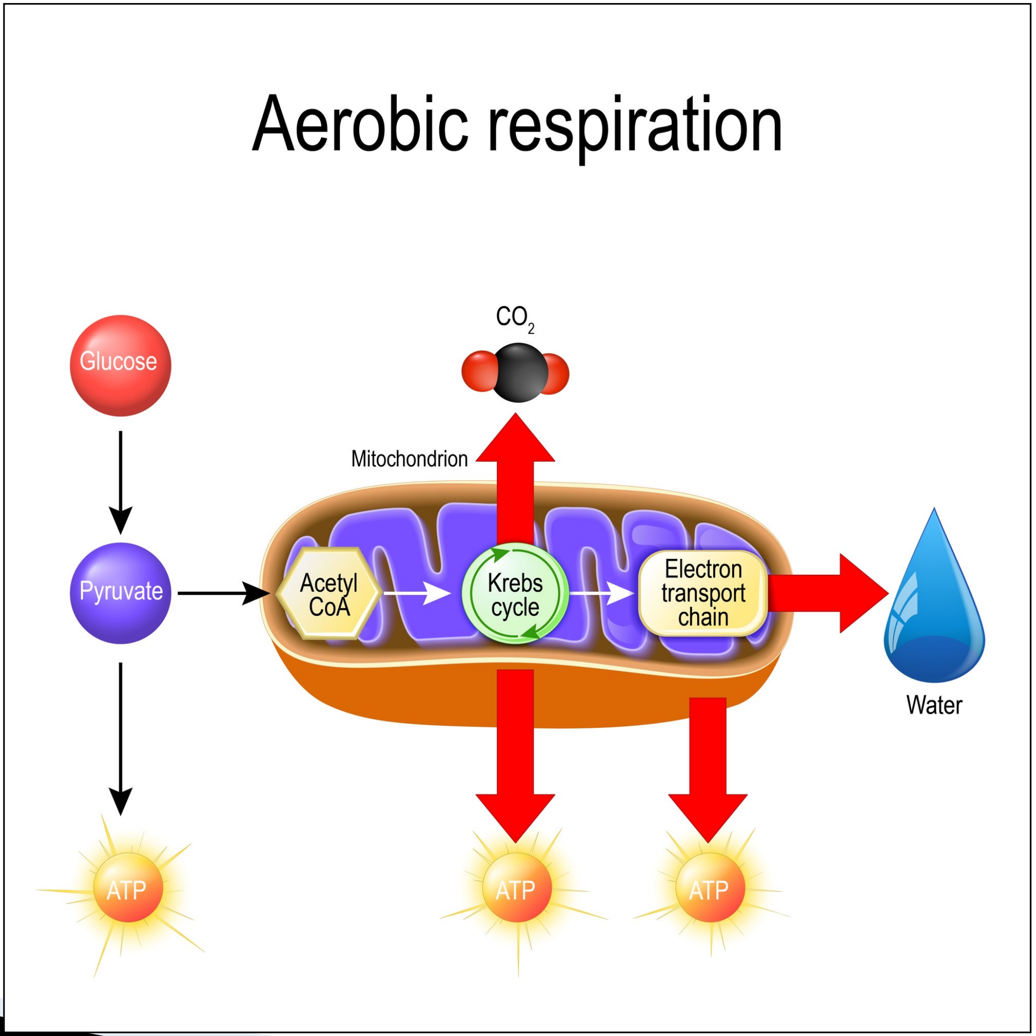
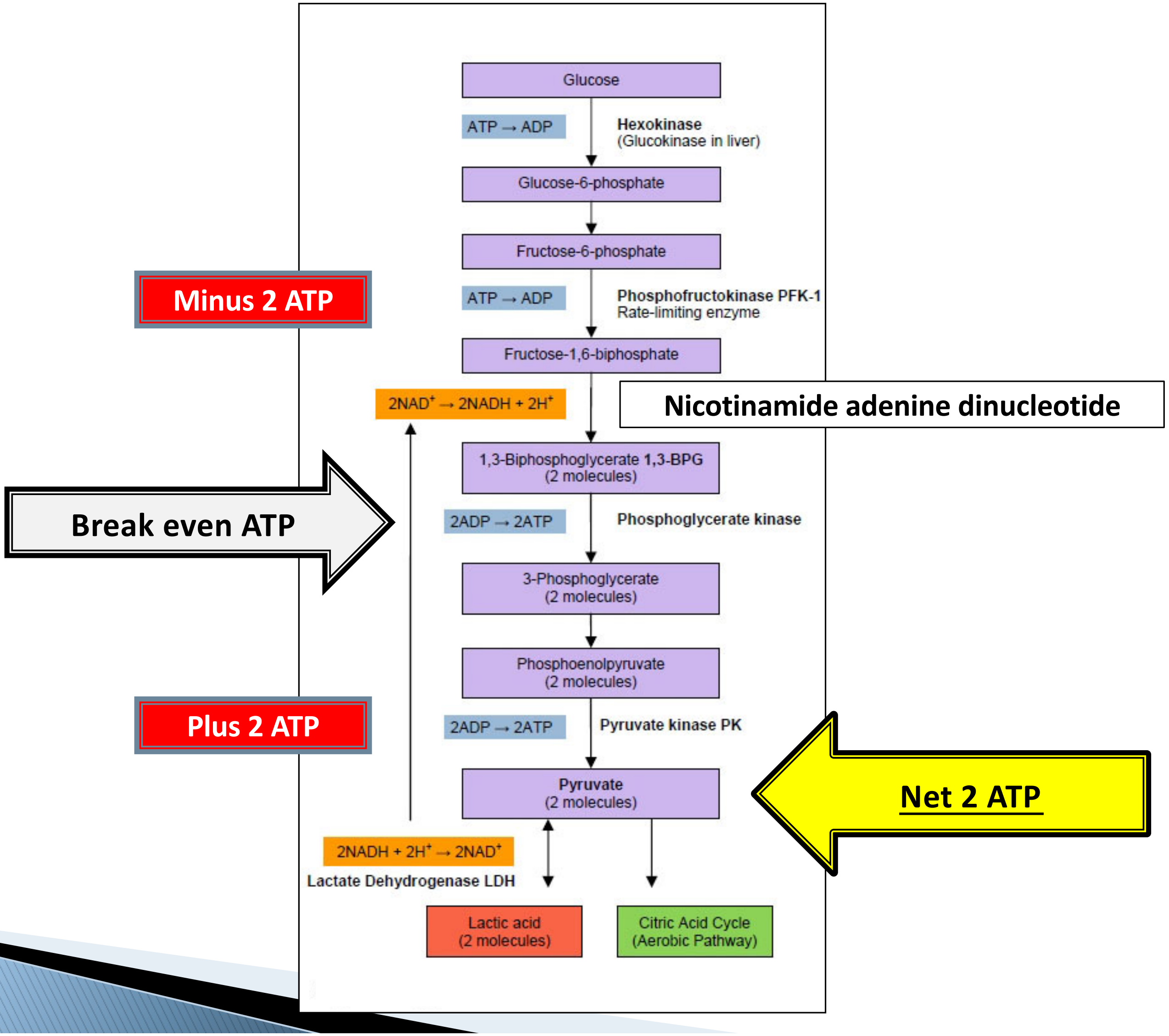


Figure 5-17 The mitochondrion

Mitochondria consist of a pair of membranes enclosing two fluid compartments, the intermembrane compartment between the outer and inner membranes and the matrix within the inner membrane. The outer membrane is smooth, but the inner membrane loops back and forth to form deep folds called cristae. Mitochondria are the site of aerobic metabolism.


Aerobic respiration
CO2
Glucose
Mitochondrion
Pyruvate
Acetyl CoA
Krebs cycle
Electron transport chain
Water
ATP
ATP
ATP



Minus 2 ATP

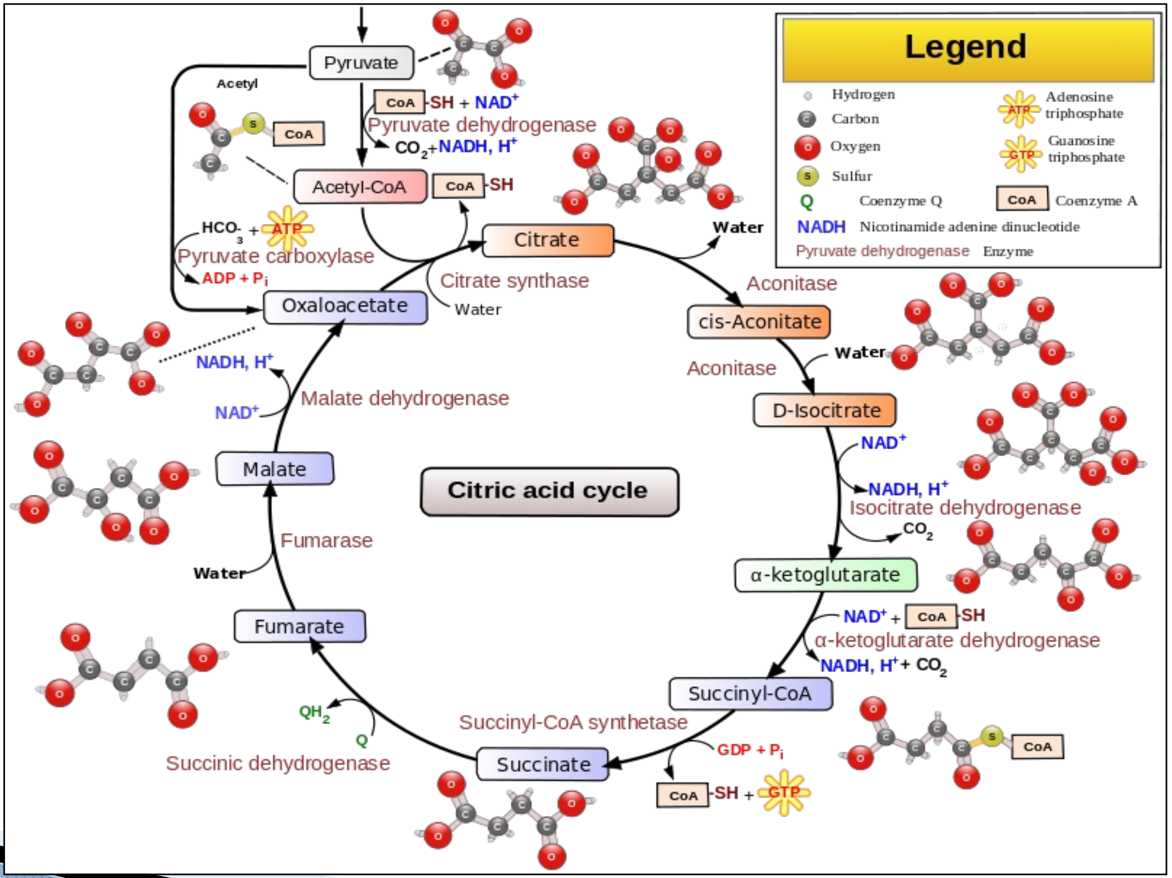
Nicotinamide adenine dinucleotide

Break even ATP

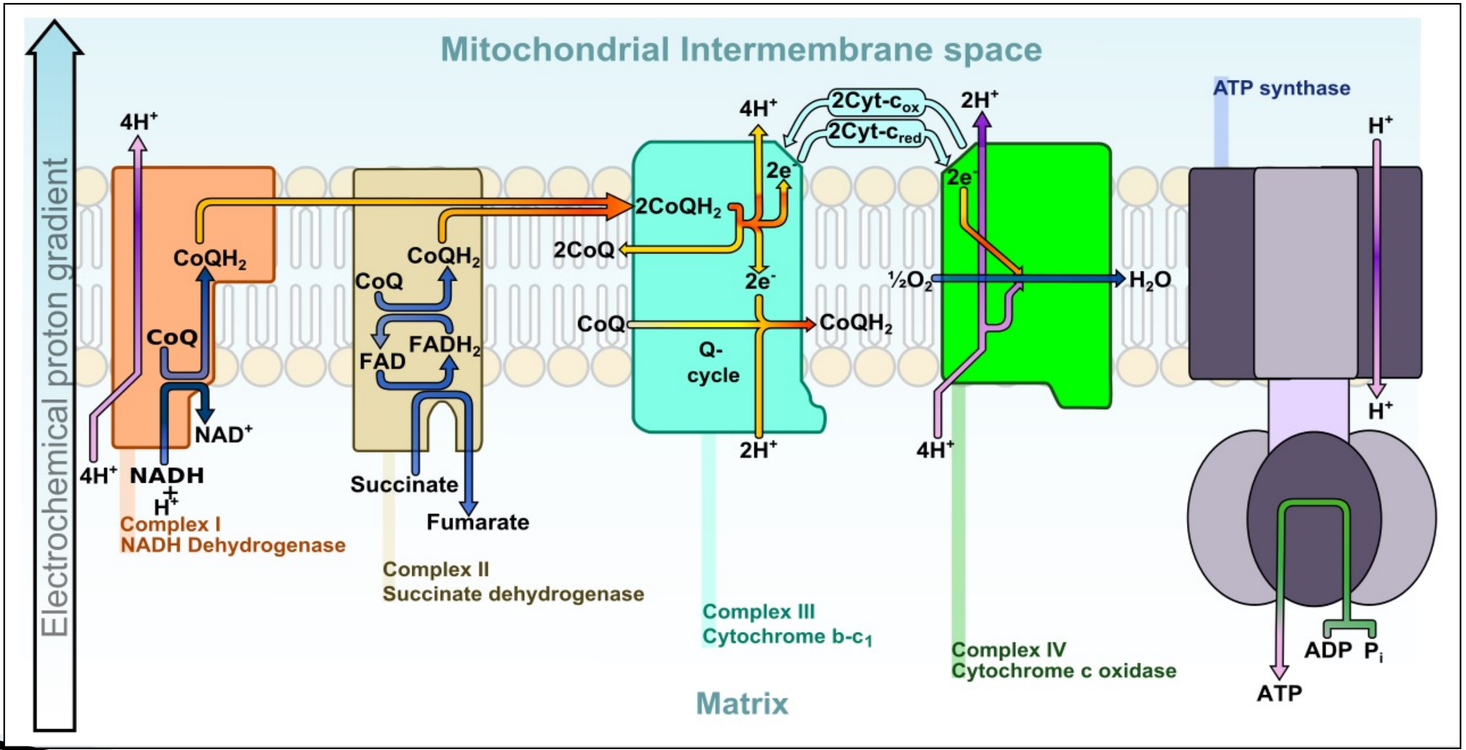
Plus 2 ATP

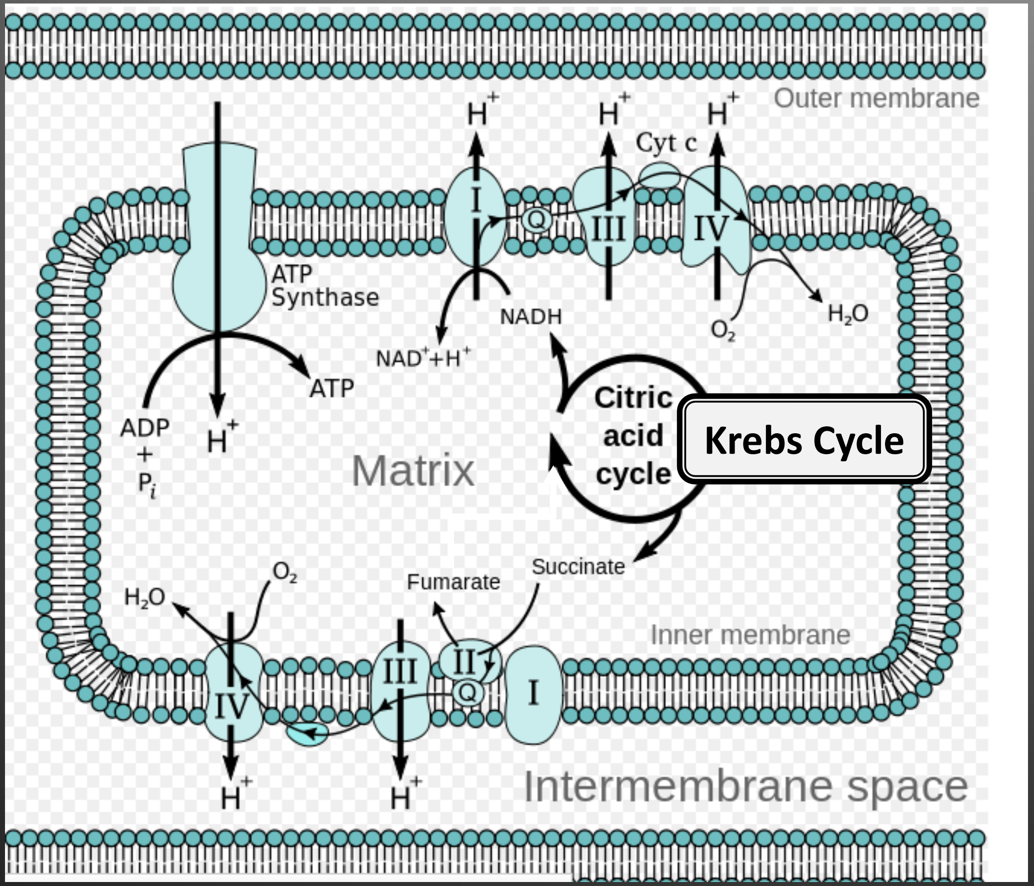
Net 2 ATP

Citric Acid Cycle *(aka Krebs Cycle)*



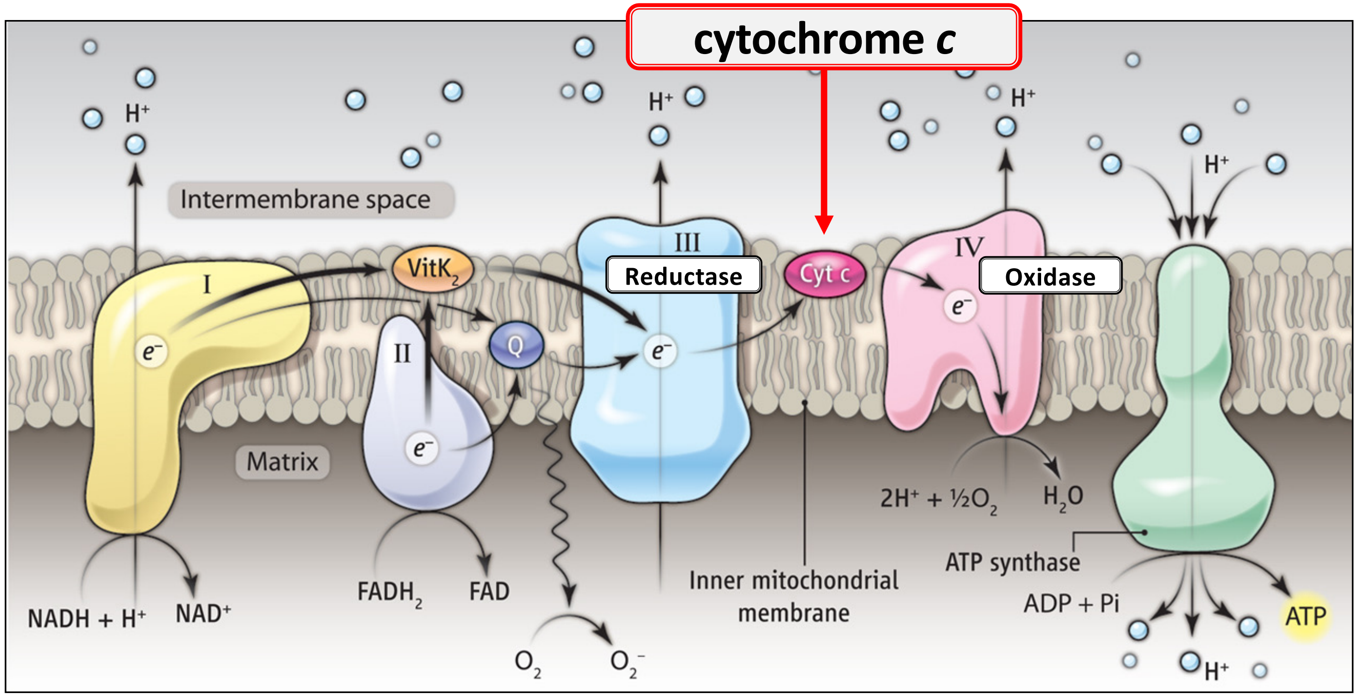
Electron Transport Chain
(aka Respiratory Chain)





Krebs Cycle

Wikipedia: Fvasconcellos 22:35, 9 September 2007 (UTC)

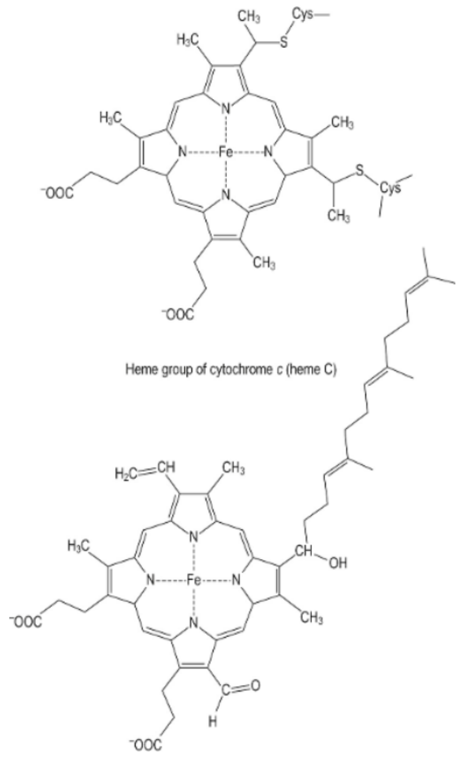


Energy obtained through the transfer of electrons (e^-) in the ETC is used by complex I (NADH coenzyme Q reductase), complex III (cytochrome bc_1), and complex IV (cytochrome c oxidase) to pump protons (H^+) from the mitochondrial matrix into the intermembrane space, creating a proton gradient. While electrons are transferred from complexes I and II to complex III by coenzyme Q (ubiquinone; Q), cytochrome c (Cyt c) carries electrons to complex IV, where molecular oxygen (O_2) is reduced to water (H_2O). ATP synthase uses the flow of H^+ back into the matrix to generate ATP from adenosine diphosphate (ADP) and inorganic phosphate (Pi). Reactive oxygen species (O_2^-) are generated by electrons that fail to complete the series. Vitamin K_2 ($VitK_2$) transfers electrons from complexes I and II to complex III.

CREDIT: Y. HAMMOND/*SCIENCE*

Cytochrome *c*

- Cytochrome *c*, a small heme protein that is loosely bound to the outer surface of the inner membrane, shuttles electrons from complex III to complex IV.
- Each cytochrome *c* carries only one electron, so the reduction of O_2 to $2H_2O$ by complex IV requires four reduced cytochrome *c* molecules.
- In response to oxidative stress and cell injury, cytochrome *c* may be released from the inner mitochondrial membrane and leak into the cytosol, inducing apoptosis (cell death).



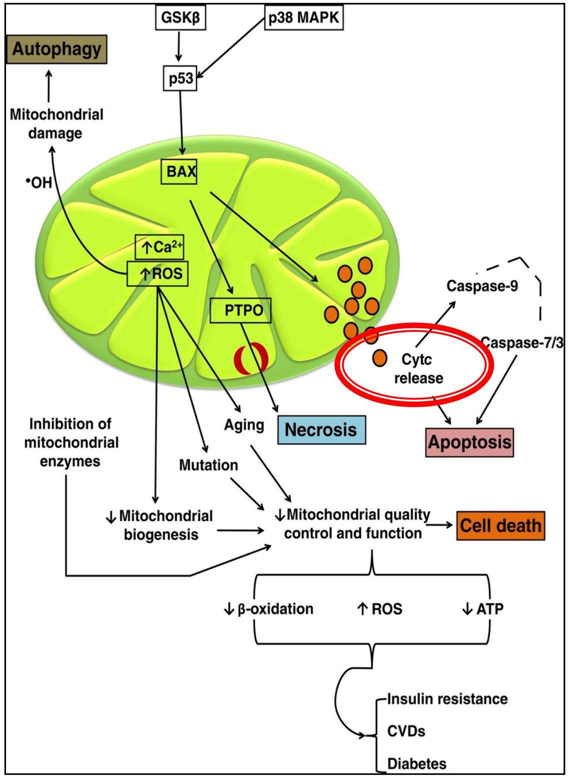
Heme group of cytochrome c (heme C)

Heme group of cytochrome a (heme A)

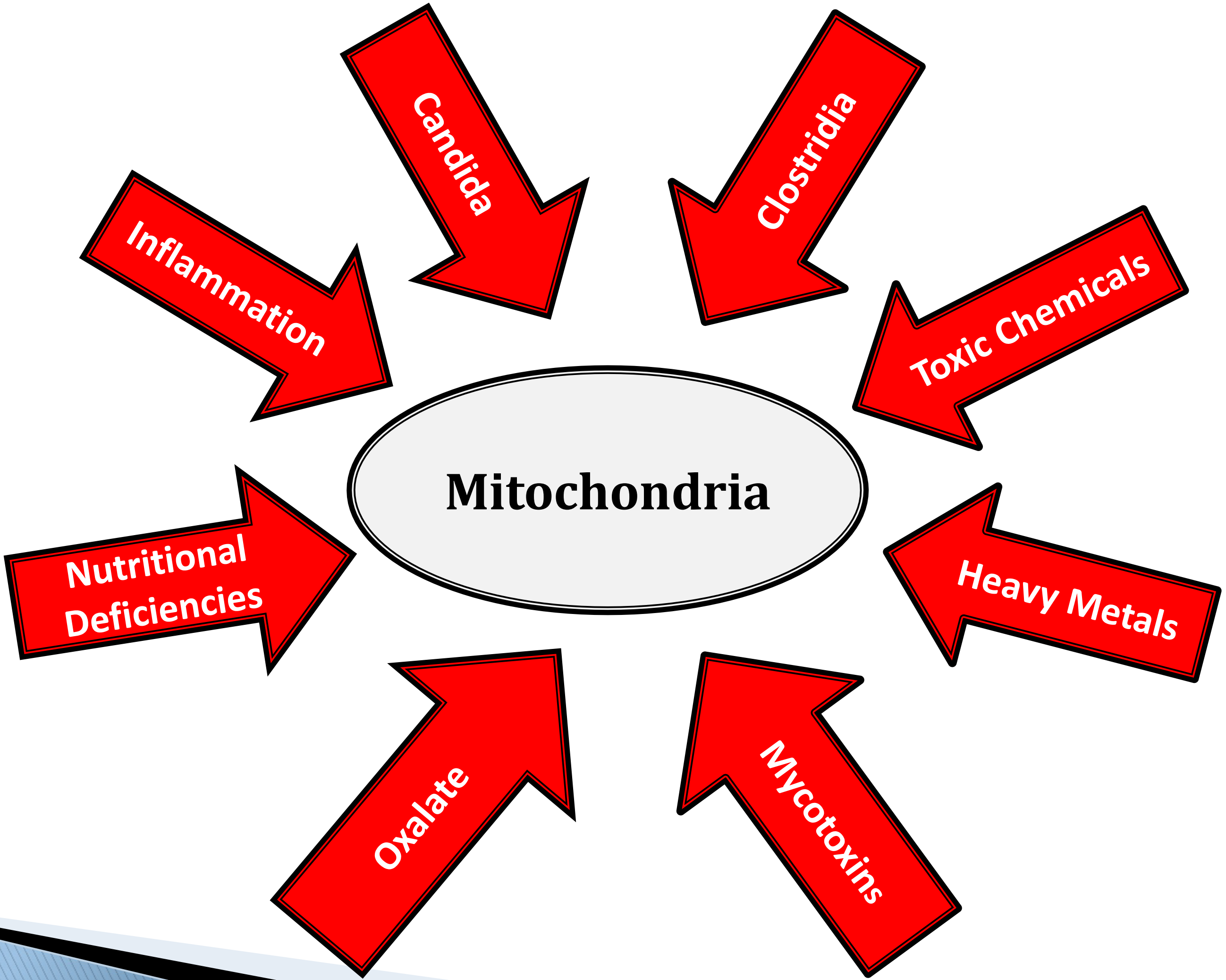
Mycotoxin-assisted mitochondrial dysfunction and cytotoxicity: Unexploited tools against proliferative disorders

Muhammad Torequl Islam, Siddhartha Kumar Mishra, Swati Tripathi, Marcus Vinícius Oliveira Barros de Alencar, João Marcelo de Castro e Sousa, Hercília Maria Lins Rolim ... See all authors

First published: 04 September 2018 | https://doi.org/10.1002/iub.1932 | Citations: 8



Source: *IUBMB Life, Volume: 70, Issue: 11, Pages: 1084-1092, First published: 04 September 2018, DOI: (10.1002/iub.1932)*



Candida

Clostridia

Inflammation

Toxic Chemicals

Mitochondria

Nutritional Deficiencies

Heavy Metals

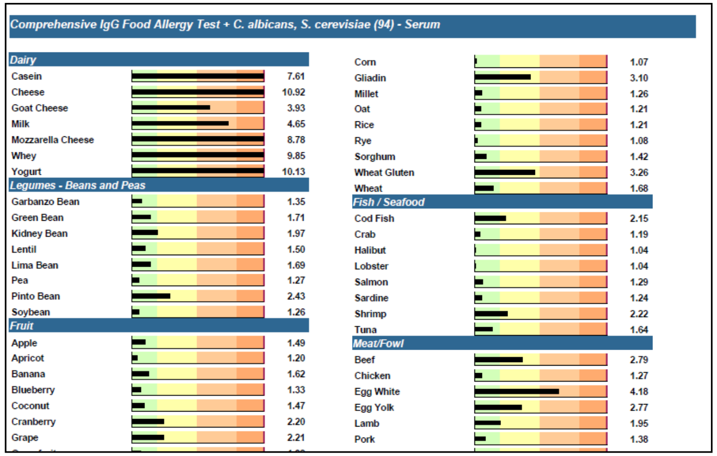
Oxalate

Mycotoxins

Glyphosate Test

GPL-TOX PROFILE

MycoTOX Profile



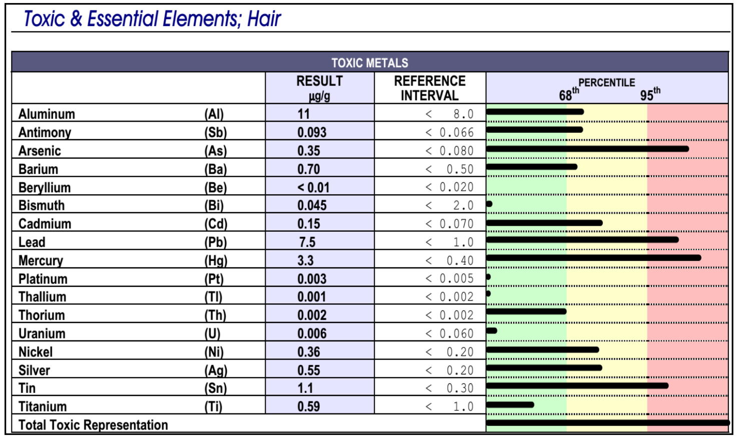
Comprehensive IgG Food Allergy Test + C. albicans, S. cerevisiae (94) - Serum

Dairy	
Casein	7.61
Cheese	10.92
Goat Cheese	3.93
Milk	4.65
Mozzarella Cheese	8.78
Whey	9.85
Yogurt	10.13
Legumes - Beans and Peas	
Garbanzo Bean	1.35
Green Bean	1.71
Kidney Bean	1.97
Lentil	1.50
Lima Bean	1.69
Pea	1.27
Pinto Bean	2.43
Soybean	1.26
Fruit	
Apple	1.49
Apricot	1.20
Banana	1.62
Blueberry	1.33
Coconut	1.47
Cranberry	2.20
Grape	2.21
Corn	1.07
Gliadin	3.10
Millet	1.26
Oat	1.21
Rice	1.21
Rye	1.08
Sorghum	1.42
Wheat Gluten	3.26
Wheat	1.68
Fish / Seafood	
Cod Fish	2.15
Crab	1.19
Halibut	1.04
Lobster	1.04
Salmon	1.29
Sardine	1.24
Shrimp	2.22
Tuna	1.64
Meat/Fowl	
Beef	2.79
Chicken	1.27
Egg White	4.18
Egg Yolk	2.77
Lamb	1.95
Pork	1.38

IgG Food Allergy Test

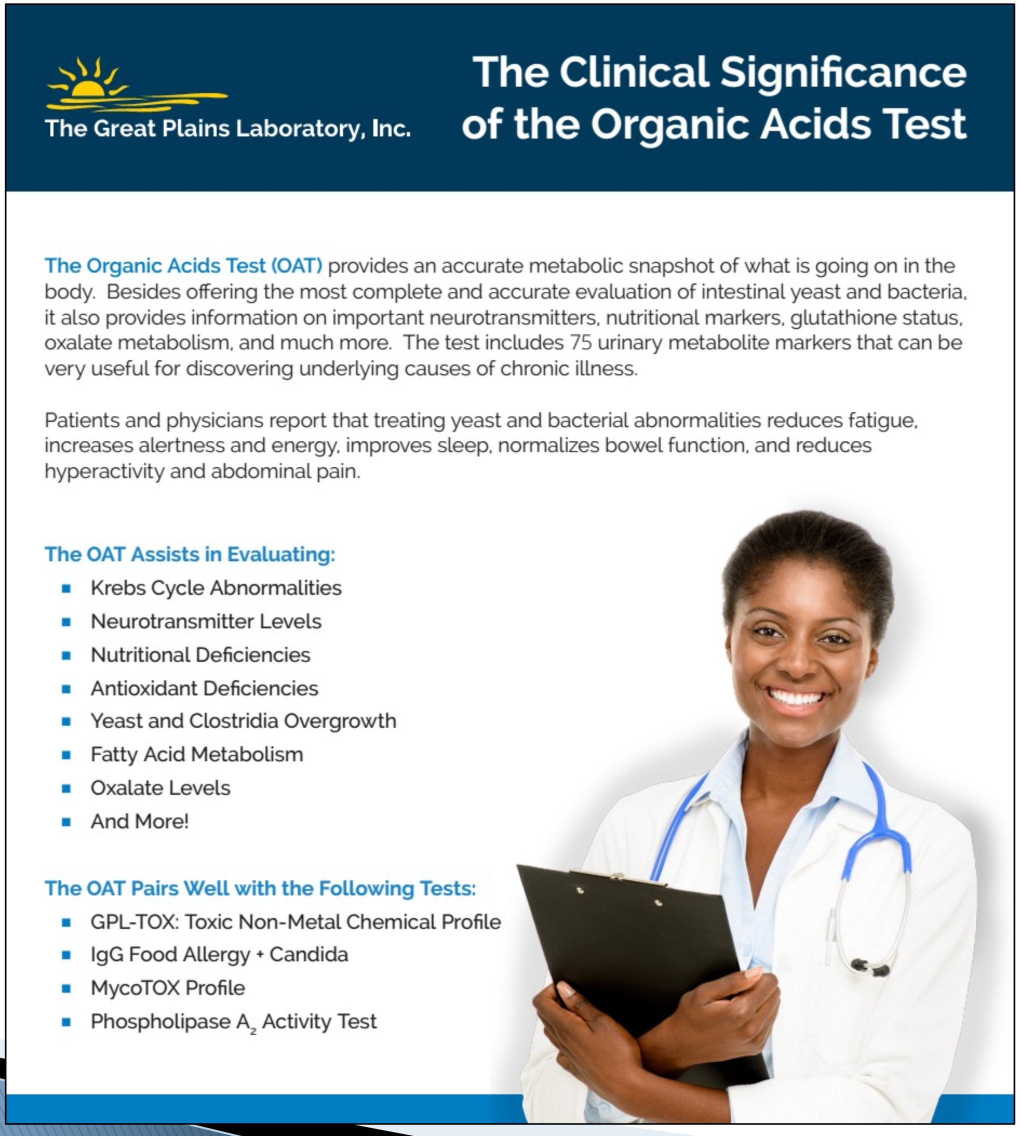
Hair Analysis

(aka hair metals)



Toxic & Essential Elements; Hair

TOXIC METALS				
		RESULT µg/g	REFERENCE INTERVAL	PERCENTILE 68th 95th
Aluminum	(Al)	11	< 8.0	
Antimony	(Sb)	0.093	< 0.066	
Arsenic	(As)	0.35	< 0.080	
Barium	(Ba)	0.70	< 0.50	
Beryllium	(Be)	< 0.01	< 0.020	
Bismuth	(Bi)	0.045	< 2.0	
Cadmium	(Cd)	0.15	< 0.070	
Lead	(Pb)	7.5	< 1.0	
Mercury	(Hg)	3.3	< 0.40	
Platinum	(Pt)	0.003	< 0.005	
Thallium	(Tl)	0.001	< 0.002	
Thorium	(Th)	0.002	< 0.002	
Uranium	(U)	0.006	< 0.060	
Nickel	(Ni)	0.36	< 0.20	
Silver	(Ag)	0.55	< 0.20	
Tin	(Sn)	1.1	< 0.30	
Titanium	(Ti)	0.59	< 1.0	
Total Toxic Representation				



The Great Plains Laboratory, Inc.

The Clinical Significance of the Organic Acids Test

The Organic Acids Test (OAT) provides an accurate metabolic snapshot of what is going on in the body. Besides offering the most complete and accurate evaluation of intestinal yeast and bacteria, it also provides information on important neurotransmitters, nutritional markers, glutathione status, oxalate metabolism, and much more. The test includes 75 urinary metabolite markers that can be very useful for discovering underlying causes of chronic illness.

Patients and physicians report that treating yeast and bacterial abnormalities reduces fatigue, increases alertness and energy, improves sleep, normalizes bowel function, and reduces hyperactivity and abdominal pain.

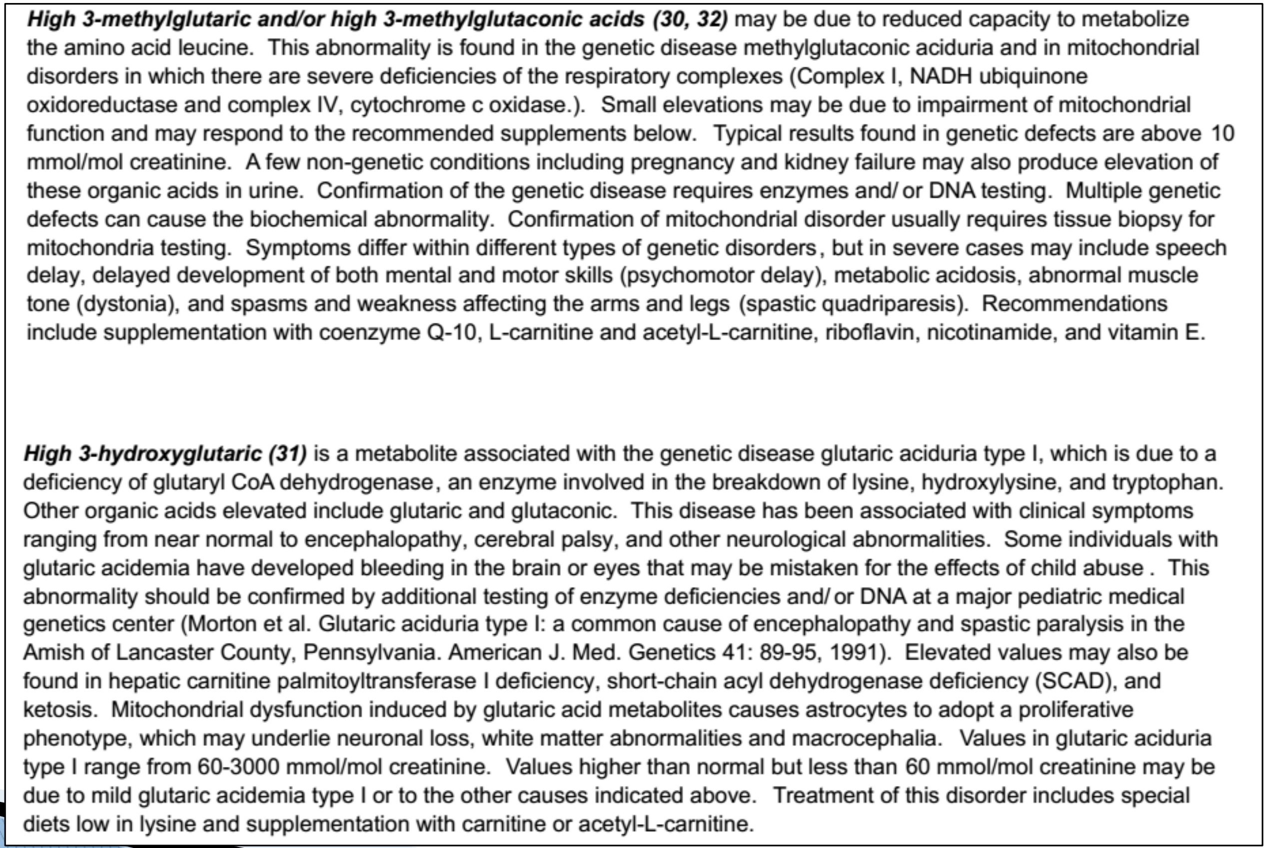
The OAT Assists in Evaluating:

- Krebs Cycle Abnormalities
- Neurotransmitter Levels
- Nutritional Deficiencies
- Antioxidant Deficiencies
- Yeast and Clostridia Overgrowth
- Fatty Acid Metabolism
- Oxalate Levels
- And More!

The OAT Pairs Well with the Following Tests:

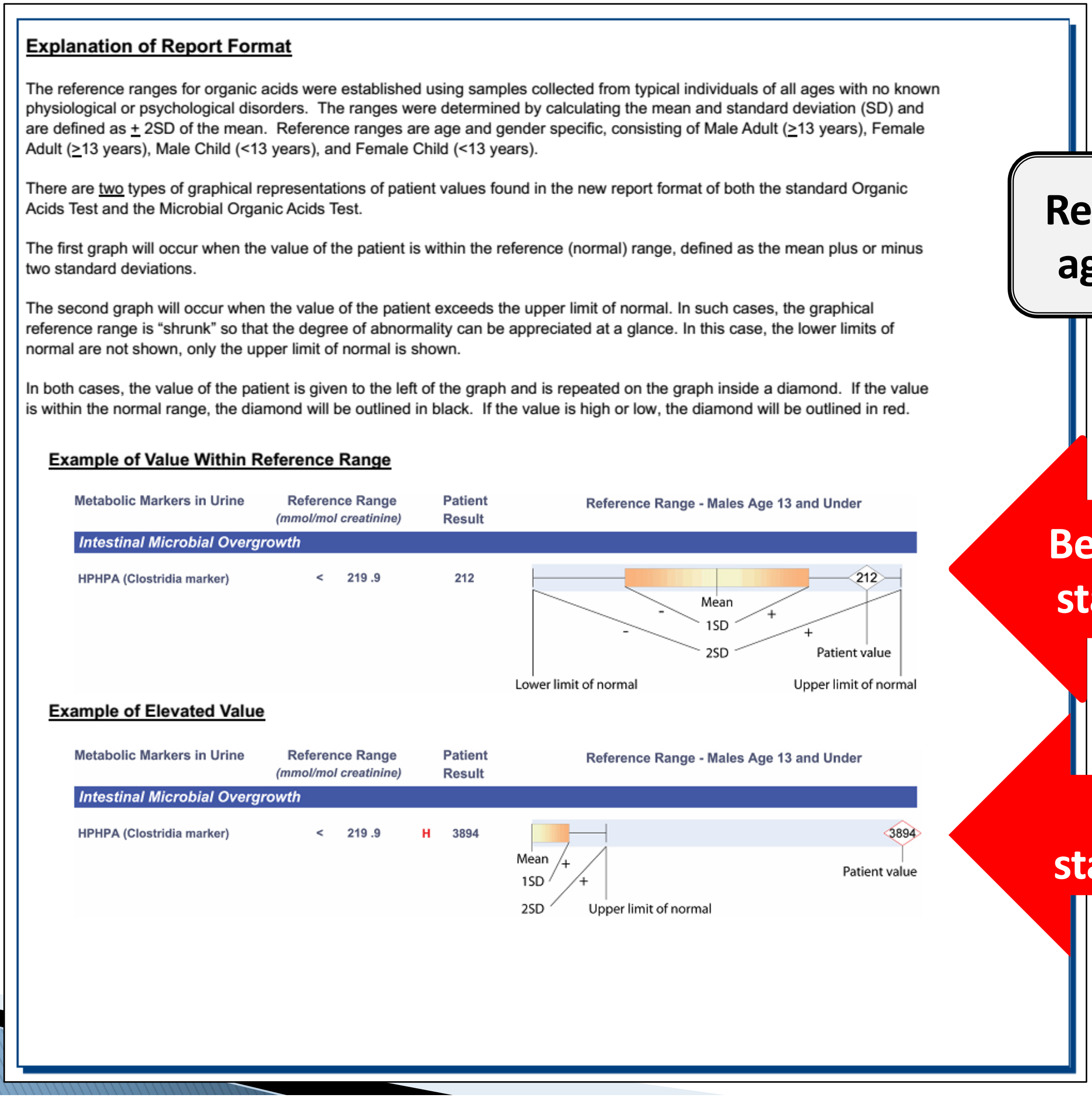
- GPL-TOX: Toxic Non-Metal Chemical Profile
- IgG Food Allergy + Candida
- MycoTOX Profile
- Phospholipase A_2 Activity Test

OAT Marker Interpretation Sections



High 3-methylglutaric and/or high 3-methylglutaconic acids (30, 32) may be due to reduced capacity to metabolize the amino acid leucine. This abnormality is found in the genetic disease methylglutaconic aciduria and in mitochondrial disorders in which there are severe deficiencies of the respiratory complexes (Complex I, NADH ubiquinone oxidoreductase and complex IV, cytochrome c oxidase.). Small elevations may be due to impairment of mitochondrial function and may respond to the recommended supplements below. Typical results found in genetic defects are above 10 mmol/mol creatinine. A few non-genetic conditions including pregnancy and kidney failure may also produce elevation of these organic acids in urine. Confirmation of the genetic disease requires enzymes and/ or DNA testing. Multiple genetic defects can cause the biochemical abnormality. Confirmation of mitochondrial disorder usually requires tissue biopsy for mitochondria testing. Symptoms differ within different types of genetic disorders, but in severe cases may include speech delay, delayed development of both mental and motor skills (psychomotor delay), metabolic acidosis, abnormal muscle tone (dystonia), and spasms and weakness affecting the arms and legs (spastic quadriparesis). Recommendations include supplementation with coenzyme Q-10, L-carnitine and acetyl-L-carnitine, riboflavin, nicotinamide, and vitamin E.

High 3-hydroxyglutaric (31) is a metabolite associated with the genetic disease glutaric aciduria type I, which is due to a deficiency of glutaryl CoA dehydrogenase, an enzyme involved in the breakdown of lysine, hydroxylysine, and tryptophan. Other organic acids elevated include glutaric and glutaconic. This disease has been associated with clinical symptoms ranging from near normal to encephalopathy, cerebral palsy, and other neurological abnormalities. Some individuals with glutaric acidemia have developed bleeding in the brain or eyes that may be mistaken for the effects of child abuse . This abnormality should be confirmed by additional testing of enzyme deficiencies and/ or DNA at a major pediatric medical genetics center (Morton et al. Glutaric aciduria type I: a common cause of encephalopathy and spastic paralysis in the Amish of Lancaster County, Pennsylvania. American J. Med. Genetics 41: 89-95, 1991). Elevated values may also be found in hepatic carnitine palmitoyltransferase I deficiency, short-chain acyl dehydrogenase deficiency (SCAD), and ketosis. Mitochondrial dysfunction induced by glutaric acid metabolites causes astrocytes to adopt a proliferative phenotype, which may underlie neuronal loss, white matter abnormalities and macrocephalia. Values in glutaric aciduria type I range from 60-3000 mmol/mol creatinine. Values higher than normal but less than 60 mmol/mol creatinine may be due to mild glutaric acidemia type I or to the other causes indicated above. Treatment of this disorder includes special diets low in lysine and supplementation with carnitine or acetyl-L-carnitine.



Explanation of Report Format

The reference ranges for organic acids were established using samples collected from typical individuals of all ages with no known physiological or psychological disorders. The ranges were determined by calculating the mean and standard deviation (SD) and are defined as ± 2SD of the mean. Reference ranges are age and gender specific, consisting of Male Adult (≥13 years), Female Adult (≥13 years), Male Child (<13 years), and Female Child (<13 years).

There are two types of graphical representations of patient values found in the new report format of both the standard Organic Acids Test and the Microbial Organic Acids Test.

The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

The second graph will occur when the value of the patient exceeds the upper limit of normal. In such cases, the graphical reference range is "shrunk" so that the degree of abnormality can be appreciated at a glance. In this case, the lower limits of normal are not shown, only the upper limit of normal is shown.

In both cases, the value of the patient is given to the left of the graph and is repeated on the graph inside a diamond. If the value is within the normal range, the diamond will be outlined in black. If the value is high or low, the diamond will be outlined in red.

Example of Value Within Reference Range

Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*		Patient Result	Reference Range - Males Age 13 and Under
Intestinal Microbial Overgrowth				
HPHPA (Clostridia marker)	< 219 .9		212	

Example of Elevated Value

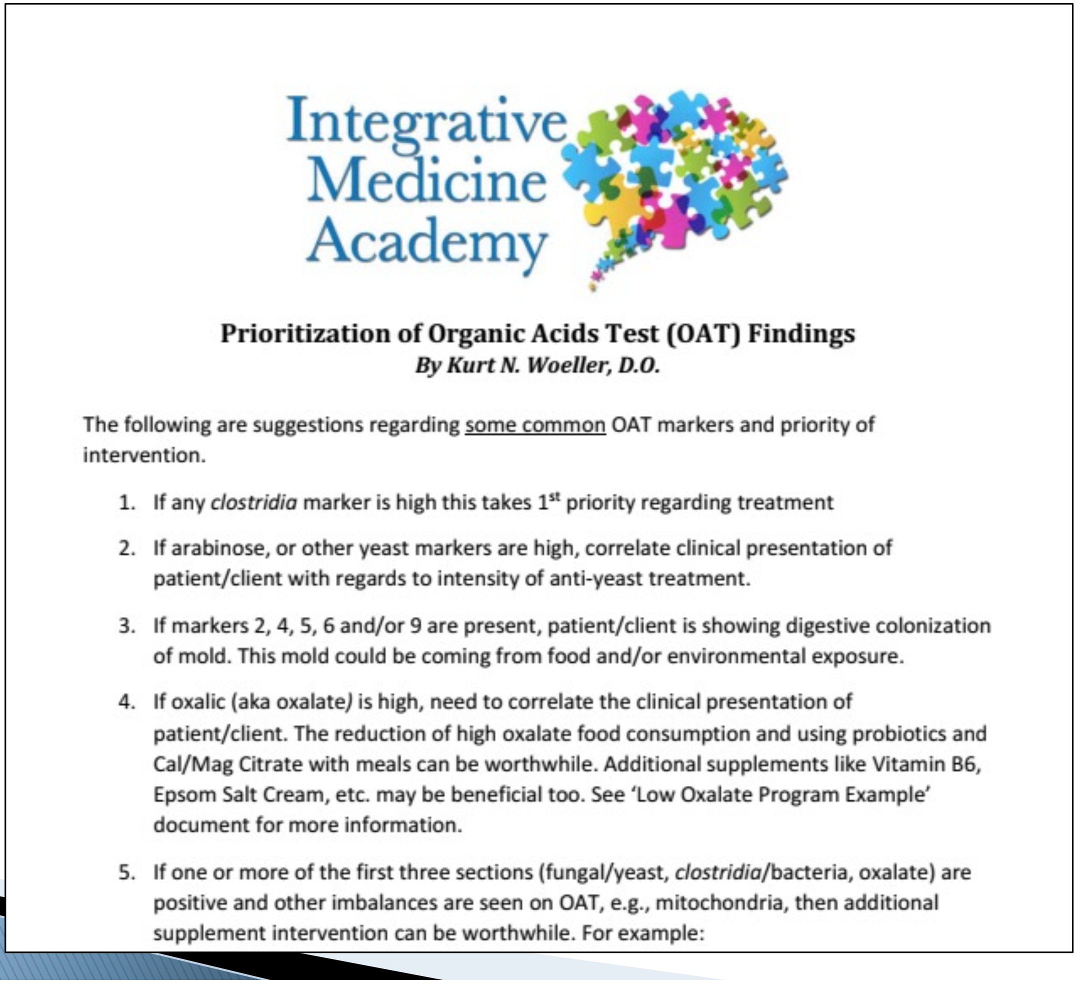
Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*		Patient Result	Reference Range - Males Age 13 and Under
Intestinal Microbial Overgrowth				
HPHPA (Clostridia marker)	< 219 .9	H	3894	

Reference ranges are age and sex specific

Between 1st and 2nd standard deviation

Above the 2nd standard deviation

Dr. Woeller OAT Lecture Support Document



Integrative Medicine Academy

Prioritization of Organic Acids Test (OAT) Findings

By Kurt N. Woeller, D.O.

The following are suggestions regarding <u>some common</u> OAT markers and priority of intervention.

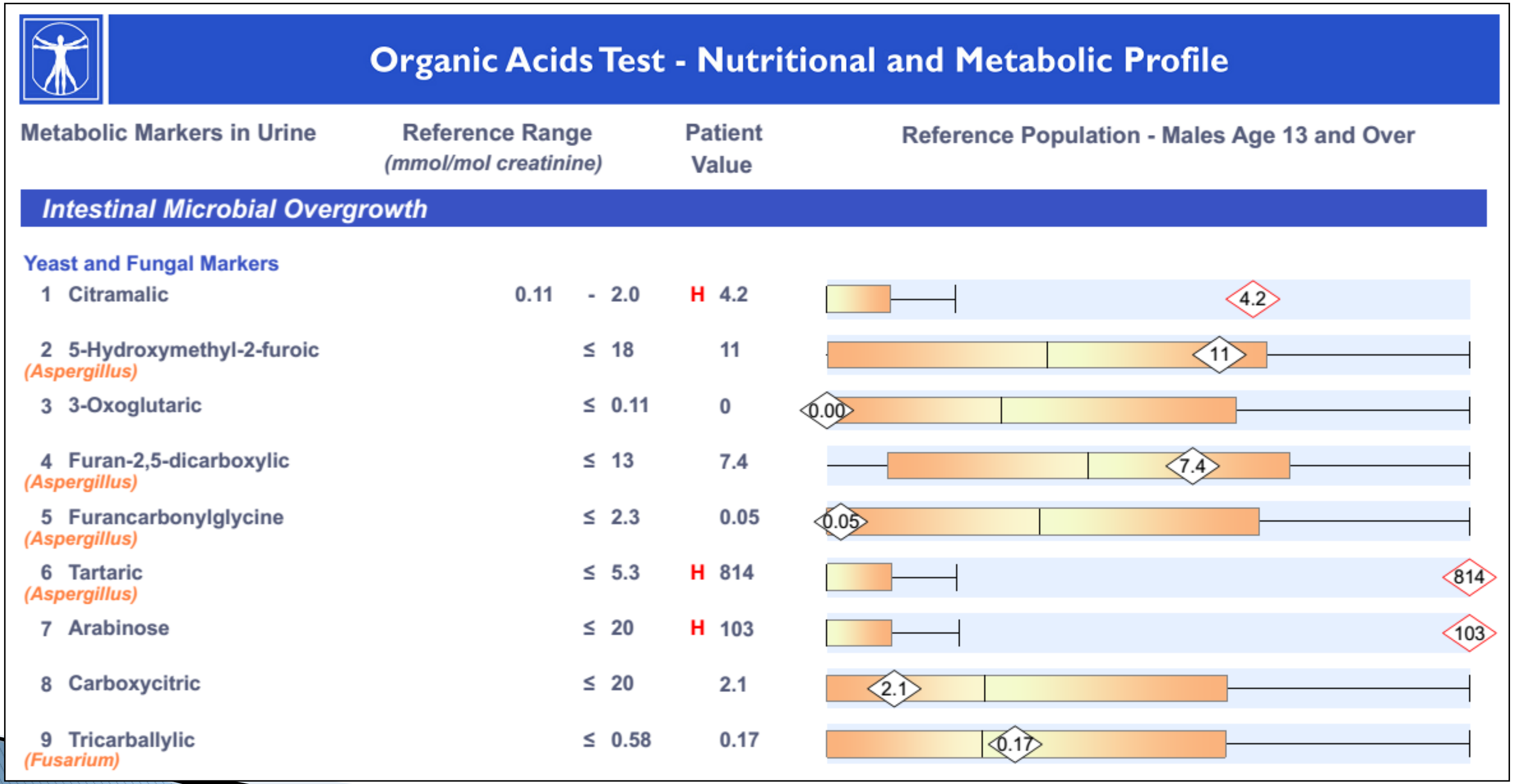
1. If any *clostridia* marker is high this takes 1st priority regarding treatment
2. If arabinose, or other yeast markers are high, correlate clinical presentation of patient/client with regards to intensity of anti-yeast treatment.
3. If markers 2, 4, 5, 6 and/or 9 are present, patient/client is showing digestive colonization of mold. This mold could be coming from food and/or environmental exposure.
4. If oxalic (aka oxalate*)* is high, need to correlate the clinical presentation of patient/client. The reduction of high oxalate food consumption and using probiotics and Cal/Mag Citrate with meals can be worthwhile. Additional supplements like Vitamin B6, Epsom Salt Cream, etc. may be beneficial too. See 'Low Oxalate Program Example' document for more information.
5. If one or more of the first three sections (fungal/yeast, *clostridia*/bacteria, oxalate) are positive and other imbalances are seen on OAT, e.g., mitochondria, then additional supplement intervention can be worthwhile. For example:

OAT Sample Report

Suggestions for reviewing an Organic Acids Test from Great Plains Laboratory

Page 1 – Yeast and Fungal Markers

(Evaluates for invasive candida and mold exposure)



Organic Acids Test - Nutritional and Metabolic Profile

Intestinal Microbial Overgrowth

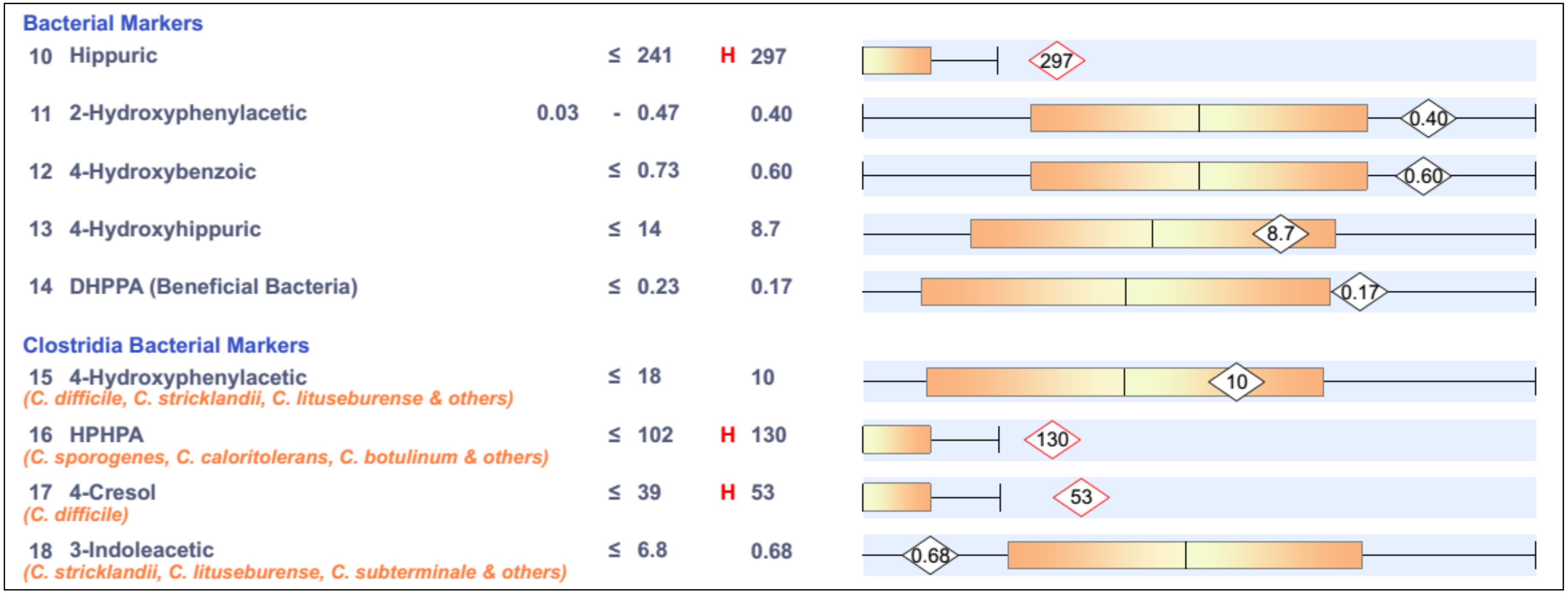
Yeast and Fungal Markers

Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*	Patient Value	Reference Population - Males Age 13 and Over
1 Citramalic	0.11 - 2.0	H 4.2	
2 5-Hydroxymethyl-2-furoic *(Aspergillus)*	≤ 18	11	
3 3-Oxoglutaric	≤ 0.11	0	
4 Furan-2,5-dicarboxylic *(Aspergillus)*	≤ 13	7.4	
5 Furancarbonylglycine *(Aspergillus)*	≤ 2.3	0.05	
6 Tartaric *(Aspergillus)*	≤ 5.3	H 814	
7 Arabinose	≤ 20	H 103	
8 Carboxycitric	≤ 20	2.1	
9 Tricarballylic *(Fusarium)*	≤ 0.58	0.17	

OAT Sample Report

Page 1 – Bacterial and Clostridia Markers

(Evaluates for dysbiosis and clostridia bacteria toxins)

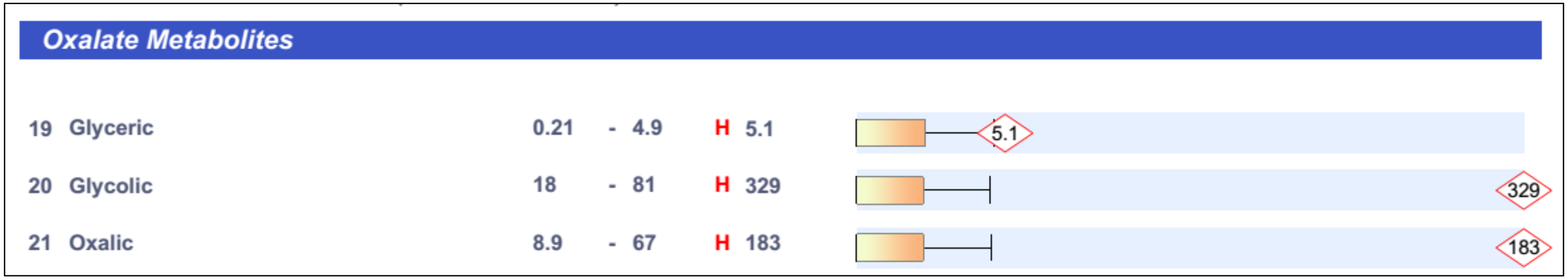


Bacterial Markers						
10	Hippuric		≤	241	H	297
11	2-Hydroxyphenylacetic	0.03	-	0.47		0.40
12	4-Hydroxybenzoic		≤	0.73		0.60
13	4-Hydroxyhippuric		≤	14		8.7
14	DHPPA (Beneficial Bacteria)		≤	0.23		0.17
Clostridia Bacterial Markers						
15	4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*		≤	18		10
16	HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*		≤	102	H	130
17	4-Cresol *(C. difficile)*		≤	39	H	53
18	3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*		≤	6.8		0.68

OAT Sample Report

Page 3 - Oxalic Acid and Metabolites

(Evaluates for high oxalate)



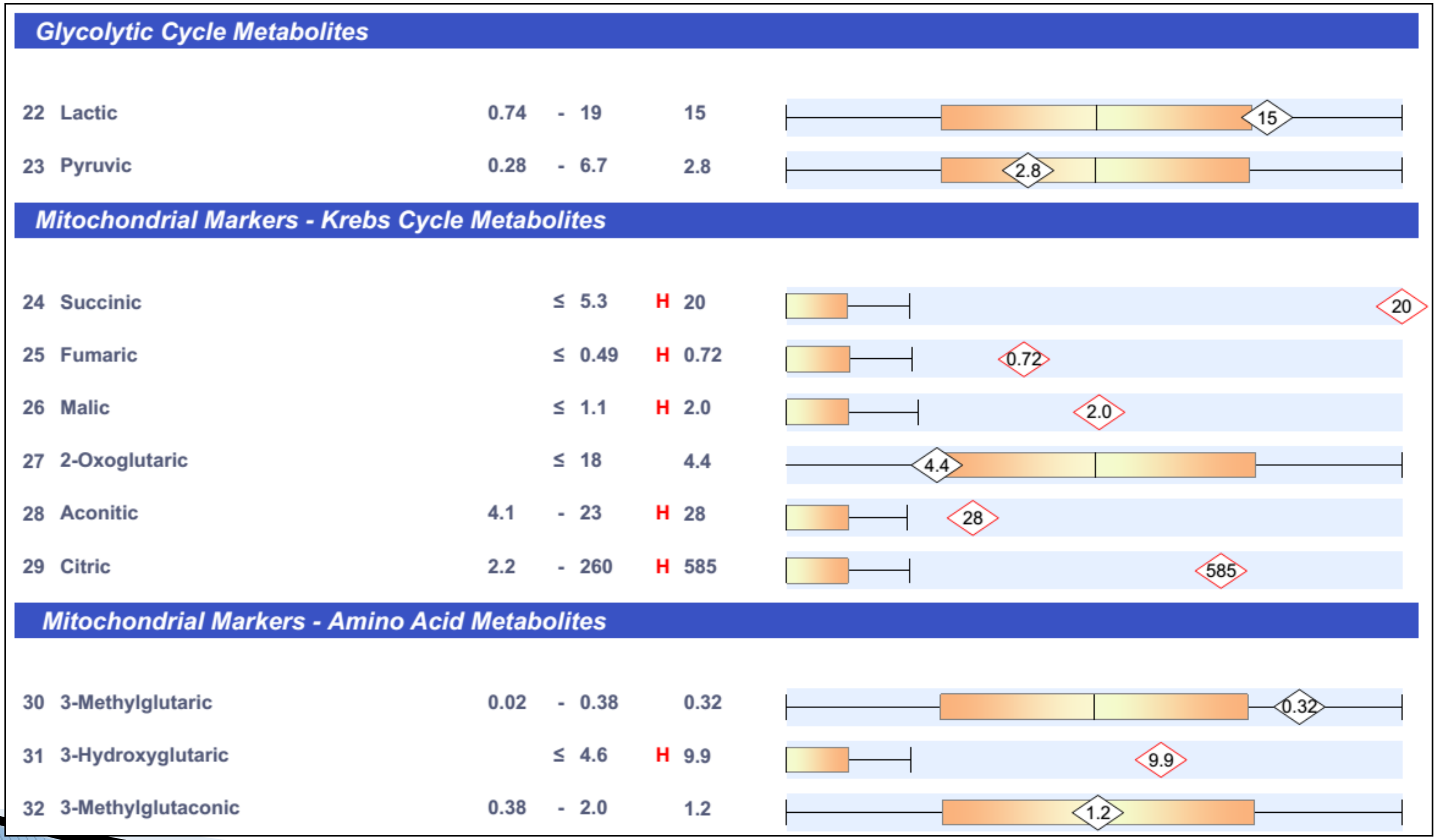
Oxalate Metabolites

19	Glyceric	0.21	-	4.9	H	5.1
20	Glycolic	18	-	81	H	329
21	Oxalic	8.9	-	67	H	183

OAT Sample Report

Page 3 – Glycolytic and Mitochondrial Metabolites

(Evaluates for mitochondrial dysfunction)



Glycolytic Cycle Metabolites

22	Lactic	0.74	-	19		15
23	Pyruvic	0.28	-	6.7		2.8

Mitochondrial Markers - Krebs Cycle Metabolites

24	Succinic		≤	5.3	H	20
25	Fumaric		≤	0.49	H	0.72
26	Malic		≤	1.1	H	2.0
27	2-Oxoglutaric		≤	18		4.4
28	Aconitic	4.1	-	23	H	28
29	Citric	2.2	-	260	H	585

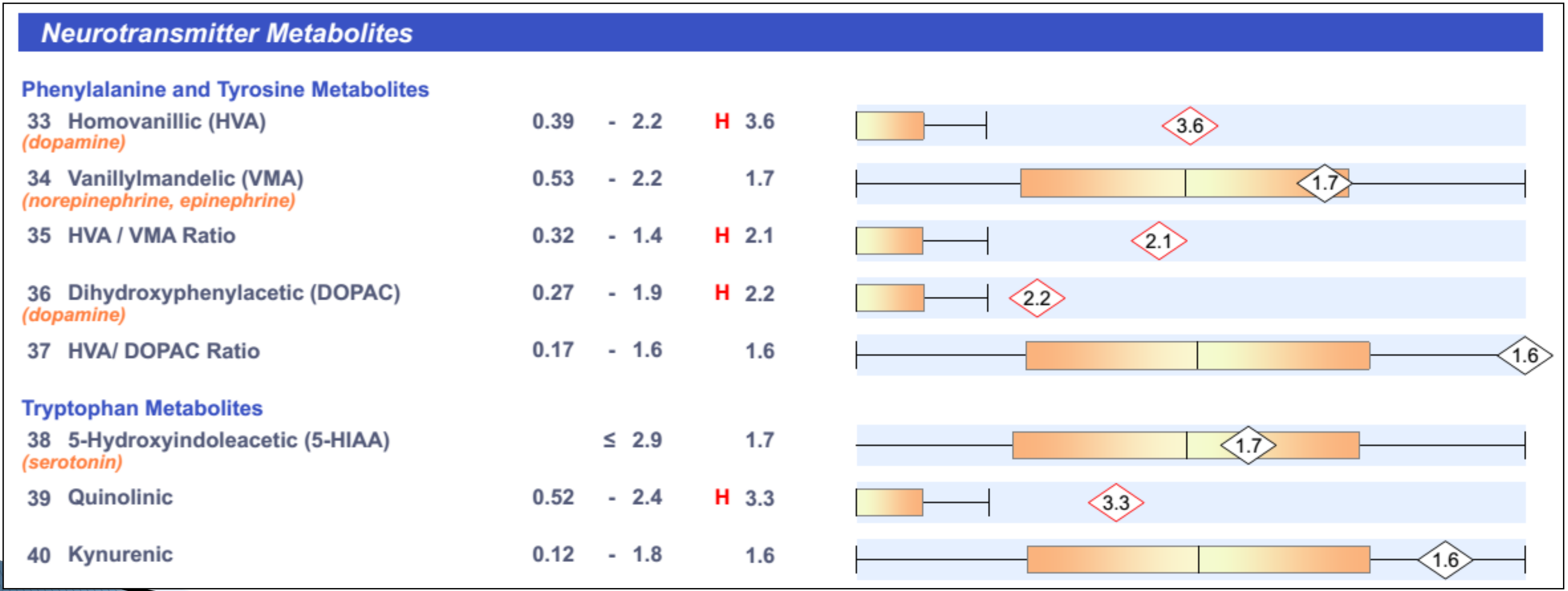
Mitochondrial Markers - Amino Acid Metabolites

30	3-Methylglutaric	0.02	-	0.38		0.32
31	3-Hydroxyglutaric		≤	4.6	H	9.9
32	3-Methylglutaconic	0.38	-	2.0		1.2

OAT Sample Report

Page 3 – Neurotransmitter Metabolites

(Evaluates for phenylalanine, tyrosine and tryptophan metabolism linked to neurotransmitter status and quinolinic acid production)



Neurotransmitter Metabolites

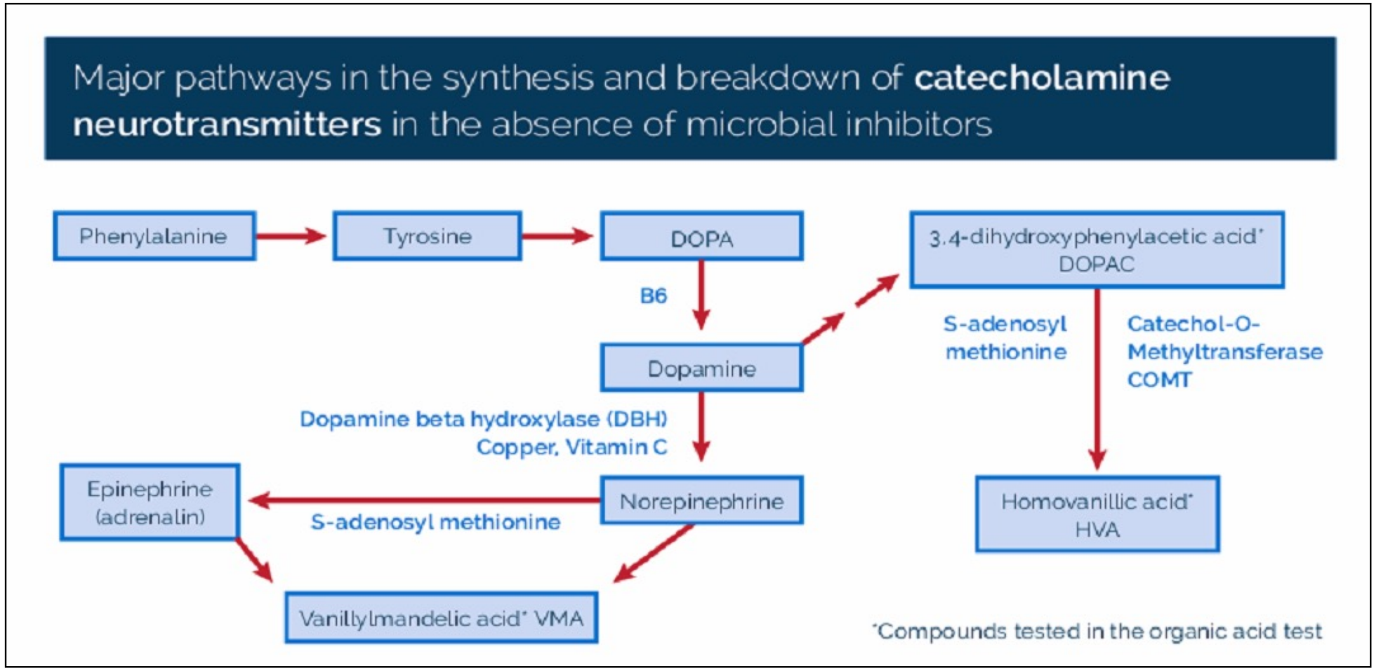
Phenylalanine and Tyrosine Metabolites

33	Homovanillic (HVA) *(dopamine)*	0.39	-	2.2	H	3.6
34	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.53	-	2.2		1.7
35	HVA / VMA Ratio	0.32	-	1.4	H	2.1
36	Dihydroxyphenylacetic (DOPAC) *(dopamine)*	0.27	-	1.9	H	2.2
37	HVA/ DOPAC Ratio	0.17	-	1.6		1.6

Tryptophan Metabolites

38	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*		≤	2.9		1.7
39	Quinolinic	0.52	-	2.4	H	3.3
40	Kynurenic	0.12	-	1.8		1.6

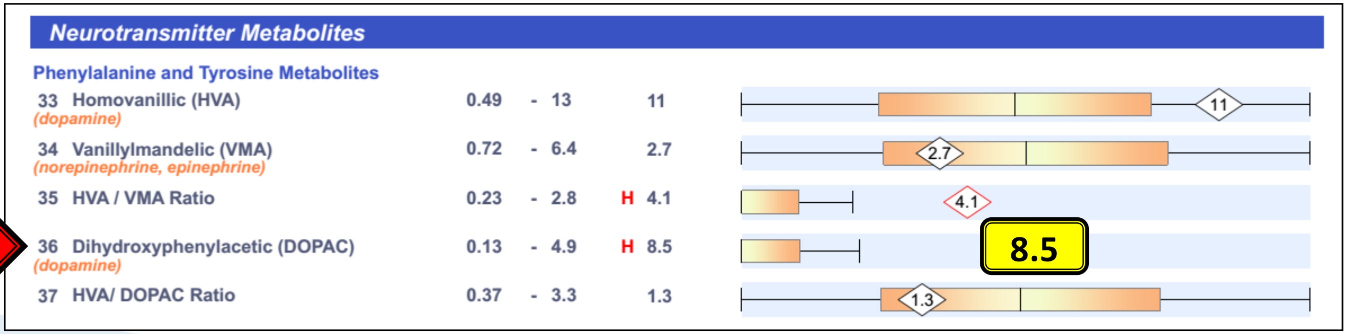
OAT Sample Report



Major pathways in the synthesis and breakdown of **catecholamine neurotransmitters** in the absence of microbial inhibitors

*Compounds tested in the organic acid test

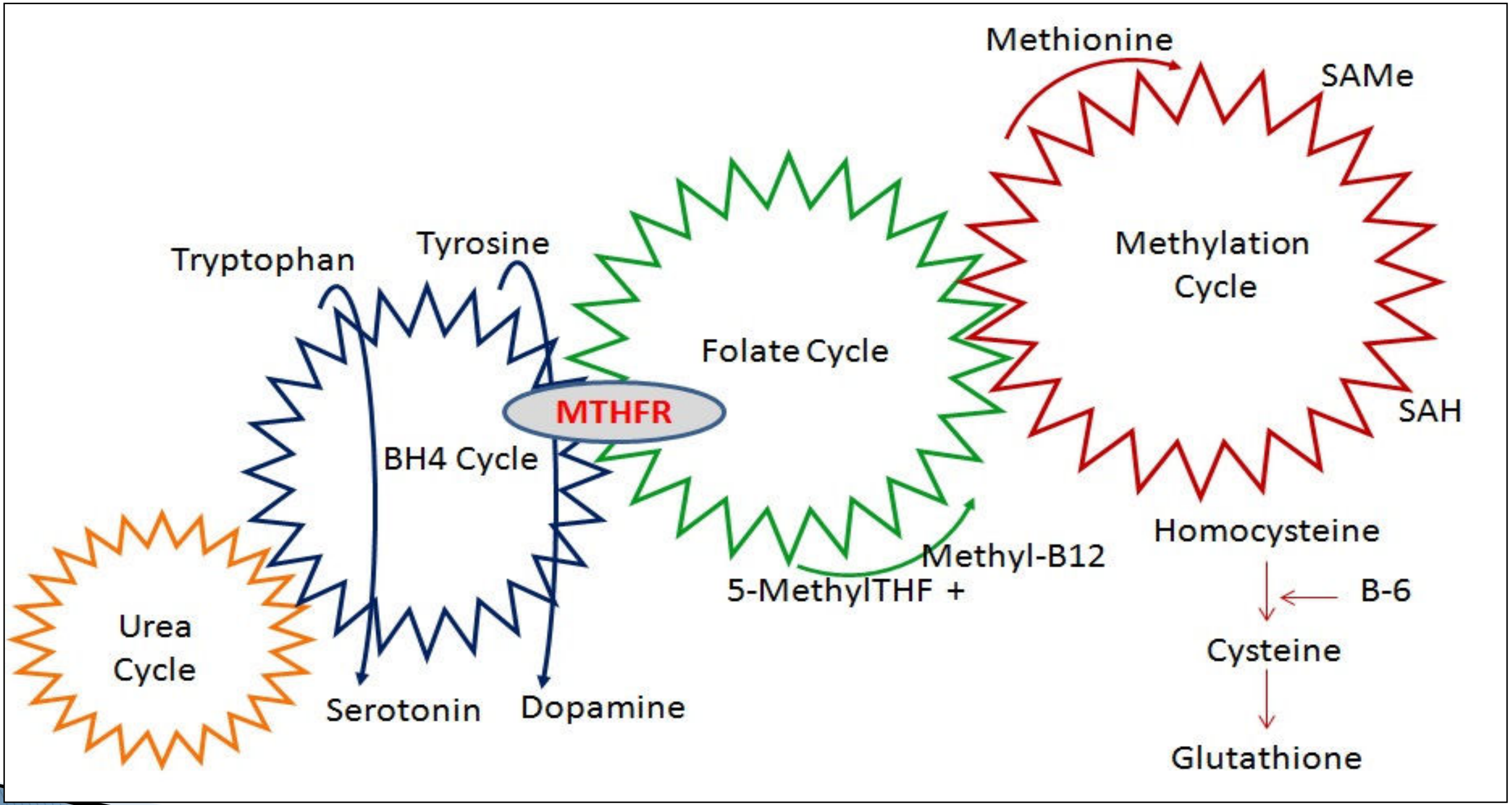
DOPAC

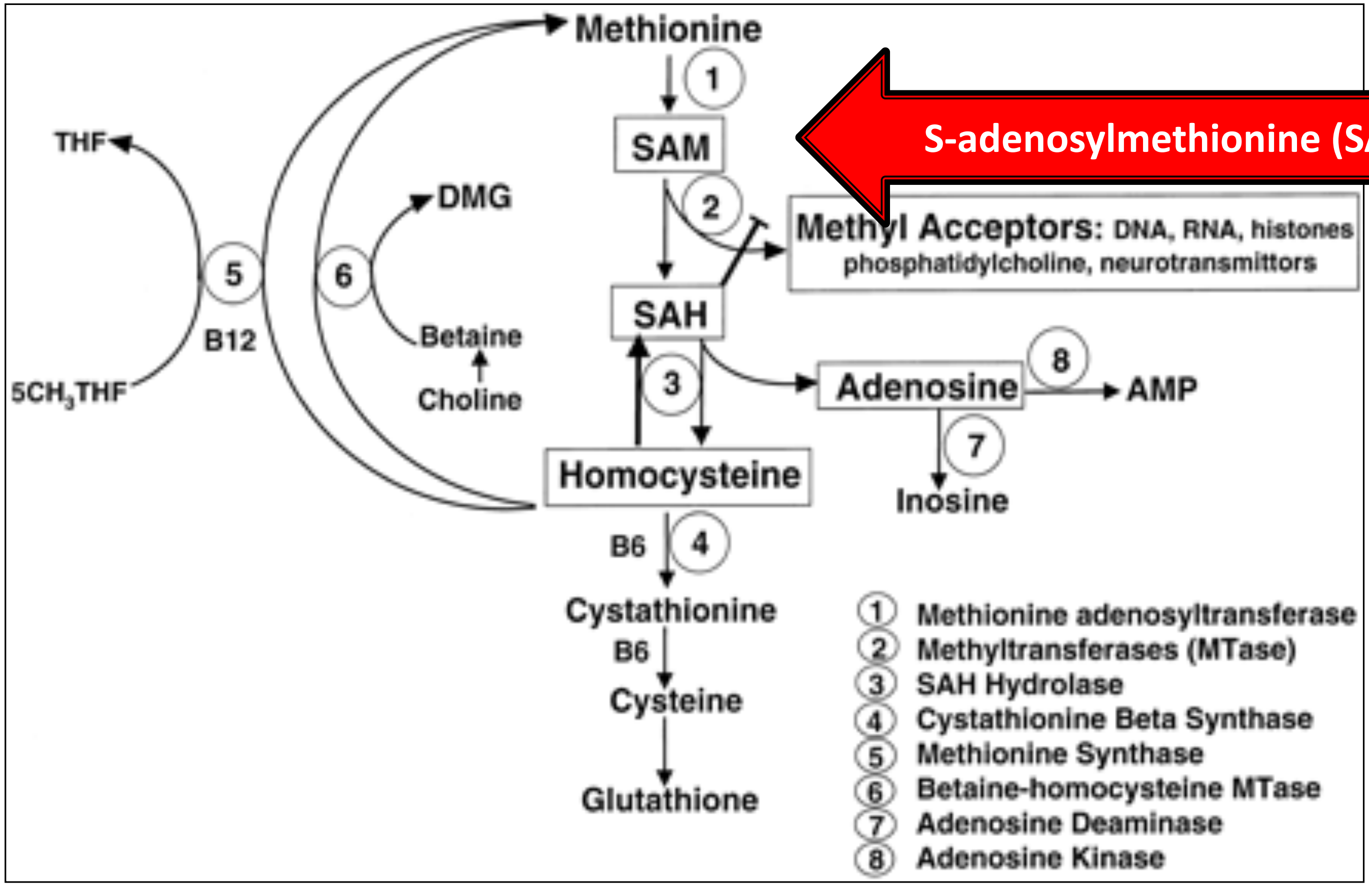


Neurotransmitter Metabolites

Phenylalanine and Tyrosine Metabolites

33	Homovanillic (HVA) *(dopamine)*	0.49	-	13		11
34	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.72	-	6.4		2.7
35	HVA / VMA Ratio	0.23	-	2.8	H	4.1
36	Dihydroxyphenylacetic (DOPAC) *(dopamine)*	0.13	-	4.9	H	8.5
37	HVA/ DOPAC Ratio	0.37	-	3.3		1.3

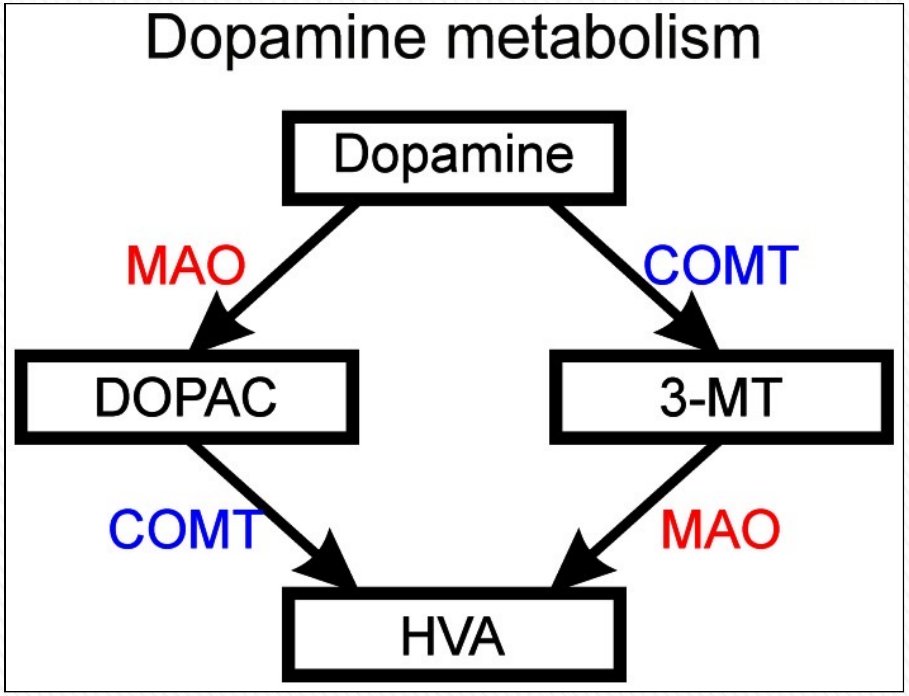

Methionine
SAMe
Methylation Cycle
Tryptophan
Tyrosine
Folate Cycle
MTHFR
SAH
BH4 Cycle
Homocysteine
Methyl-B12
5-MethylTHF +
B-6
Urea Cycle
Cysteine
Serotonin
Dopamine
Glutathione



S-adenosylmethionine (SAMe)

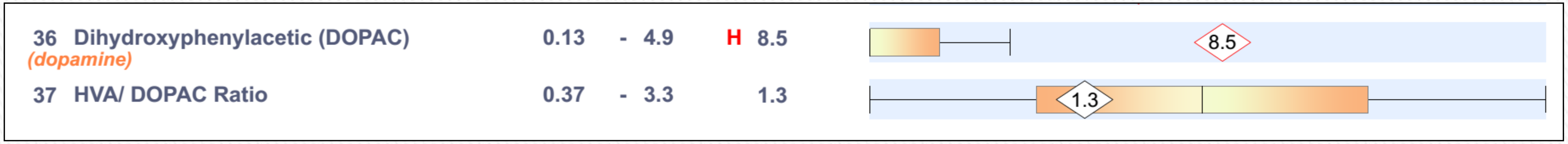
Source: ***Jill James, Ph.D***

Dopamine metabolism

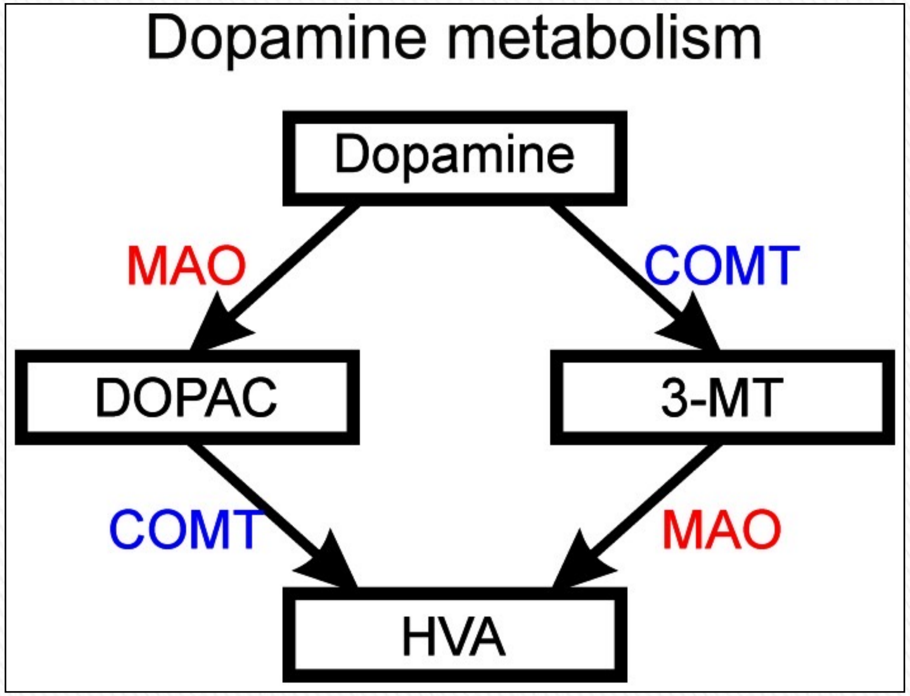


High DOPAC (examples)

- Dopamine Beta-Hydroxylase inhibition:
  - *Polymorphism*
  - *Clostridia toxin inhibition*
  - *Vitamin C and/or copper deficiency*
- Deficiency of SAMe:
  - *SAMe 200mg to 400mg BID*
- Catechol-O-methyltransferase (COMT) polymorphism.
- Magnesium deficiency
- Increased L-Tyrosine and/or Phenylalanine consumption.



36	**Dihydroxyphenylacetic (DOPAC)** *(dopamine)*	0.13 - 4.9	H	8.5
37	**HVA/ DOPAC Ratio**	0.37 - 3.3		1.3



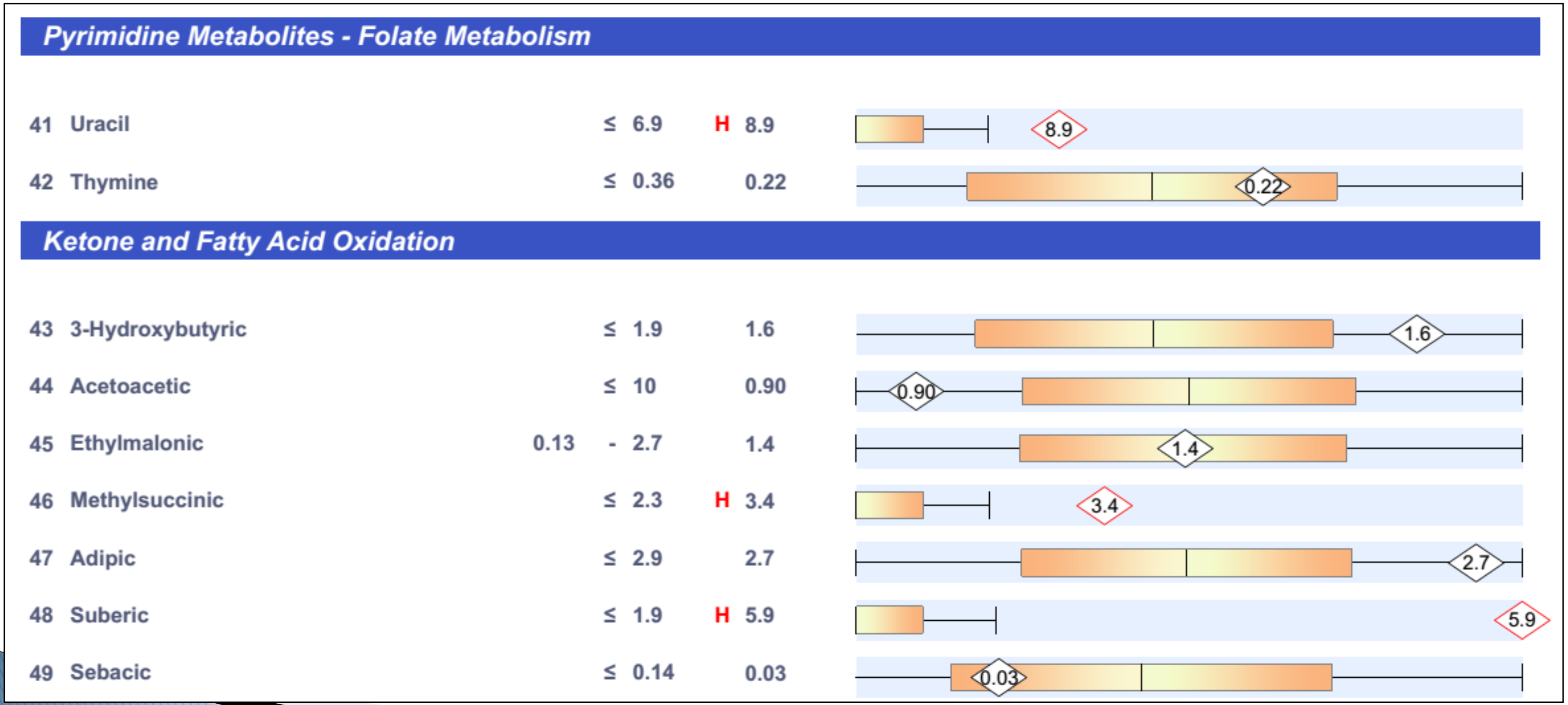
Low DOPAC (examples)

- Polymorphism of MAO enzyme
- Decreased intake or absorption of L-Tyrosine and/or Phenylalanine.
- Decreased BH4 *(tetrahydrobiopterin).*
- Deficiency of Vitamin B6
- MAO inhibitors, i.e. drugs, certain supplements like turmeric and kava.

36	**Dihydroxyphenylacetic (DOPAC)** *(dopamine)*	0.27	- 1.9		0.72
37	**HVA/ DOPAC Ratio**	0.17	- 1.6	H	1.8

Page 4 – Pyrimidines and Fatty Acids

(Evaluates for folate metabolism, as well as fatty acid metabolism problems which can contribute to mitochondrial dysfunction)



Pyrimidine Metabolites - Folate Metabolism

41	Uracil		≤	6.9	H	8.9
42	Thymine		≤	0.36		0.22

Ketone and Fatty Acid Oxidation

43	3-Hydroxybutyric		≤	1.9		1.6
44	Acetoacetic		≤	10		0.90
45	Ethylmalonic	0.13	-	2.7		1.4
46	Methylsuccinic		≤	2.3	H	3.4
47	Adipic		≤	2.9		2.7
48	Suberic		≤	1.9	H	5.9
49	Sebacic		≤	0.14		0.03

OAT Sample Report

Page 4 – Nutritional Markers

(Evaluates for various nutrient imbalances)

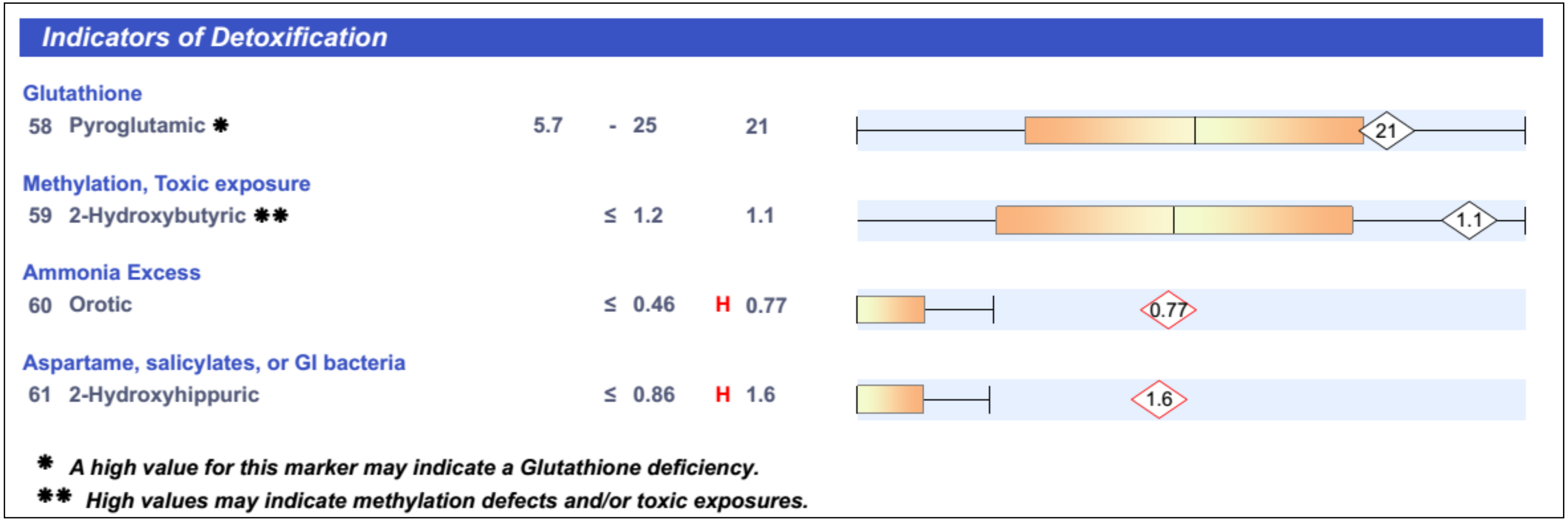
Nutritional Markers

Vitamin B12						
50	Methylmalonic ✱		≤	2.3		2.2
Vitamin B6						
51	Pyridoxic (B6)		≤	26	H	58
Vitamin B5						
52	Pantothenic (B5)		≤	5.4	H	164
Vitamin B2 (Riboflavin)						
53	Glutaric ✱		≤	0.43		0.21
Vitamin C						
54	Ascorbic	10	-	200		10
Vitamin Q10 (CoQ10)						
55	3-Hydroxy-3-methylglutaric ✱		≤	26	H	28
Glutathione Precursor and Chelating Agent						
56	N-Acetylcysteine (NAC)		≤	0.13		0.02
Biotin (Vitamin H)						
57	Methylcitric ✱	0.15	-	1.7	H	2.3

OAT Sample Report

Page 5 – Indicators of Detoxification

(Evaluates for glutathione deficiency and other imbalances)



Indicators of Detoxification

Glutathione				
58	Pyroglutamic ✱	5.7 - 25		21
Methylation, Toxic exposure				
59	2-Hydroxybutyric ✱✱	≤ 1.2		1.1
Ammonia Excess				
60	Orotic	≤ 0.46	H	0.77
Aspartame, salicylates, or GI bacteria				
61	2-Hydroxyhippuric	≤ 0.86	H	1.6

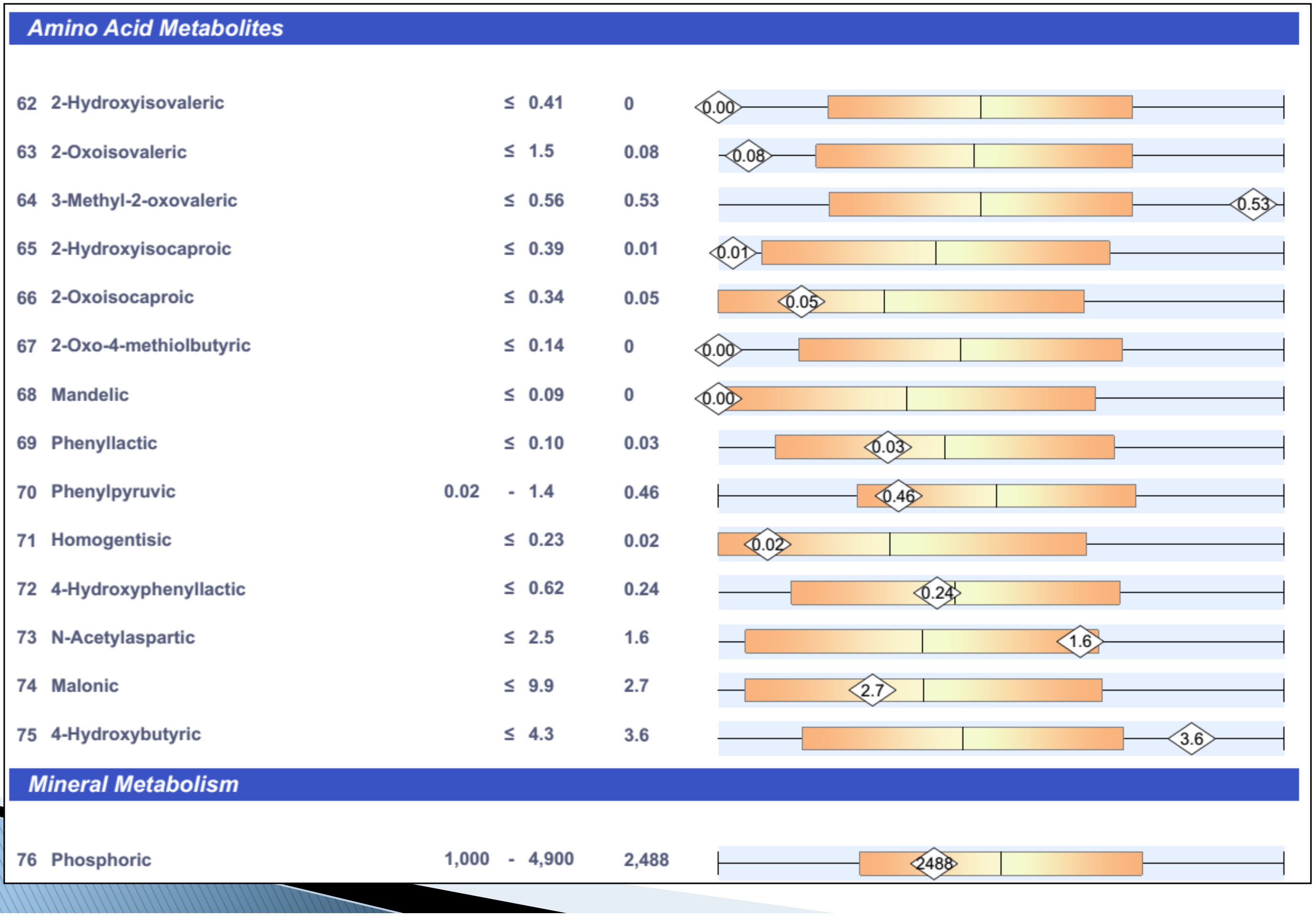
✱ *A high value for this marker may indicate a Glutathione deficiency.*

✱✱ *High values may indicate methylation defects and/or toxic exposures.*

OAT Sample Report

Page 5 – Amino Acid Metabolites & Phosphoric Acid

(Measures inborn errors of metabolism and other metabolic imbalances)



Amino Acid Metabolites

62	2-Hydroxyisovaleric	≤ 0.41	0
63	2-Oxoisovaleric	≤ 1.5	0.08
64	3-Methyl-2-oxovaleric	≤ 0.56	0.53
65	2-Hydroxyisocaproic	≤ 0.39	0.01
66	2-Oxoisocaproic	≤ 0.34	0.05
67	2-Oxo-4-methiolbutyric	≤ 0.14	0
68	Mandelic	≤ 0.09	0
69	Phenyllactic	≤ 0.10	0.03
70	Phenylpyruvic	0.02 - 1.4	0.46
71	Homogentisic	≤ 0.23	0.02
72	4-Hydroxyphenyllactic	≤ 0.62	0.24
73	N-Acetylaspartic	≤ 2.5	1.6
74	Malonic	≤ 9.9	2.7
75	4-Hydroxybutyric	≤ 4.3	3.6

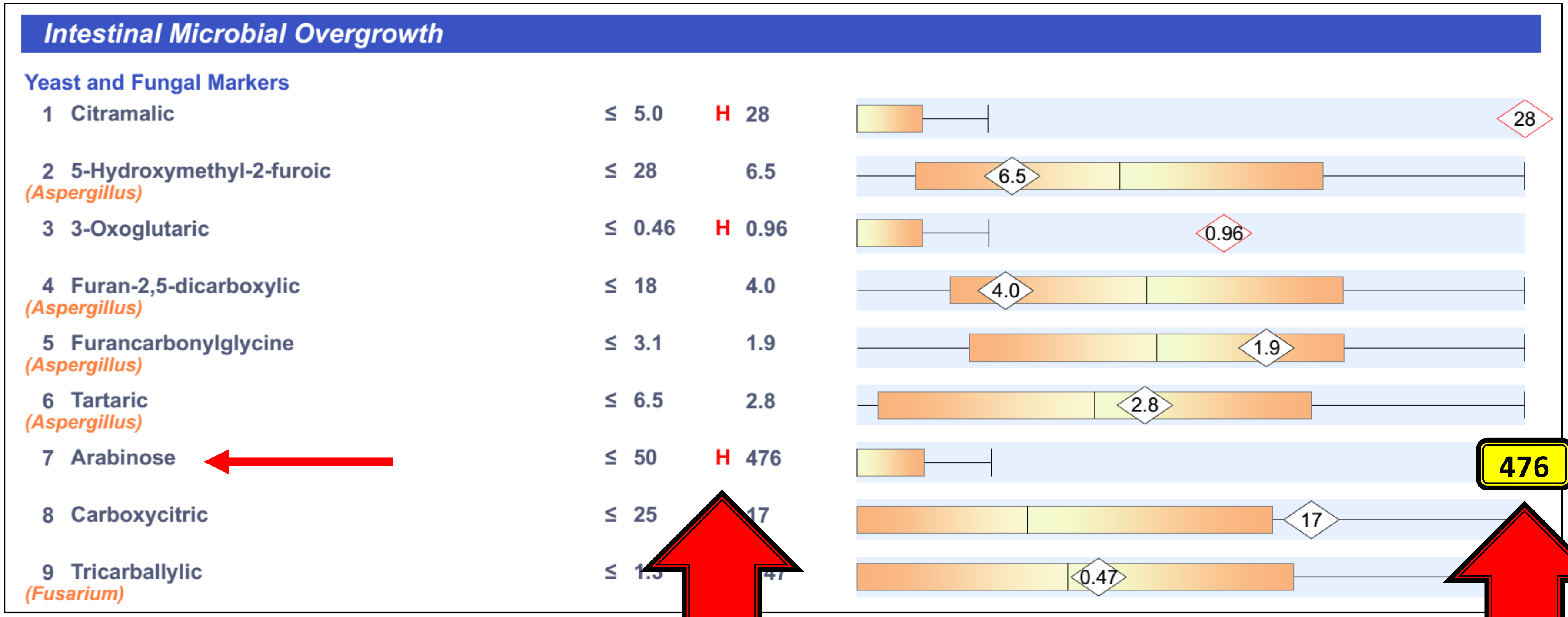
Mineral Metabolism

76	Phosphoric	1,000 - 4,900	2,488

**OAT
Sample
Report**

Yeast/Fungal Assessment

More information to come in Lecture #2

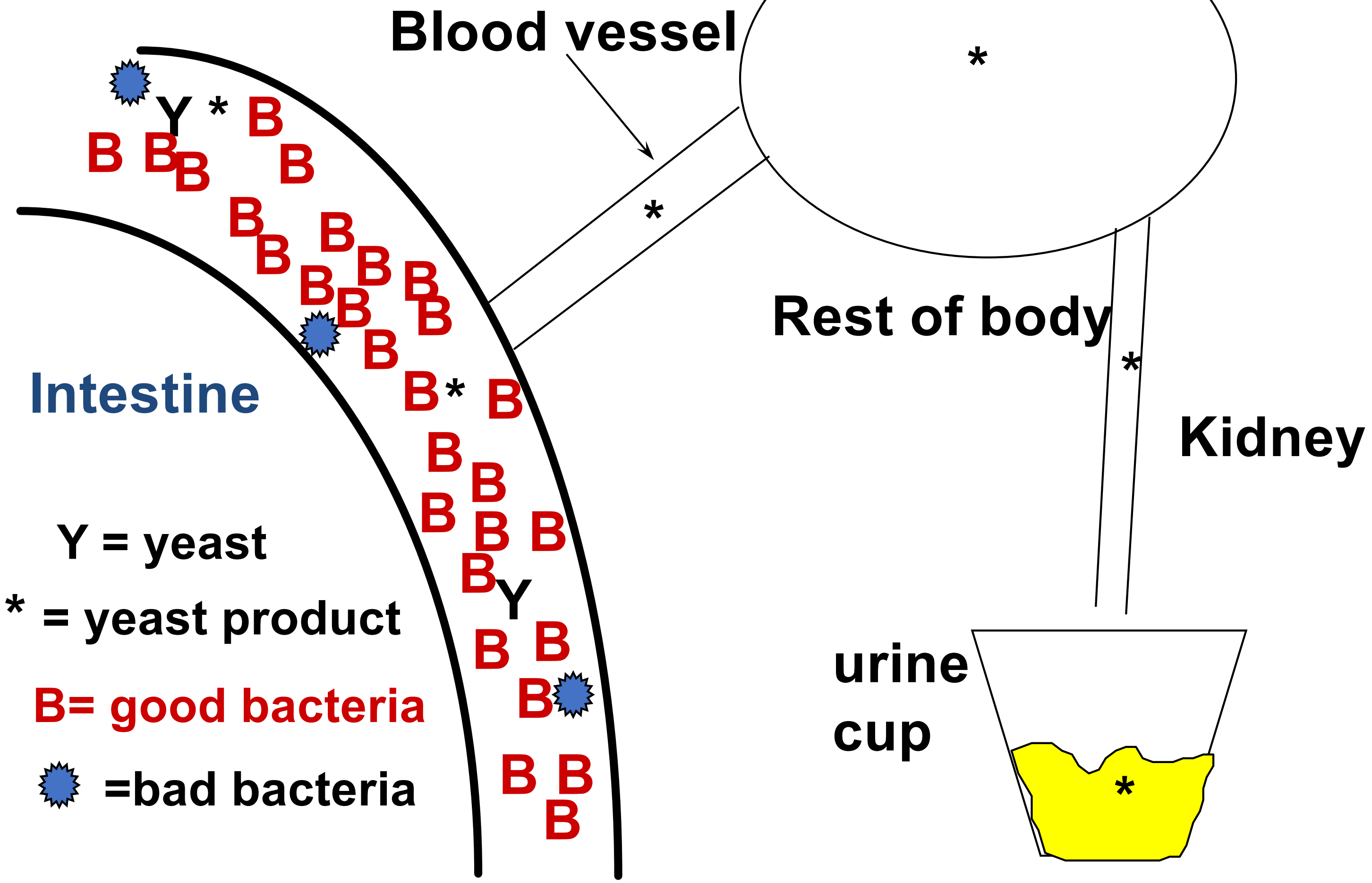


Intestinal Microbial Overgrowth

Yeast and Fungal Markers

1	**Citramalic**	≤ 5.0	H	28
2	**5-Hydroxymethyl-2-furoic** *(Aspergillus)*	≤ 28		6.5
3	**3-Oxoglutaric**	≤ 0.46	H	0.96
4	**Furan-2,5-dicarboxylic** *(Aspergillus)*	≤ 18		4.0
5	**Furancarbonylglycine** *(Aspergillus)*	≤ 3.1		1.9
6	**Tartaric** *(Aspergillus)*	≤ 6.5		2.8
7	**Arabinose**	≤ 50	H	476
8	**Carboxycitric**	≤ 25		17
9	**Tricarballylic** *(Fusarium)*	≤ 1.3		0.47

Normal Intestine



Blood vessel

Rest of body

Kidney

urine cup

Intestine

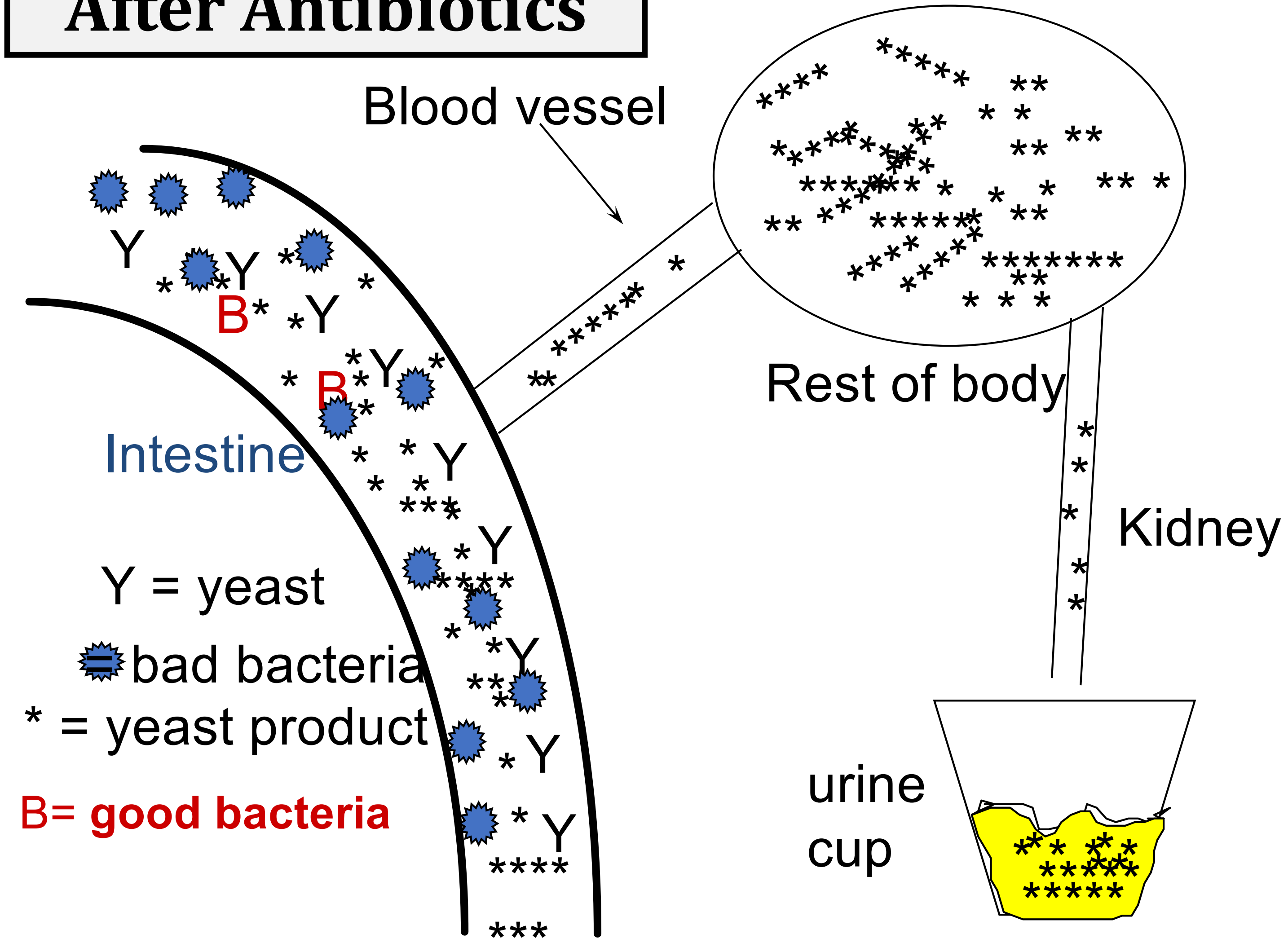
Y = yeast

* = yeast product

B= good bacteria

● =bad bacteria

After Antibiotics



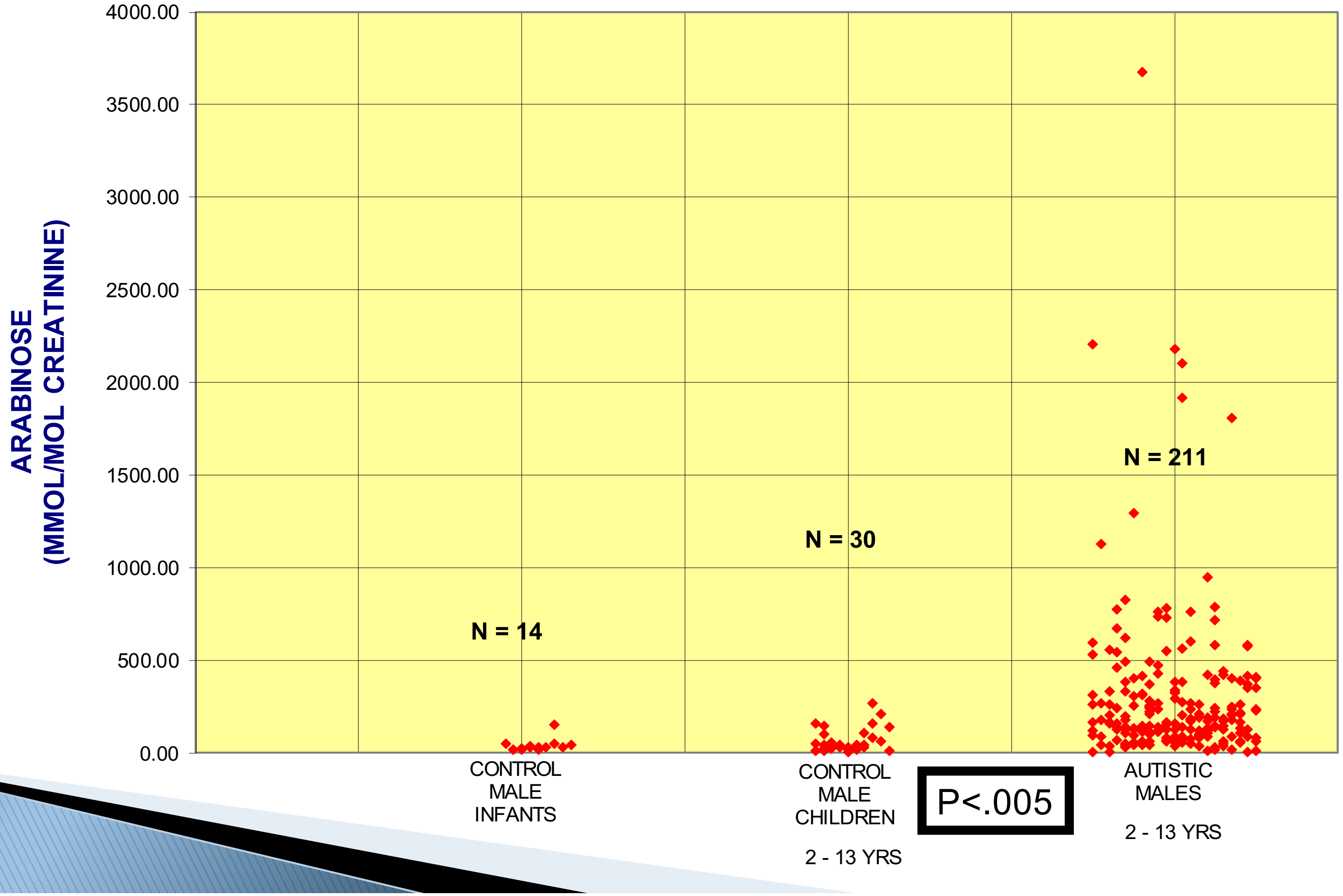
Y = yeast

● = bad bacteria

* = yeast product

B= good bacteria

Shaw, W., et al Assessment of antifungal drug therapy in autism by measurement of suspected microbial metabolites in urine with GC/MS. Clinical Practice of Alternative Medicine: 15-26,2000



Conditions in which Candida may be a factor

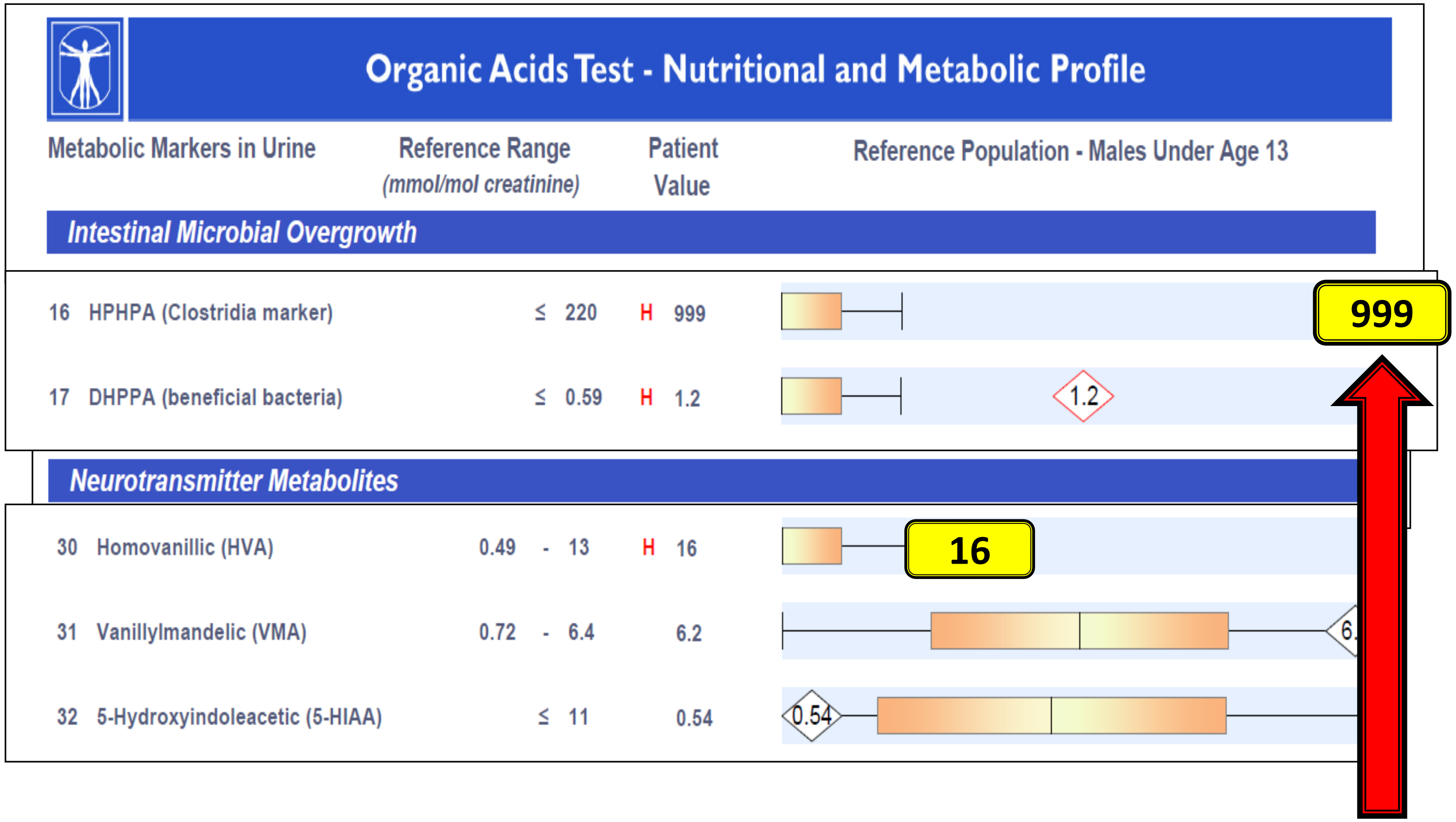
- Autism
- Alzheimer's disease
- Systemic lupus erythematosus (SLE)
- Fibromyalgia
- Chronic fatigue syndrome & CFIDS
- HIV infection
- Schizophrenia

- Colitis
- Depression
- PMS
- Vaginal yeast infection
- Multiple sclerosis
- Interstitial cystitis
- Seizures
- Irritable bowel
- Cancer

Clostridia Bacteria
Toxin Assessment

More information to come in Lecture #3

HPHPA

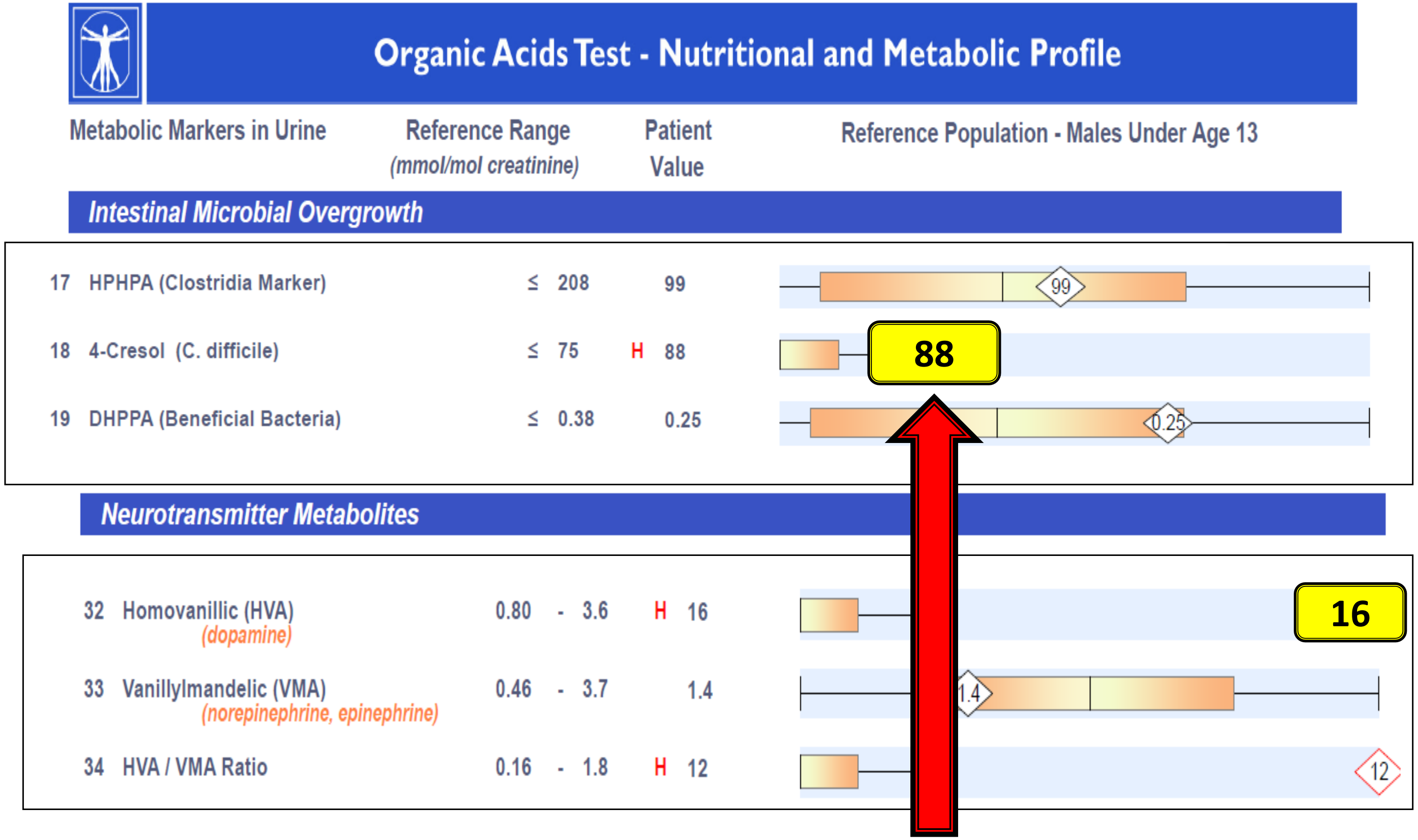


Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	
Intestinal Microbial Overgrowth			
16 HPHPA (Clostridia marker)	≤ 220	H	999
17 DHPPA (beneficial bacteria)	≤ 0.59	H	1.2
Neurotransmitter Metabolites			
30 Homovanillic (HVA)	0.49 - 13	H	16
31 Vanillylmandelic (VMA)	0.72 - 6.4		6.2
32 5-Hydroxyindoleacetic (5-HIAA)	≤ 11		0.54

Reference Population - Males Under Age 13

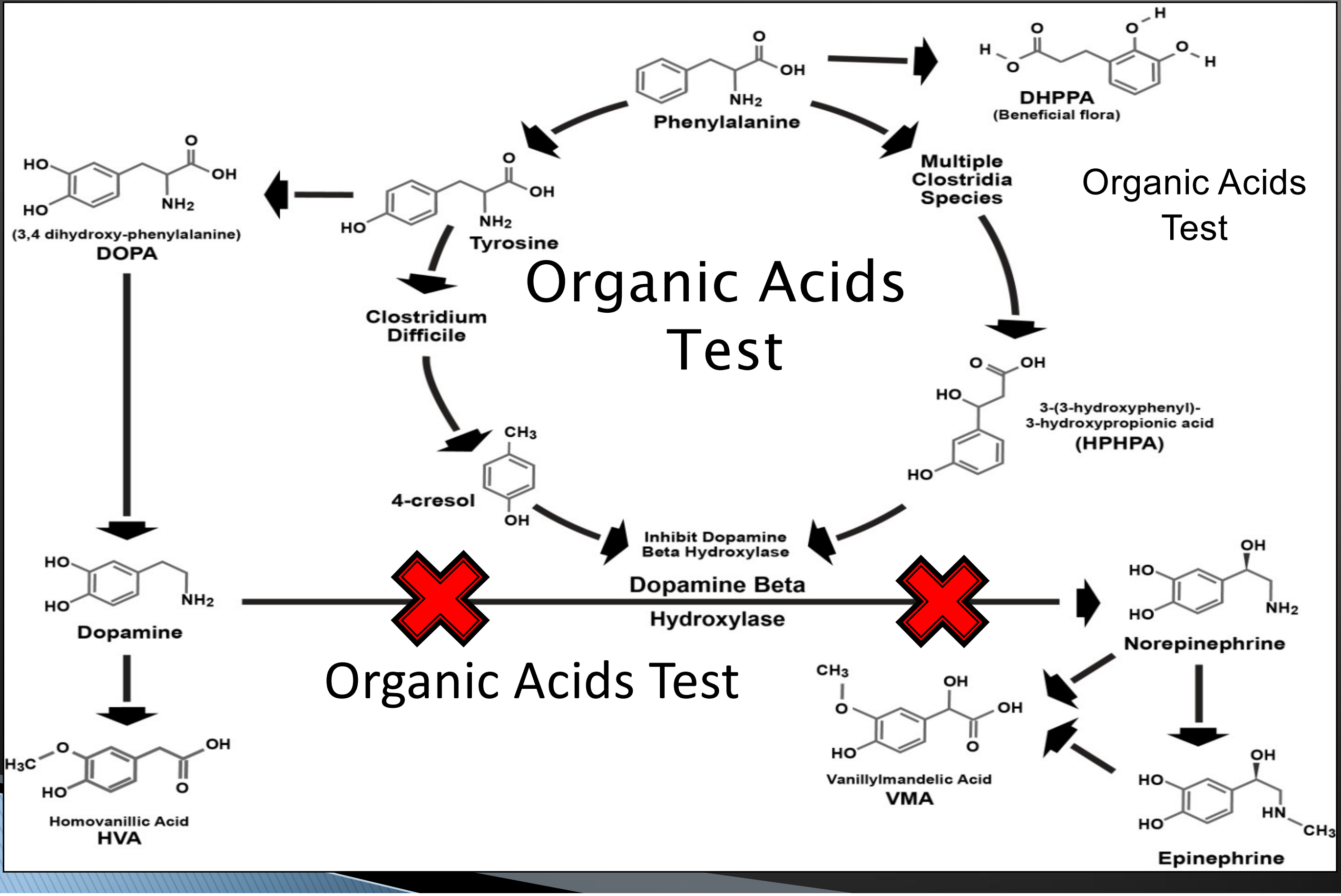
4-Cresol



Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
Intestinal Microbial Overgrowth				
17 HPHPA (Clostridia Marker)	≤ 208		99	99
18 4-Cresol (C. difficile)	≤ 75	H	88	88
19 DHPPA (Beneficial Bacteria)	≤ 0.38		0.25	0.25
Neurotransmitter Metabolites				
32 Homovanillic (HVA) *(dopamine)*	0.80 - 3.6	H	16	16
33 Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.46 - 3.7		1.4	1.4
34 HVA / VMA Ratio	0.16 - 1.8	H	12	12

Effect of Certain Intestinal Bacteria Toxins on Neurotransmitters

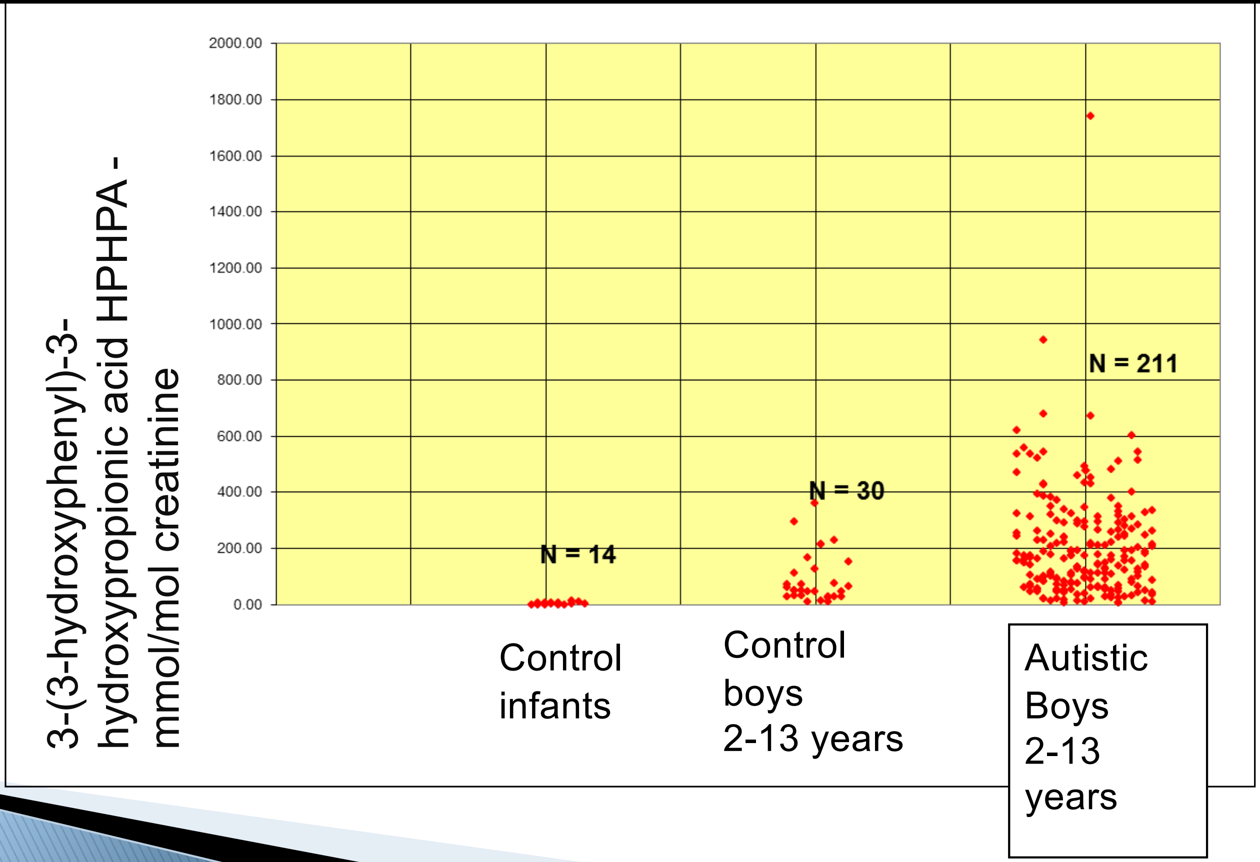


Organic Acids Test

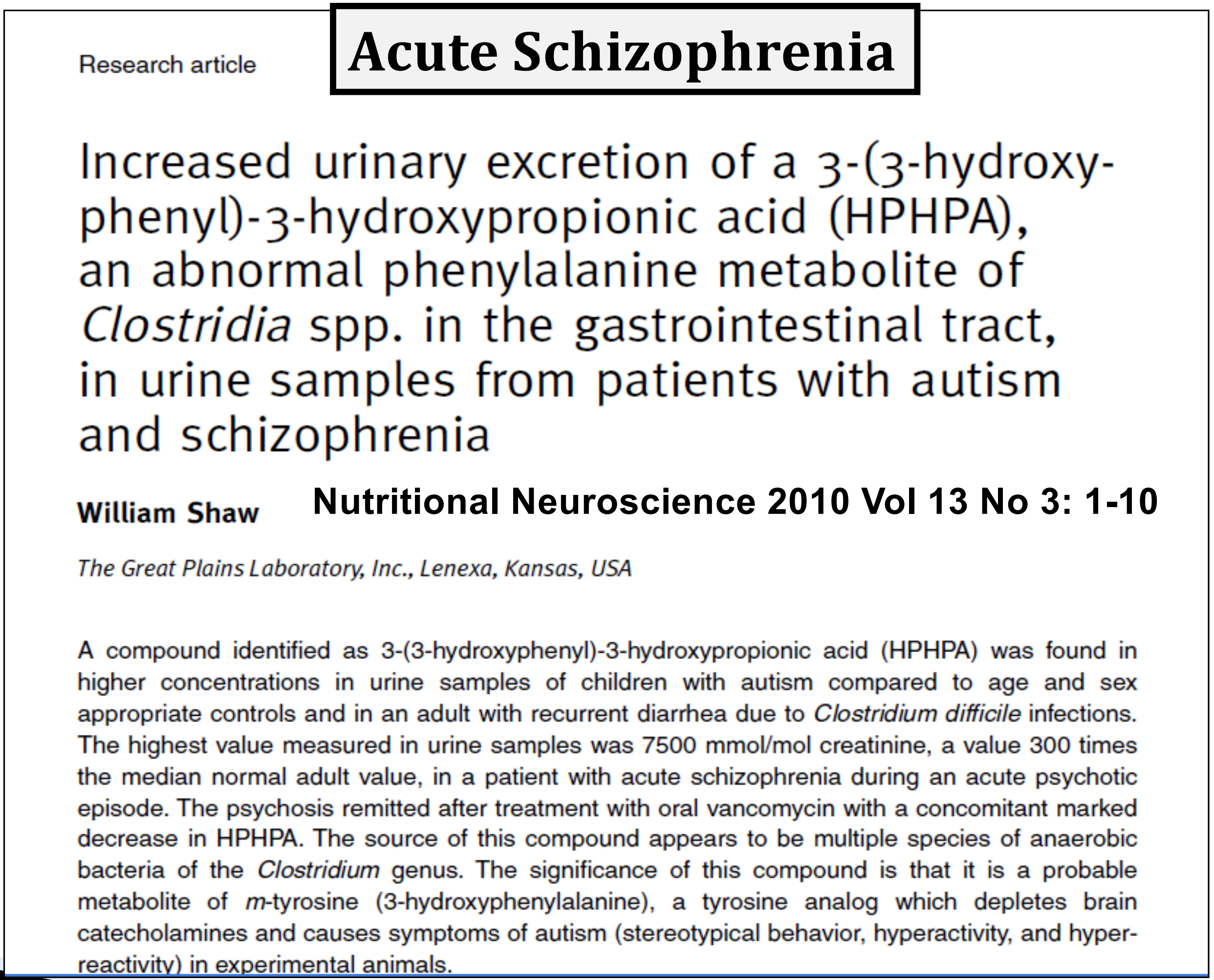
Organic Acids Test

Organic Acids Test

Distribution of values for HPHPA Clostridia metabolite in urine samples of male infants, control boys, and boys with autism.



Acute Schizophrenia



Research article

Increased urinary excretion of a 3-(3-hydroxyphenyl)-3-hydroxypropionic acid (HPHPA), an abnormal phenylalanine metabolite of *Clostridia* spp. in the gastrointestinal tract, in urine samples from patients with autism and schizophrenia

William Shaw

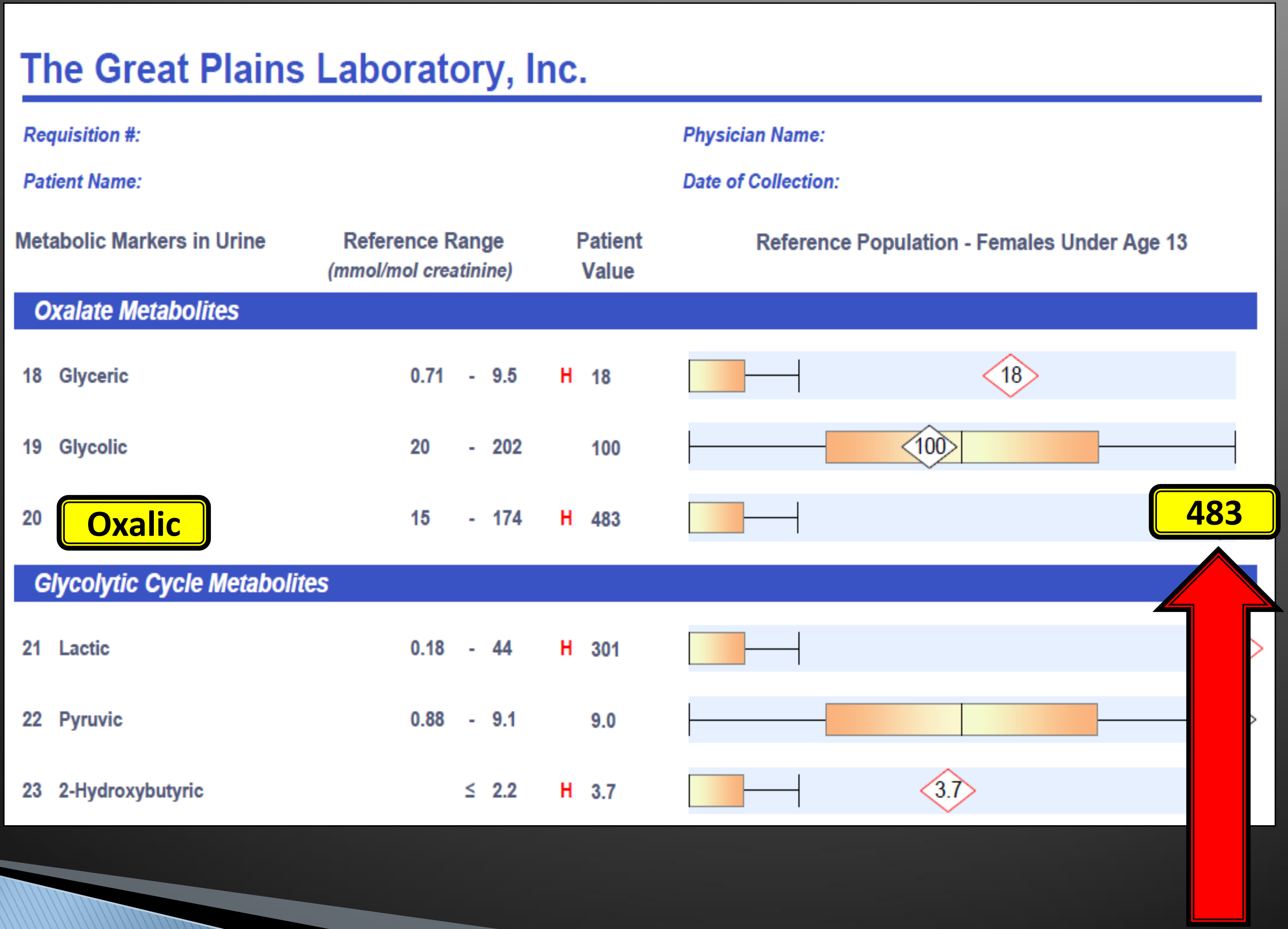
The Great Plains Laboratory, Inc., Lenexa, Kansas, USA

Nutritional Neuroscience 2010 Vol 13 No 3: 1-10

A compound identified as 3-(3-hydroxyphenyl)-3-hydroxypropionic acid (HPHPA) was found in higher concentrations in urine samples of children with autism compared to age and sex appropriate controls and in an adult with recurrent diarrhea due to *Clostridium difficile* infections. The highest value measured in urine samples was 7500 mmol/mol creatinine, a value 300 times the median normal adult value, in a patient with acute schizophrenia during an acute psychotic episode. The psychosis remitted after treatment with oral vancomycin with a concomitant marked decrease in HPHPA. The source of this compound appears to be multiple species of anaerobic bacteria of the *Clostridium* genus. The significance of this compound is that it is a probable metabolite of *m*-tyrosine (3-hydroxyphenylalanine), a tyrosine analog which depletes brain catecholamines and causes symptoms of autism (stereotypical behavior, hyperactivity, and hyper-reactivity) in experimental animals.

Oxalate Assessment

More information to come in Lecture #4



The Great Plains Laboratory, Inc.

Requisition #: *Physician Name:*

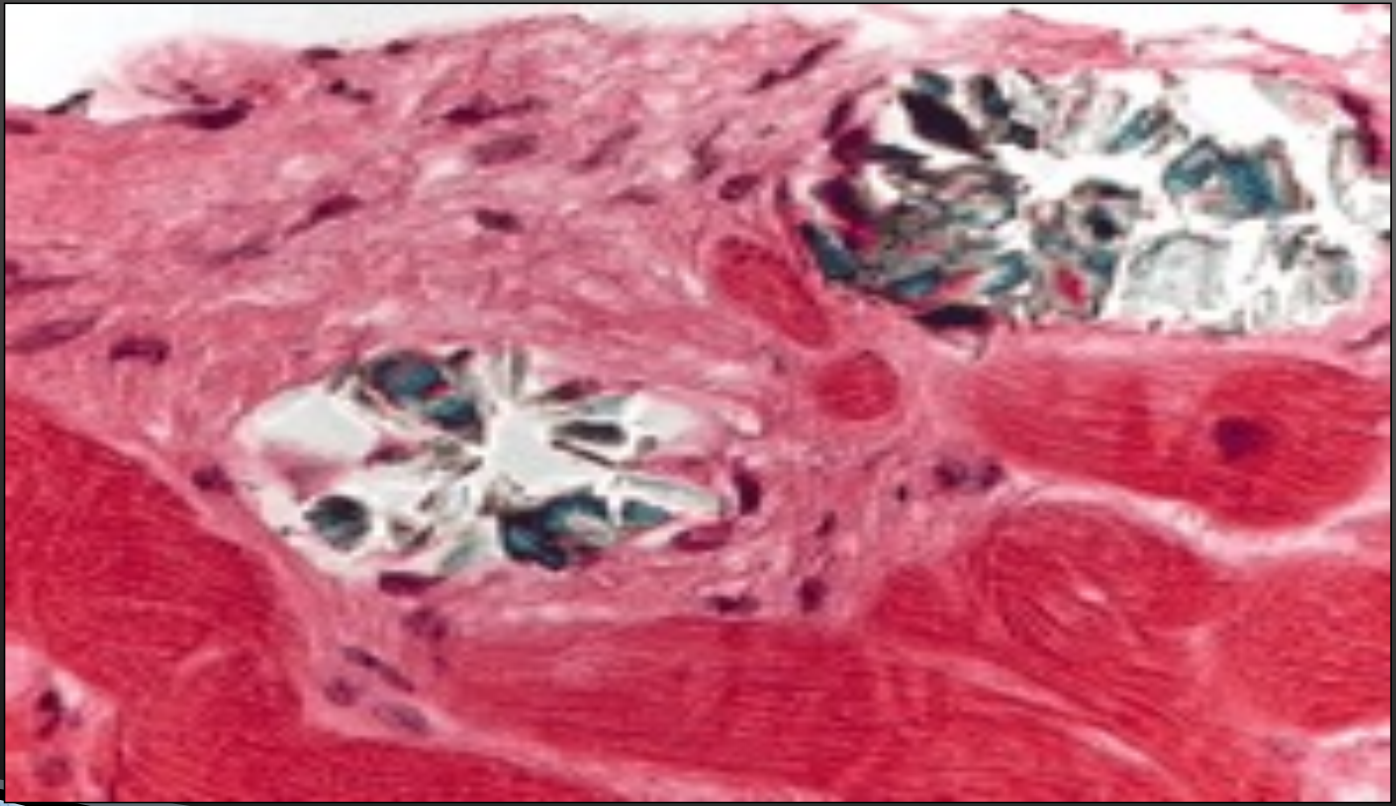
Patient Name: *Date of Collection:*

Metabolic Markers in Urine		Reference Range (*mmol/mol creatinine*)			Patient Value		Reference Population - Females Under Age 13
Oxalate Metabolites							
18	Glyceric	0.71	-	9.5	H	18	18
19	Glycolic	20	-	202		100	100
20	**Oxalic**	15	-	174	H	483	**483**
Glycolytic Cycle Metabolites							
21	Lactic	0.18	-	44	H	301	
22	Pyruvic	0.88	-	9.1		9.0	
23	2-Hydroxybutyric		≤	2.2	H	3.7	3.7

Oxalate Staghorn in Kidney

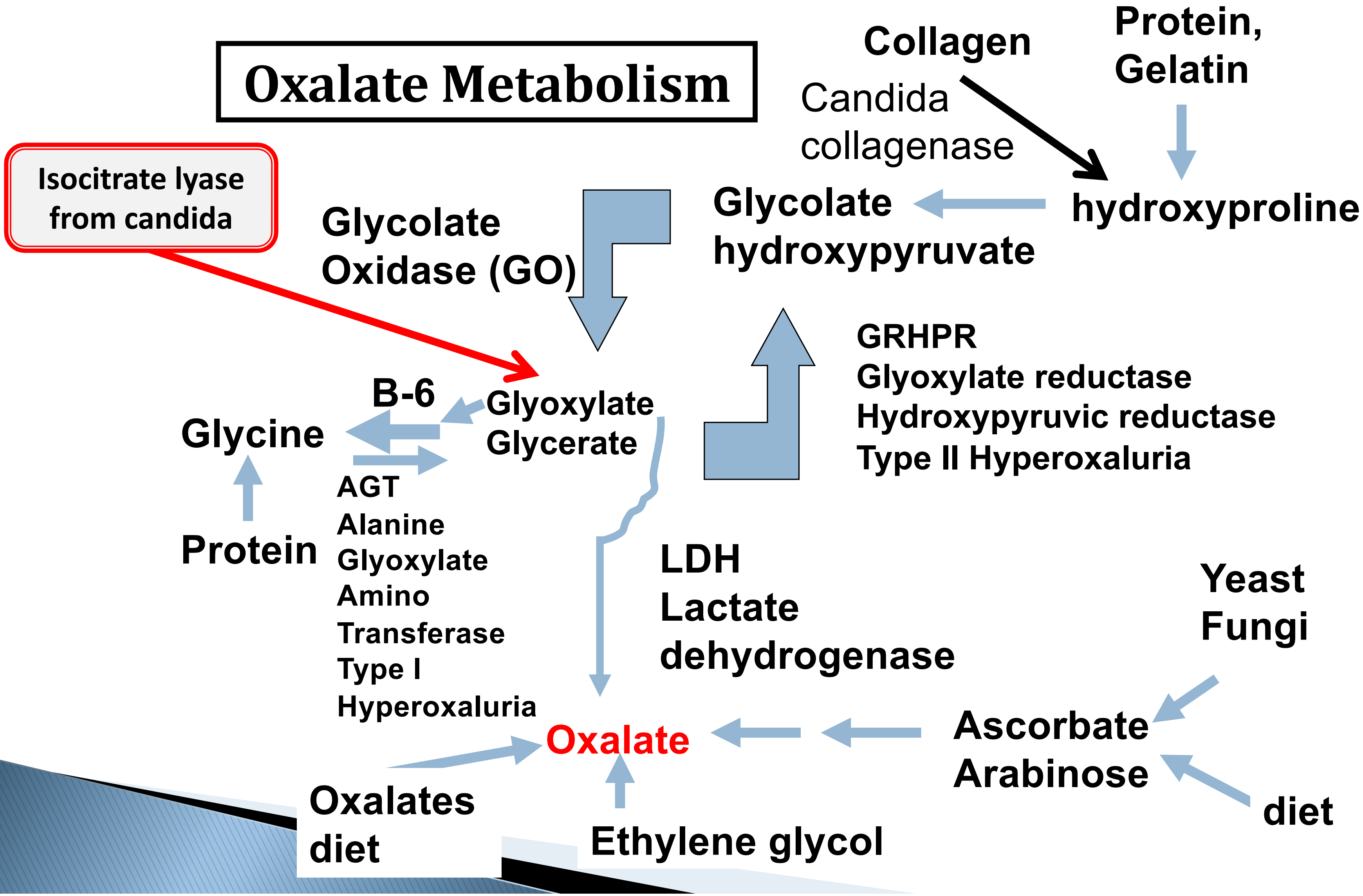
75-90% of kidney stones are oxalates. 10-15 percent of adults will be diagnosed with a kidney stone in their lifetime.

Oxalate Crystals in the Heart



Oxalate Crystals in Leg Lesions

Oxalate Metabolism



Collagen

Protein,
Gelatin

Candida
collagenase

hydroxyproline

Glycolate
hydroxypyruvate

Isocitrate lyase
from candida

Glycolate
Oxidase (GO)

GRHPR
Glyoxylate reductase
Hydroxypyruvic reductase
Type II Hyperoxaluria

B-6

Glyoxylate
Glycerate

Glycine

Protein

AGT
Alanine
Glyoxylate
Amino
Transferase
Type I
Hyperoxaluria

LDH
Lactate
dehydrogenase

Yeast
Fungi

Ascorbate
Arabinose

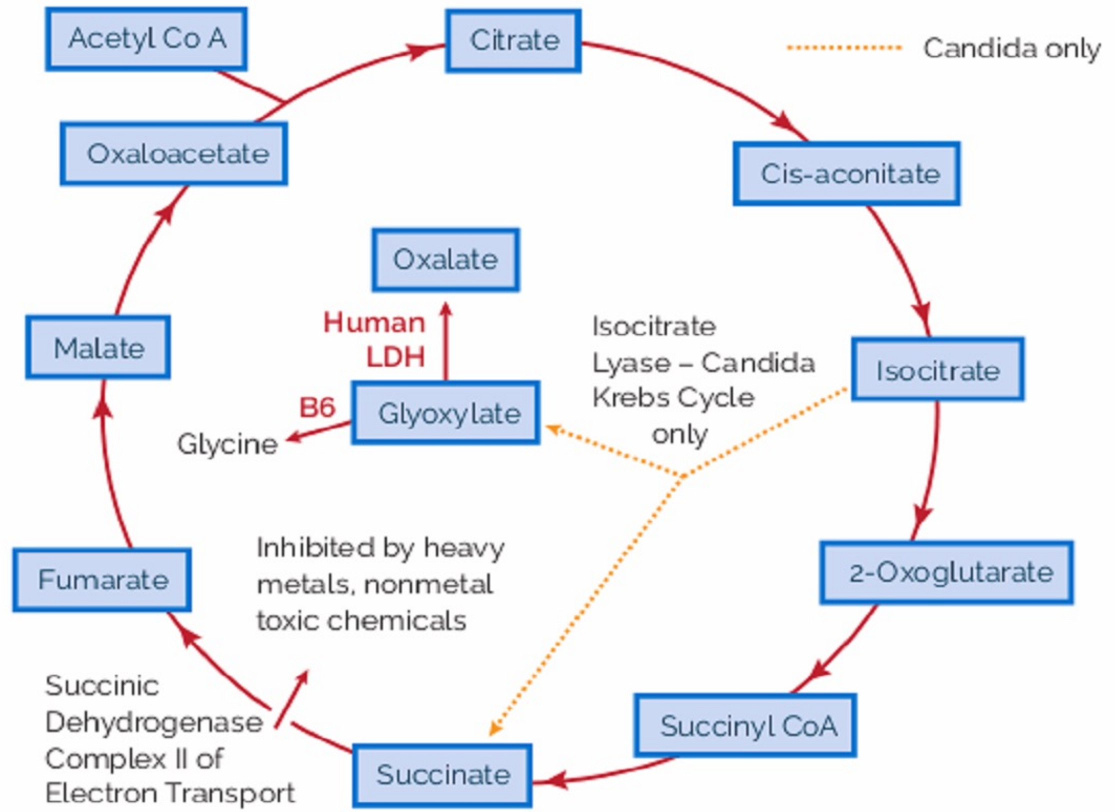
diet

Oxalate

Oxalates
diet

Ethylene glycol

Human Krebs Cycle showing Candida Krebs Cycle variant that causes excess Oxalate via Glyoxylate



Acetyl Co A

Citrate

Candida only

Oxaloacetate

Cis-aconitate

Oxalate

Human LDH

Isocitrate Lyase – Candida Krebs Cycle only

Malate

Isocitrate

B6

Glyoxylate

Glycine

Inhibited by heavy metals, nonmetal toxic chemicals

Fumarate

2-Oxoglutarate

Succinic Dehydrogenase Complex II of Electron Transport

Succinyl CoA

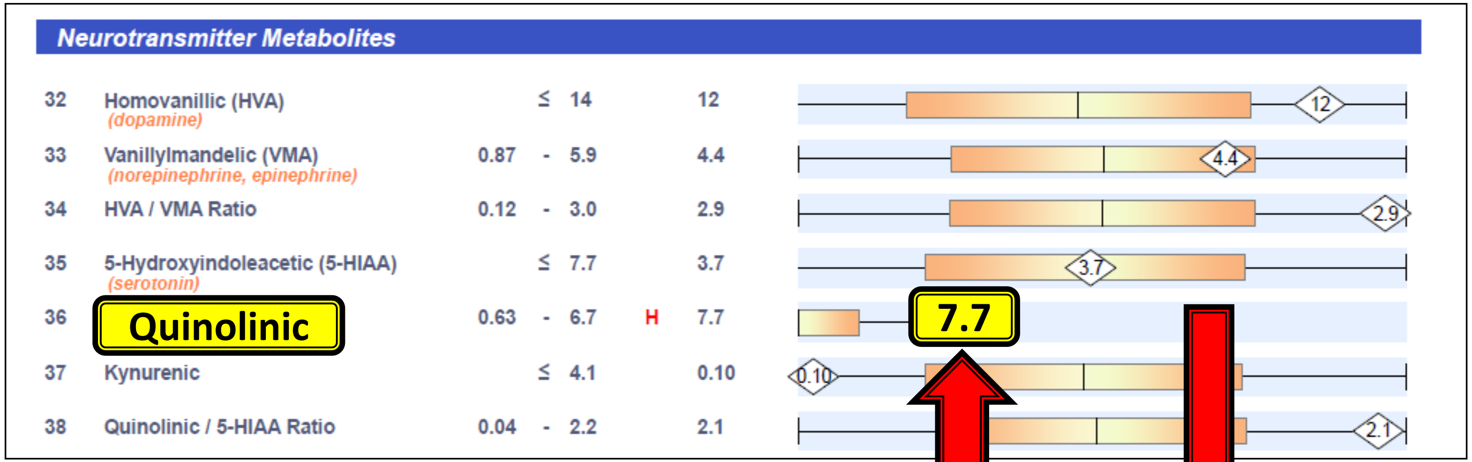
Succinate

Various health problems in which high oxalate may play a role

- Arthritis
- Behavior problems in children
- Interstitial cystitis
- Joint pain
- Fibromyalgia
- Heart disease
- Heavy metal problems
- Mitochondrial dysfunction
- Osteoporosis
- Thyroid disorders

Quinolinic Acid *(and neurochemical)* Assessment

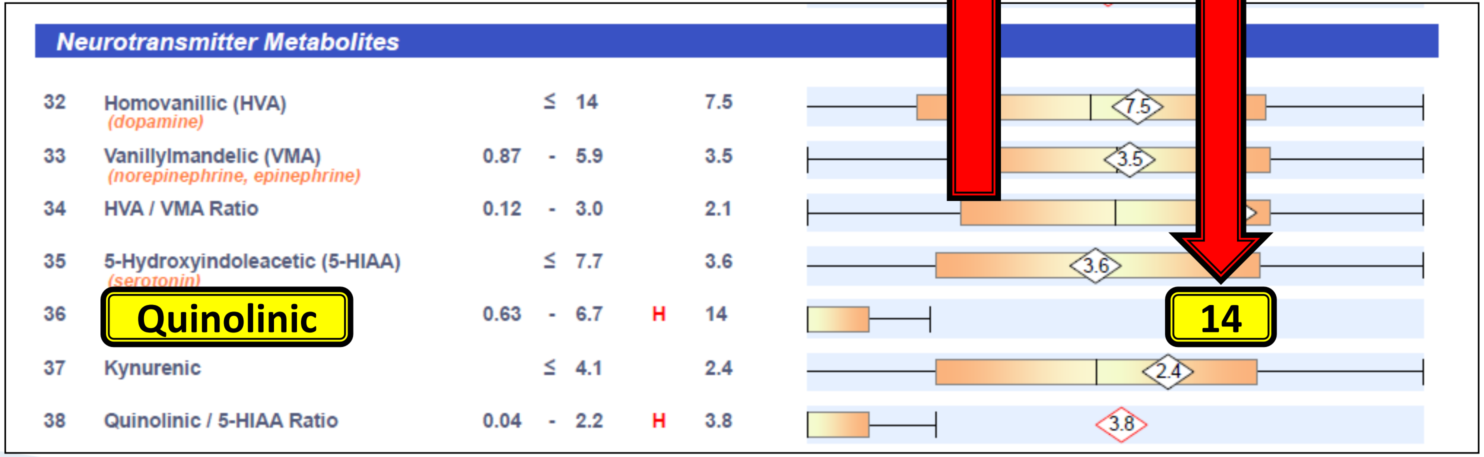
More information to come in Lecture #5



Neurotransmitter Metabolites

32	Homovanillic (HVA) *(dopamine)*		≤ 14		12
33	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.87	- 5.9		4.4
34	HVA / VMA Ratio	0.12	- 3.0		2.9
35	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*		≤ 7.7		3.7
36	**Quinolinic**	0.63	- 6.7	H	7.7
37	Kynurenic		≤ 4.1		0.10
38	Quinolinic / 5-HIAA Ratio	0.04	- 2.2		2.1

7.7

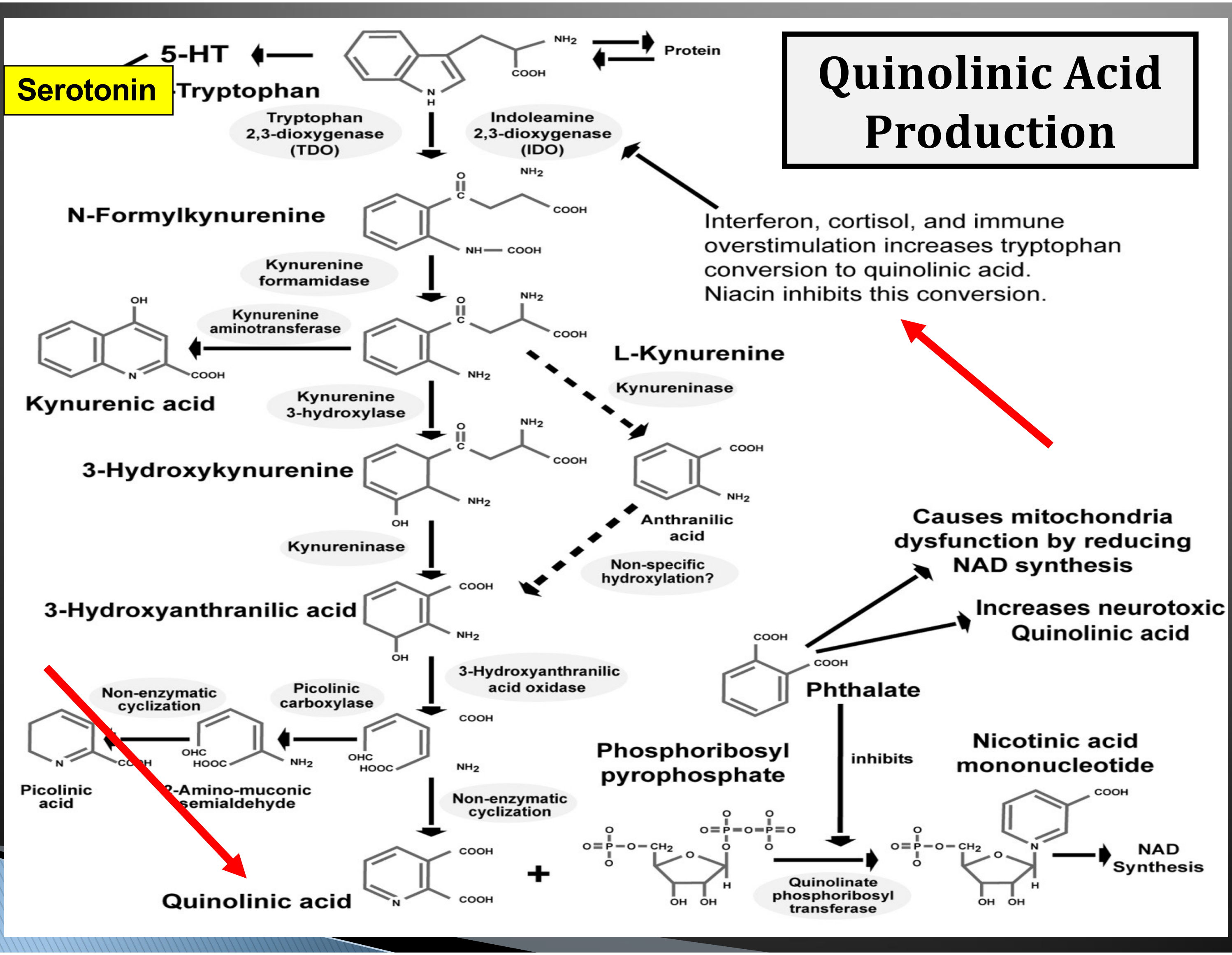


Neurotransmitter Metabolites

32	Homovanillic (HVA) *(dopamine)*		≤ 14		7.5
33	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.87	- 5.9		3.5
34	HVA / VMA Ratio	0.12	- 3.0		2.1
35	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*		≤ 7.7		3.6
36	**Quinolinic**	0.63	- 6.7	H	14
37	Kynurenic		≤ 4.1		2.4
38	Quinolinic / 5-HIAA Ratio	0.04	- 2.2	H	3.8

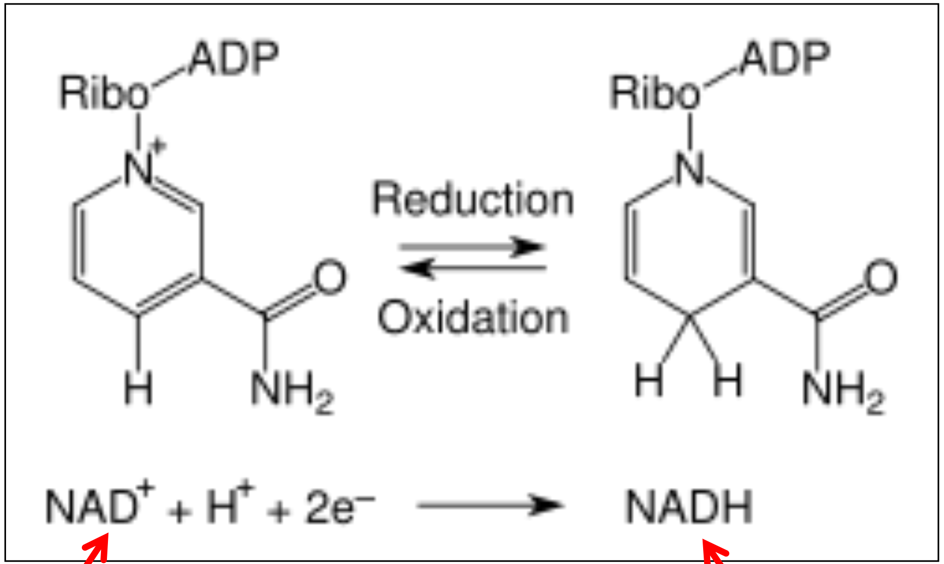
14

Quinolinic Acid Production



Interferon, cortisol, and immune overstimulation increases tryptophan conversion to quinolinic acid.
Niacin inhibits this conversion.

Nicotinamide adenine dinucleotide *(hydrogen)*

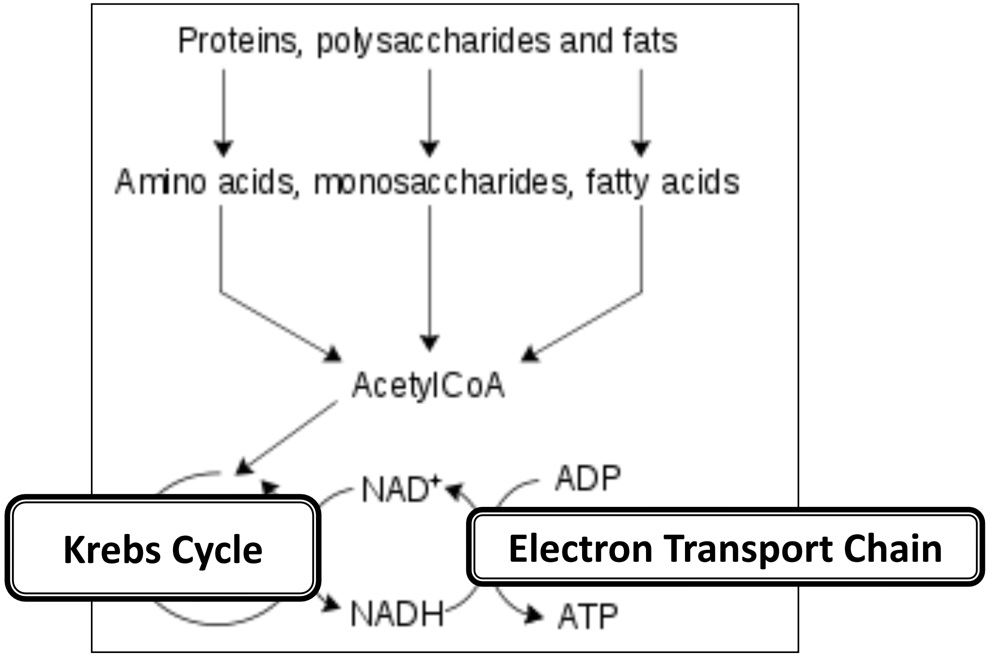


$$NAD^+ + H^+ + 2e^- \longrightarrow NADH$$

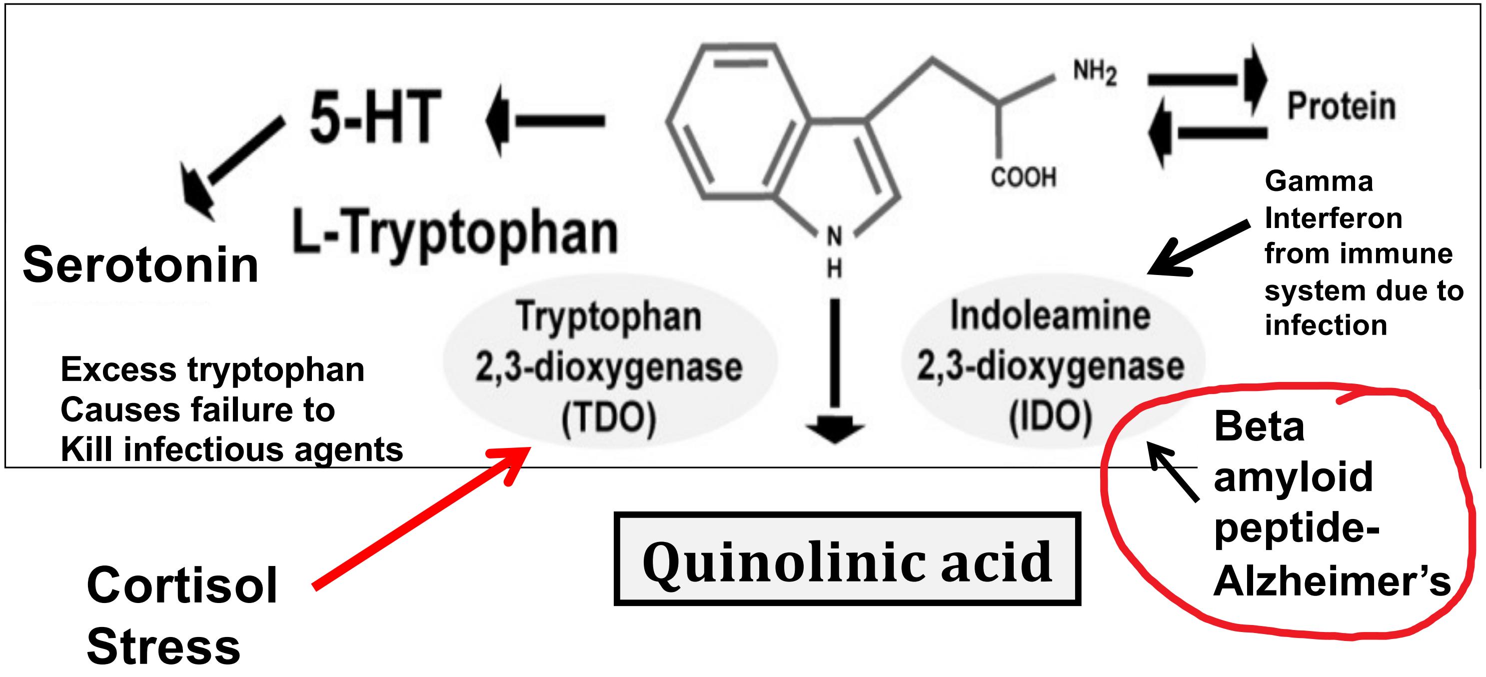
Oxidized

Reduced

Redox Reactions



- **Oxidation** is the *loss* of electrons or an *increase* in oxidation state by a molecule, atom, or ion.
- **Reduction** is the *gain* of electrons or a *decrease* in oxidation state by a molecule, atom, or ion.



5-HT

Serotonin

L-Tryptophan

Protein

Gamma Interferon from immune system due to infection

Excess tryptophan
Causes failure to
Kill infectious agents

Tryptophan 2,3-dioxygenase (TDO)

Indoleamine 2,3-dioxygenase (IDO)

Beta amyloid peptide- Alzheimer’s

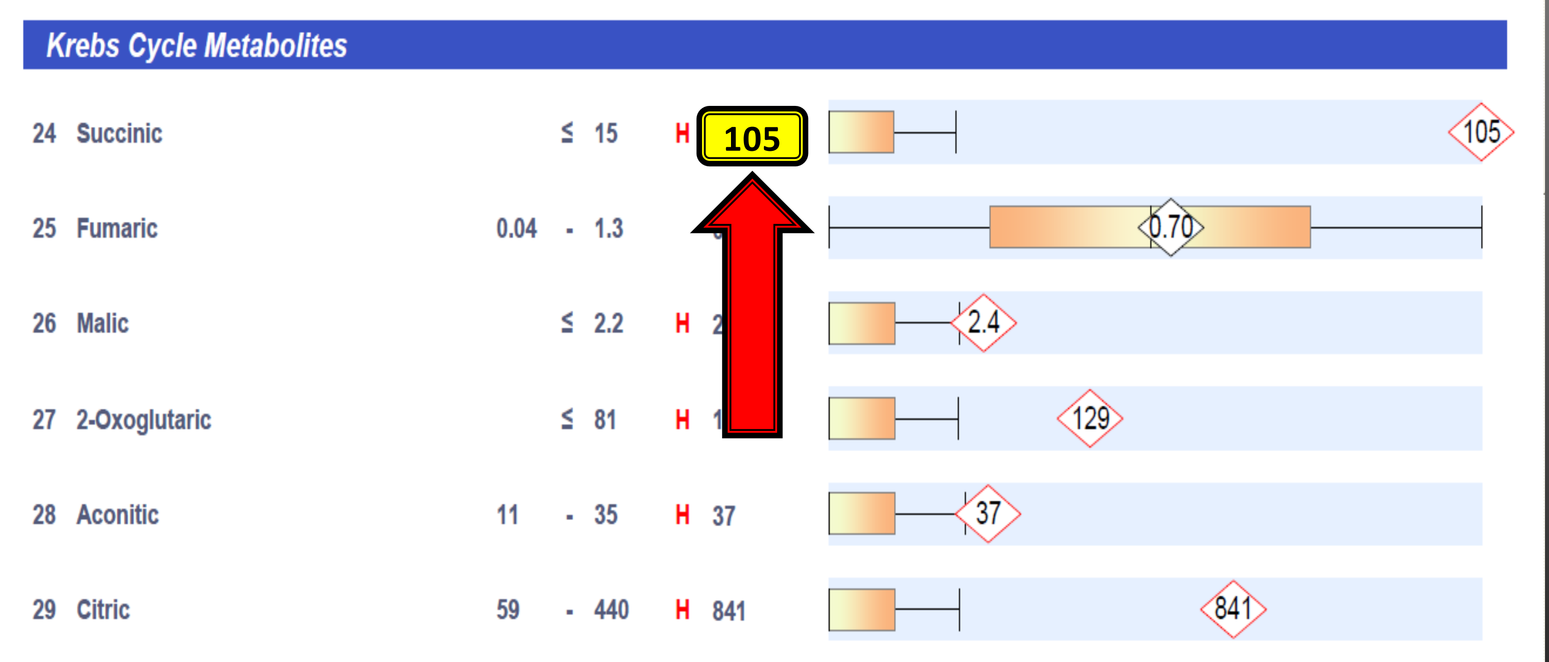
Quinolinic acid

Cortisol
Stress

Kills cells containing bacteria, viruses, parasites. May also damage infectious organisms themselves. IDO causes drastic reduction in tryptophan for protein synthesis needed by infected cells and infectious organisms - tryptophan at very low levels.

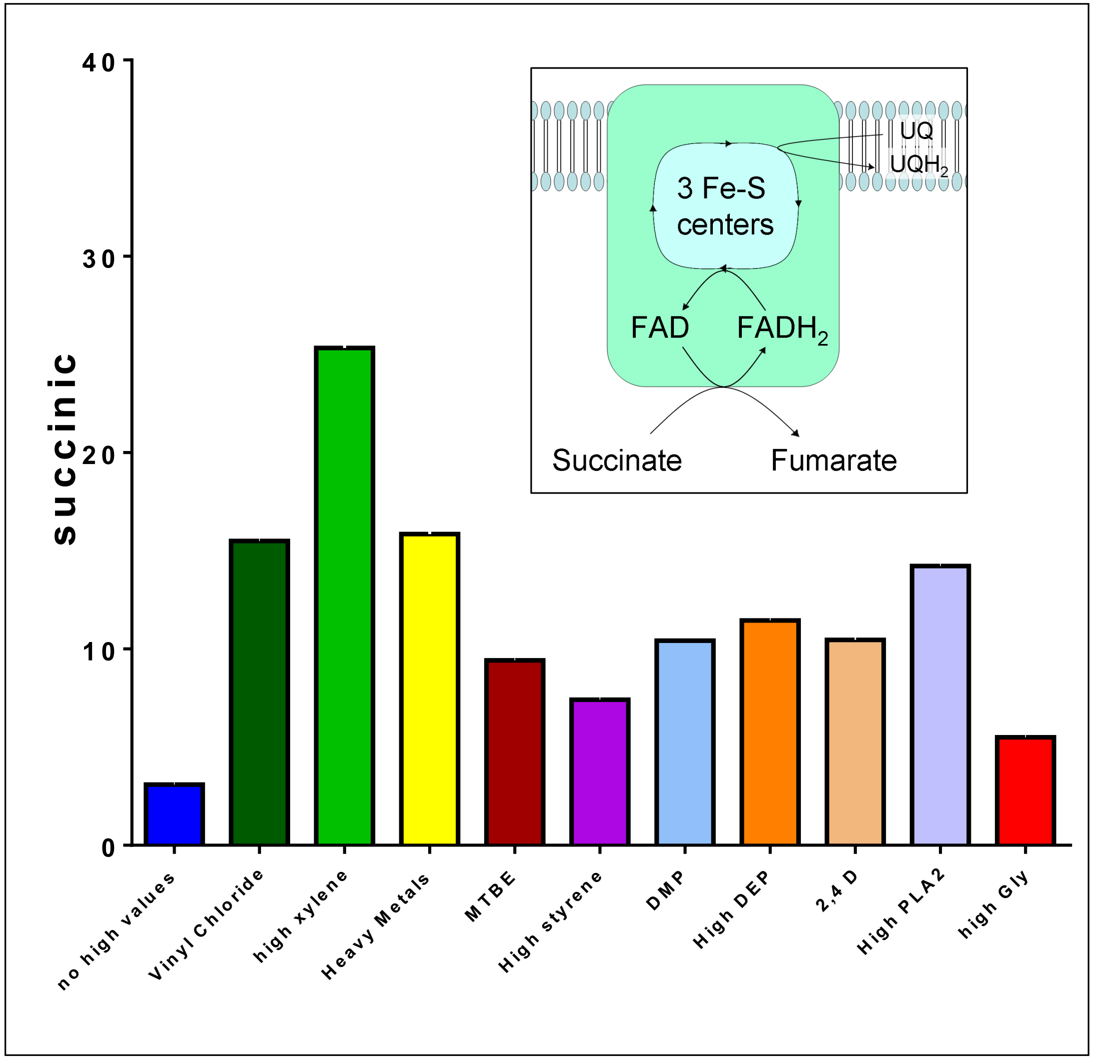
Mitochondria Dysfunction Assessment

Krebs Cycle Metabolites



Krebs Cycle Metabolites

24	Succinic		≤	15	H	105
25	Fumaric	0.04	-	1.3		
26	Malic		≤	2.2	H	2
27	2-Oxoglutaric		≤	81	H	1
28	Aconitic	11	-	35	H	37
29	Citric	59	-	440	H	841


40
30
20
10
0
succinic
no high values
Vinyl Chloride
high xylene
Heavy Metals
MTBE
High styrene
DMP
High DEP
2,4 D
High PLA2
high Gly
UQ
UQH2
3 Fe-S centers
FAD
FADH2
Succinate
Fumarate

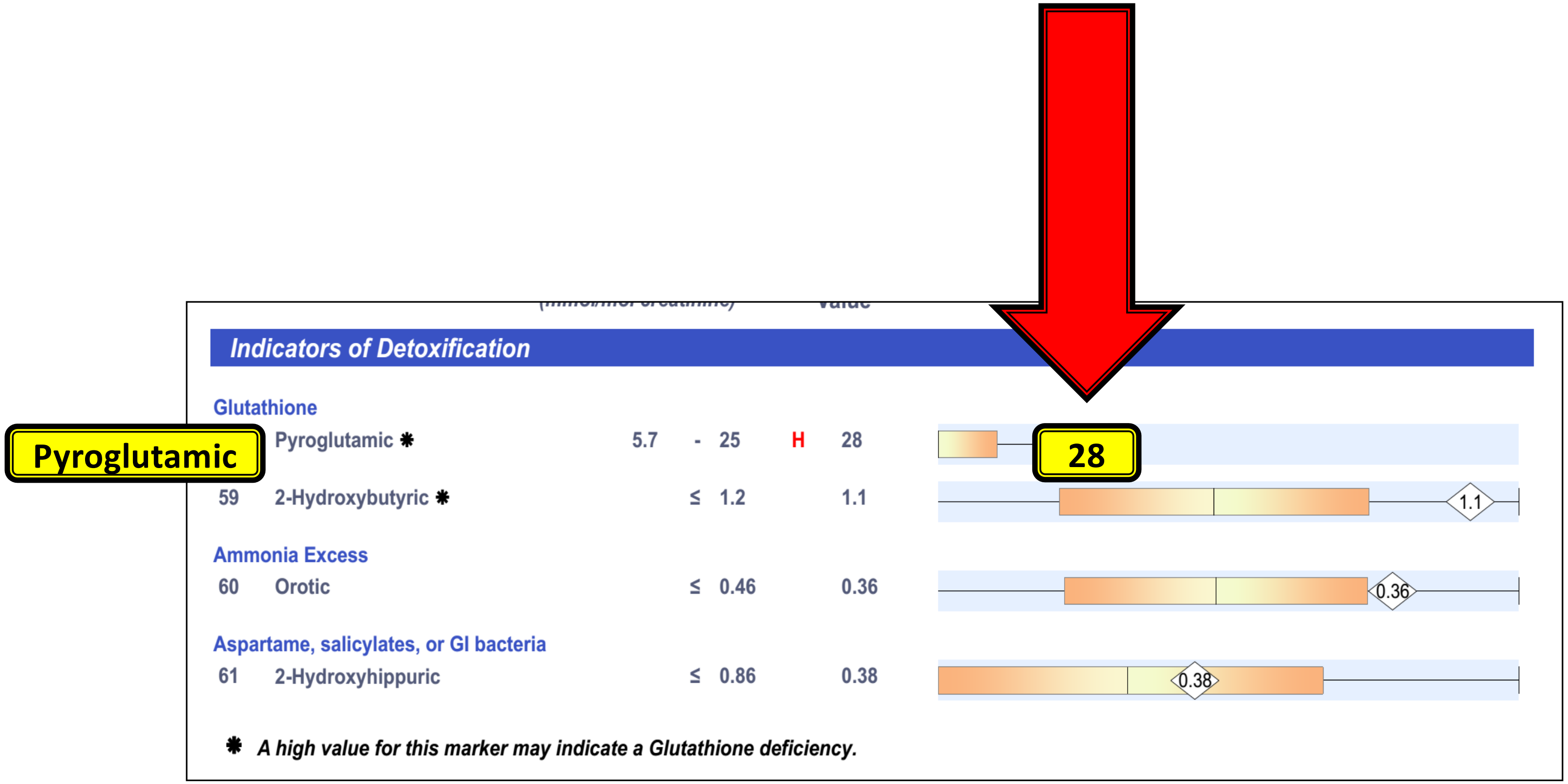
GPL OAT Course Attendee

Mitochondrial Markers - Krebs Cycle Metabolites

24	**Succinic**		≤	5.3	H	5.4
25	Fumaric		≤	0.49	H	1.0
26	Malic		≤	1.1		0.85
27	2-Oxoglutaric		≤	18		18
28	Aconitic	4.1	-	23		15
29	Citric	2.2	-	260	H	594

Mitochondrial Markers - Amino Acid Metabolites

30	3-Methylglutaric	0.02	-	0.38	H	0.72
31	3-Hydroxyglutaric		≤	4.6	H	7.2
32	3-Methylglutaconic	0.38	-	2.0		1.2



Indicators of Detoxification

Glutathione

	Pyroglutamic ✱	5.7	- 25	H	28
59	2-Hydroxybutyric ✱		≤ 1.2		1.1

Ammonia Excess

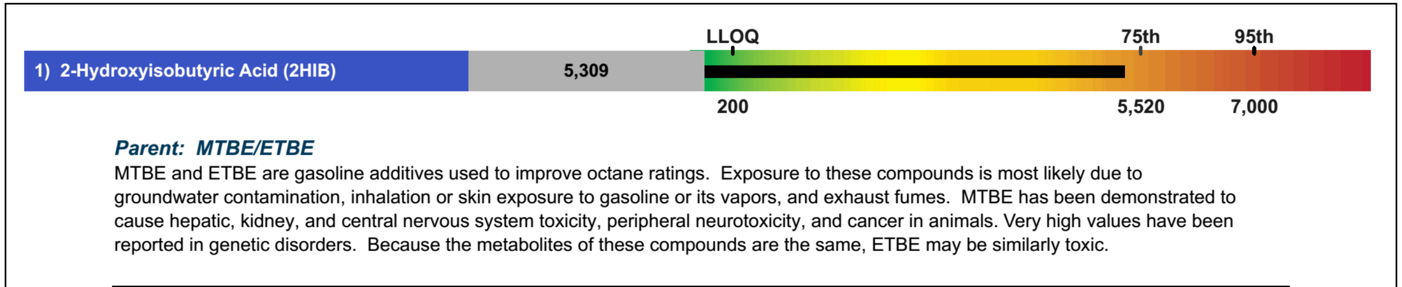
60	Orotic		≤ 0.46		0.36

Aspartame, salicylates, or GI bacteria

61	2-Hydroxyhippuric		≤ 0.86		0.38

✱ *A high value for this marker may indicate a Glutathione deficiency.*

GPL-TOX PROFILE

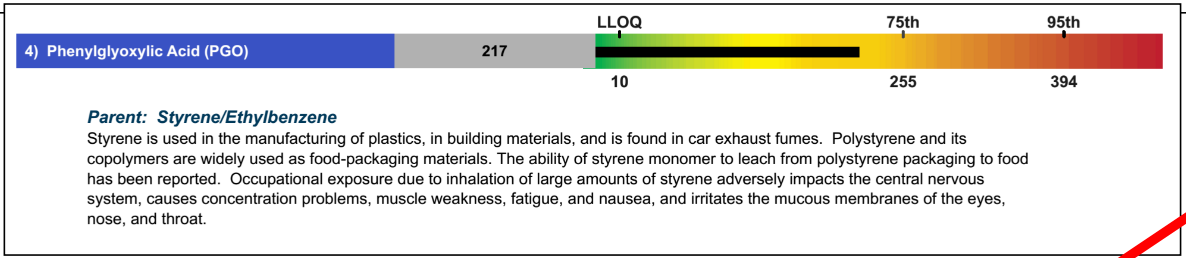

LLOQ 75th 95th

1) 2-Hydroxyisobutyric Acid (2HIB) 5,309

200 5,520 7,000

Parent: MTBE/ETBE

MTBE and ETBE are gasoline additives used to improve octane ratings. Exposure to these compounds is most likely due to groundwater contamination, inhalation or skin exposure to gasoline or its vapors, and exhaust fumes. MTBE has been demonstrated to cause hepatic, kidney, and central nervous system toxicity, peripheral neurotoxicity, and cancer in animals. Very high values have been reported in genetic disorders. Because the metabolites of these compounds are the same, ETBE may be similarly toxic.

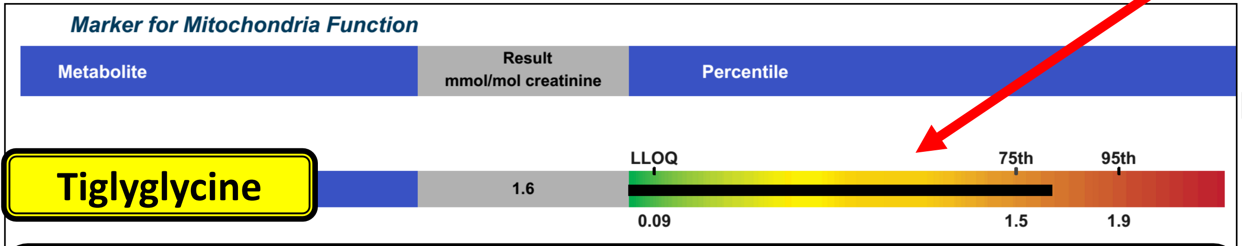

LLOQ 75th 95th

4) Phenylglyoxylic Acid (PGO) 217

10 255 394

Parent: Styrene/Ethylbenzene

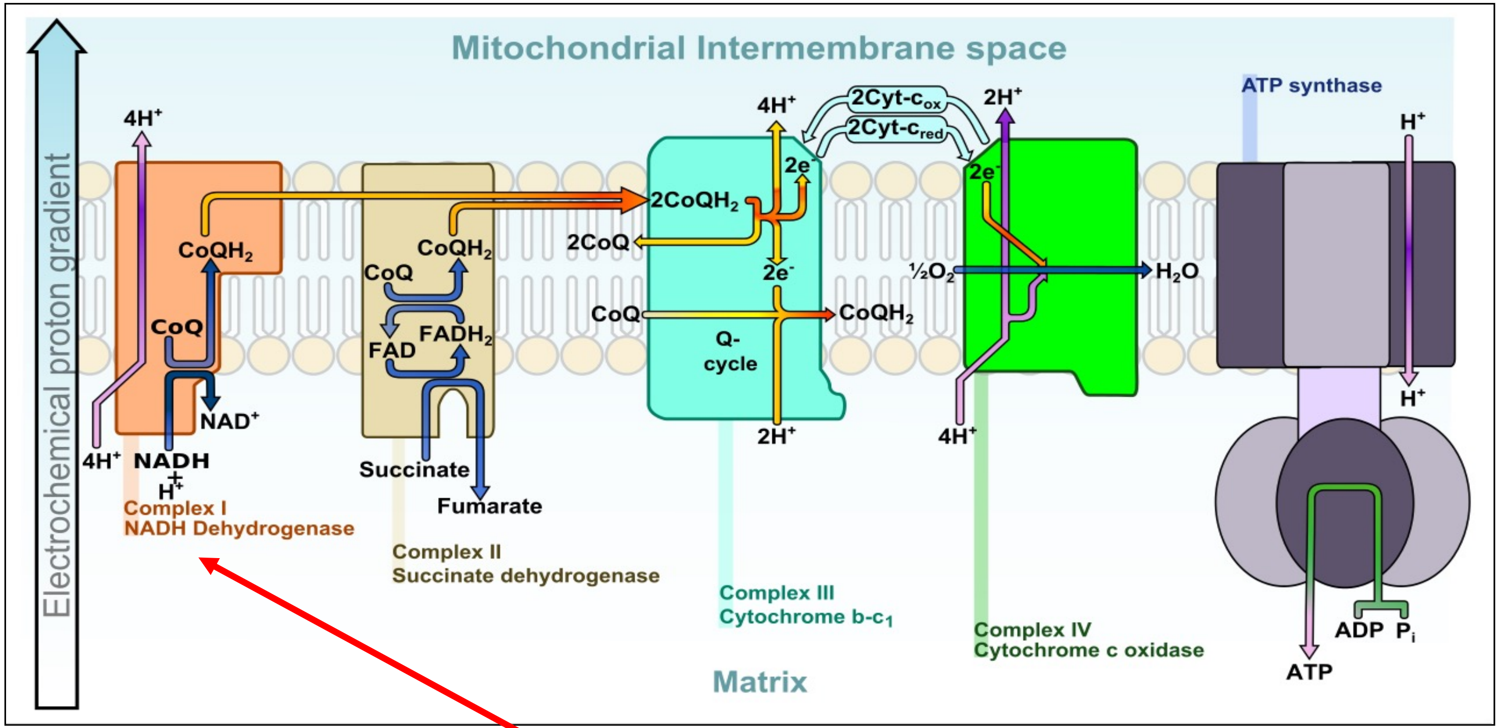
Styrene is used in the manufacturing of plastics, in building materials, and is found in car exhaust fumes. Polystyrene and its copolymers are widely used as food-packaging materials. The ability of styrene monomer to leach from polystyrene packaging to food has been reported. Occupational exposure due to inhalation of large amounts of styrene adversely impacts the central nervous system, causes concentration problems, muscle weakness, fatigue, and nausea, and irritates the mucous membranes of the eyes, nose, and throat.


Marker for Mitochondria Function

Metabolite	Result mmol/mol creatinine	Percentile
Tiglyglycine	1.6	LLOQ 0.09; 75th 1.5; 95th 1.9

Tiglyglycine linked to mitochondrial DNA mutations from infection, inflammation, toxins and nutritional deficiencies.

Electron Transport Chain
(aka Respiratory Chain)



Complex I

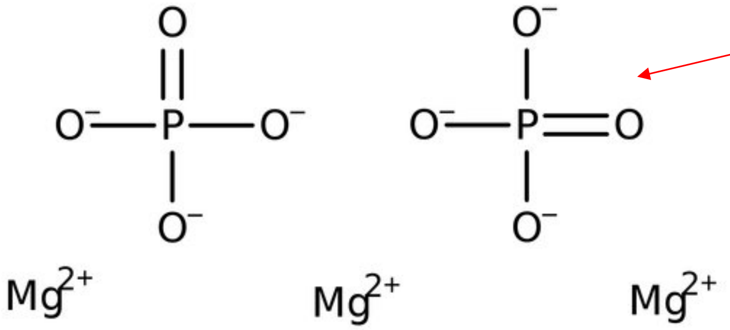
Supplement Support for Mitochondrial Function *(examples)*

General supplement support and antioxidant therapy can be helpful for mitochondrial issues.

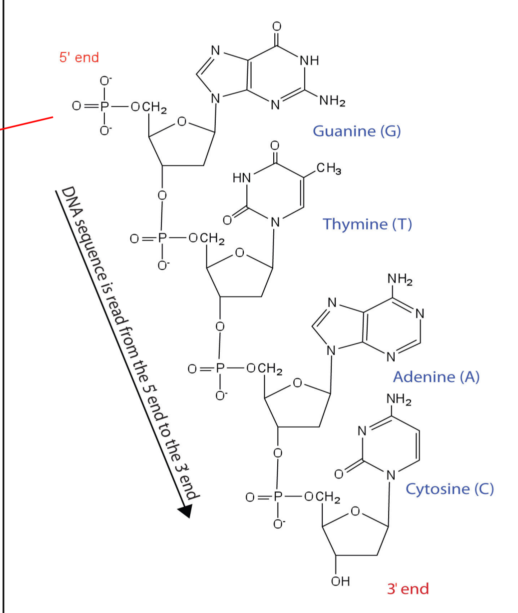
Examples:

- **L-Carnitine** – helps with fatty acid transport
- **CoQ10 (Ubiquinol)**
- **Thiamine (B1), Pyridoxine (B6), Riboflavin (B2)** - *all support mitochondrial function.*
- **Antioxidants** – *help to decrease oxidative stress*
- **'Mitochondrial Cocktail'** – *combination of ingredients for balanced mitochondrial support, e.g., CoQ10, NADH.*

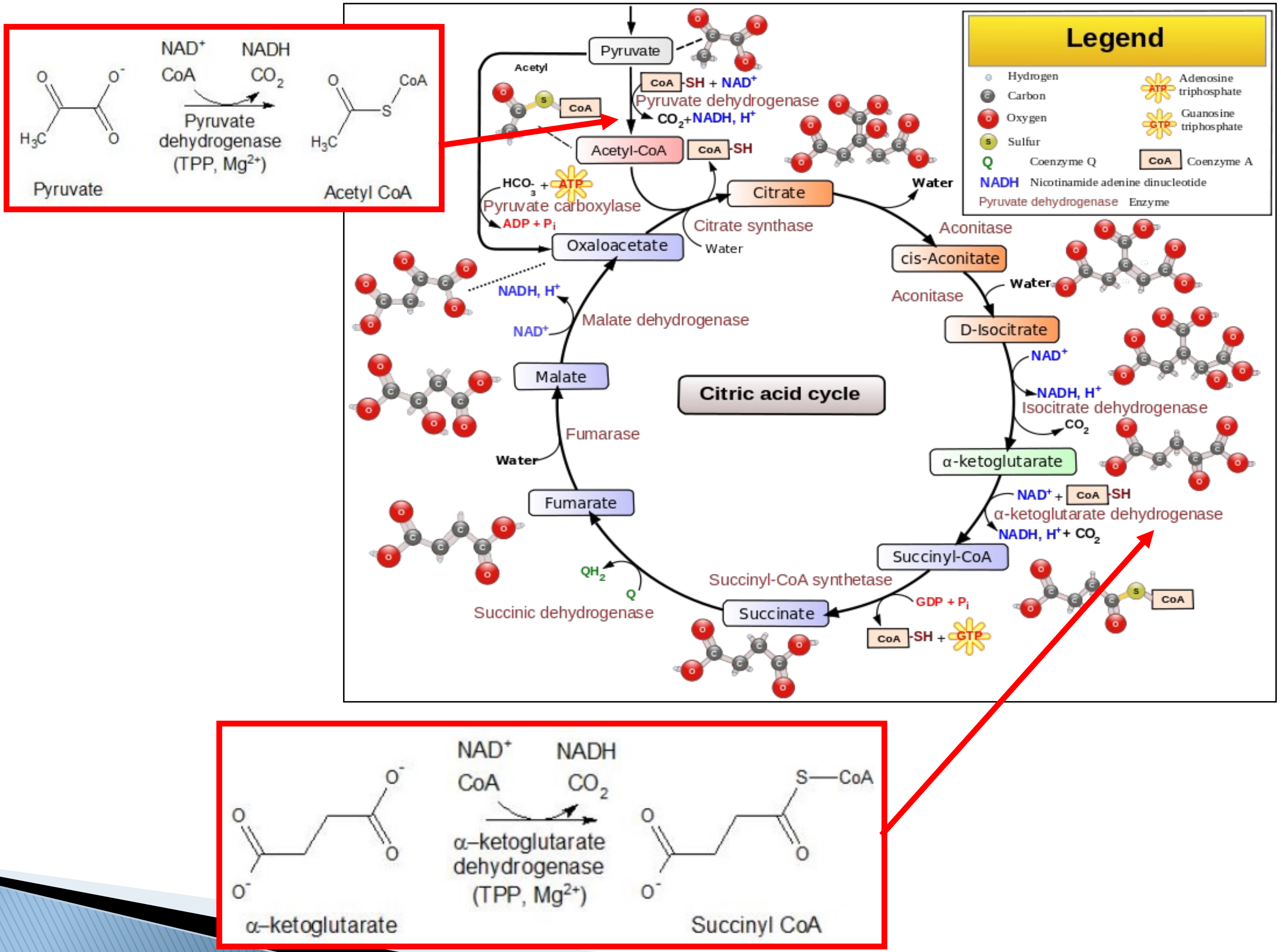
- At the cellular level Mg^{2+} competes with Ca^{2+}, as well as protons (+) or amines ($-NH_2^+$), for binding affinity to various anions *(negatively charged)* found in the mitochondria, cytosol, and nucleus.
- More than 1/2 of the magnesium found in the nucleus is associated with nucleic acids and free nucleotides which are polyanionic groups.



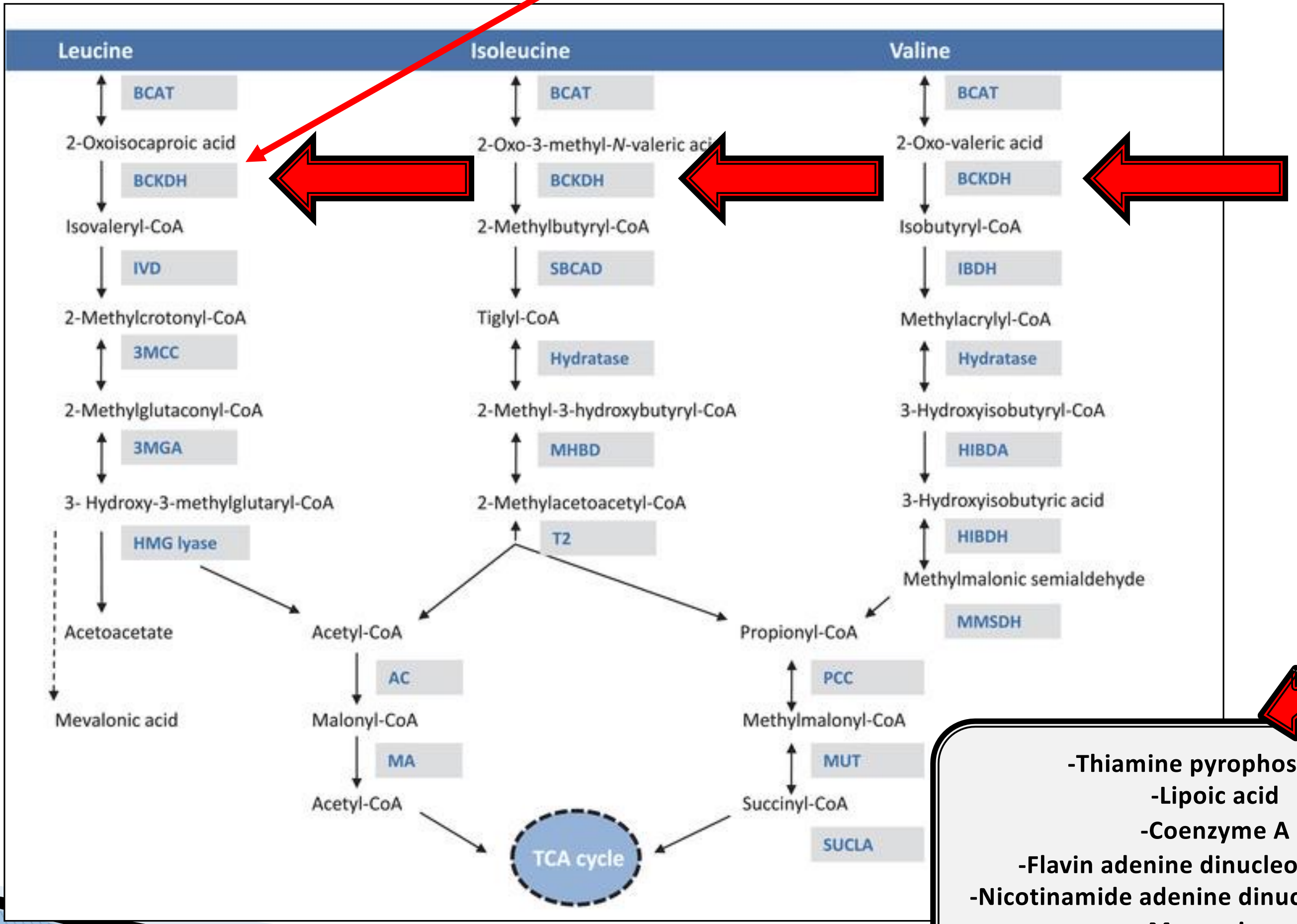
Magnesium Phosphate



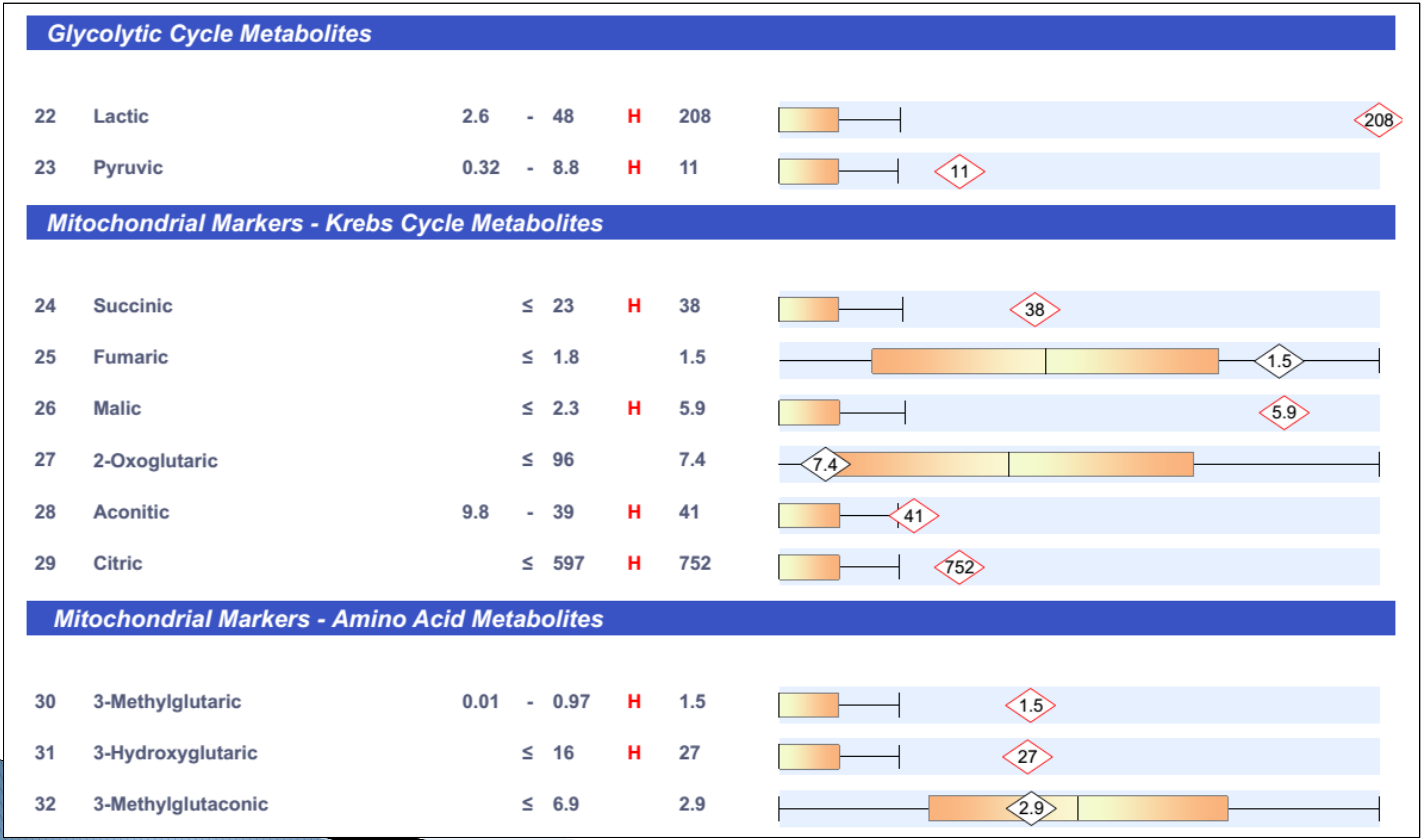
Source: https://coolgyan.org/chemistry/magnesium-phosphate/


NAD+
NADH
CoA
CO2
Pyruvate dehydrogenase (TPP, Mg2+)
Pyruvate
Acetyl CoA
Legend
Hydrogen
Carbon
Oxygen
Sulfur
Q Coenzyme Q
NADH Nicotinamide adenine dinucleotide
Pyruvate dehydrogenase Enzyme
ATP Adenosine triphosphate
GTP Guanosine triphosphate
CoA Coenzyme A
Pyruvate
Acetyl
CoA-SH + NAD+
Pyruvate dehydrogenase
CO2+NADH, H+
Acetyl-CoA
CoA-SH
HCO3- + ATP
Pyruvate carboxylase
ADP + Pi
Citrate
Citrate synthase
Water
Oxaloacetate
Aconitase
cis-Aconitate
Water
Aconitase
D-Isocitrate
NAD+
NADH, H+
Isocitrate dehydrogenase
CO2
α-ketoglutarate
NAD+ + CoA-SH
α-ketoglutarate dehydrogenase
NADH, H+ + CO2
Succinyl-CoA
Succinyl-CoA synthetase
GDP + Pi
CoA-SH + GTP
Succinate
Succinic dehydrogenase
QH2
Q
Fumarate
Water
Fumarase
Malate
NAD+
NADH, H+
Malate dehydrogenase
Citric acid cycle
NAD+
NADH
CoA
CO2
α–ketoglutarate dehydrogenase (TPP, Mg2+)
α–ketoglutarate
Succinyl CoA

Branched Chain Alpha-Ketoacid Dehydrogenase (Complex)



-Thiamine pyrophosphate
-Lipoic acid
-Coenzyme A
-Flavin adenine dinucleotide (FAD)
-Nicotinamide adenine dinucleotide (NAD^+)
Magnesium



Glycolytic Cycle Metabolites

22	Lactic	2.6	-	48	H	208
23	Pyruvic	0.32	-	8.8	H	11

Mitochondrial Markers - Krebs Cycle Metabolites

24	Succinic		≤	23	H	38
25	Fumaric		≤	1.8		1.5
26	Malic		≤	2.3	H	5.9
27	2-Oxoglutaric		≤	96		7.4
28	Aconitic	9.8	-	39	H	41
29	Citric		≤	597	H	752

Mitochondrial Markers - Amino Acid Metabolites

30	3-Methylglutaric	0.01	-	0.97	H	1.5
31	3-Hydroxyglutaric		≤	16	H	27
32	3-Methylglutaconic		≤	6.9		2.9

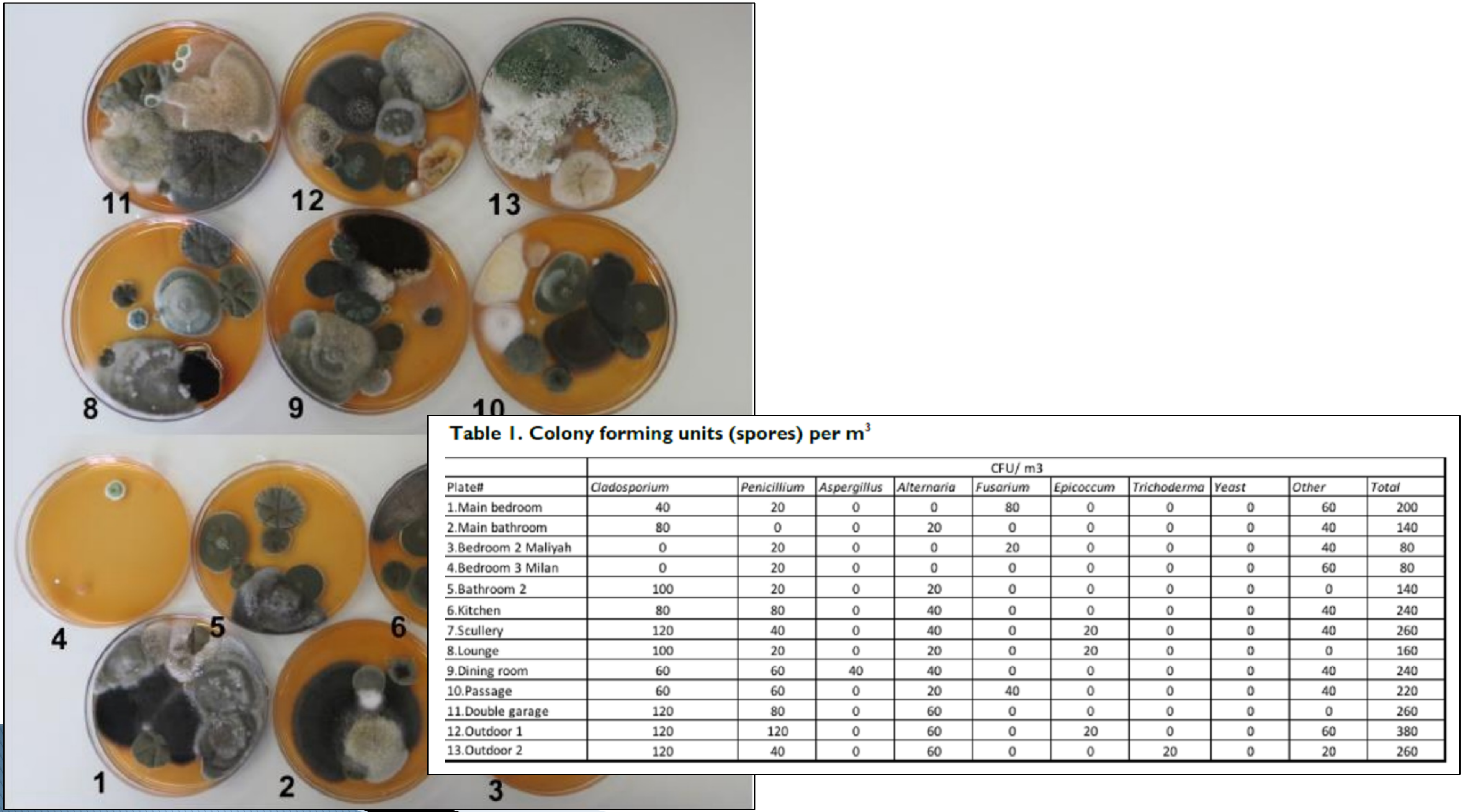
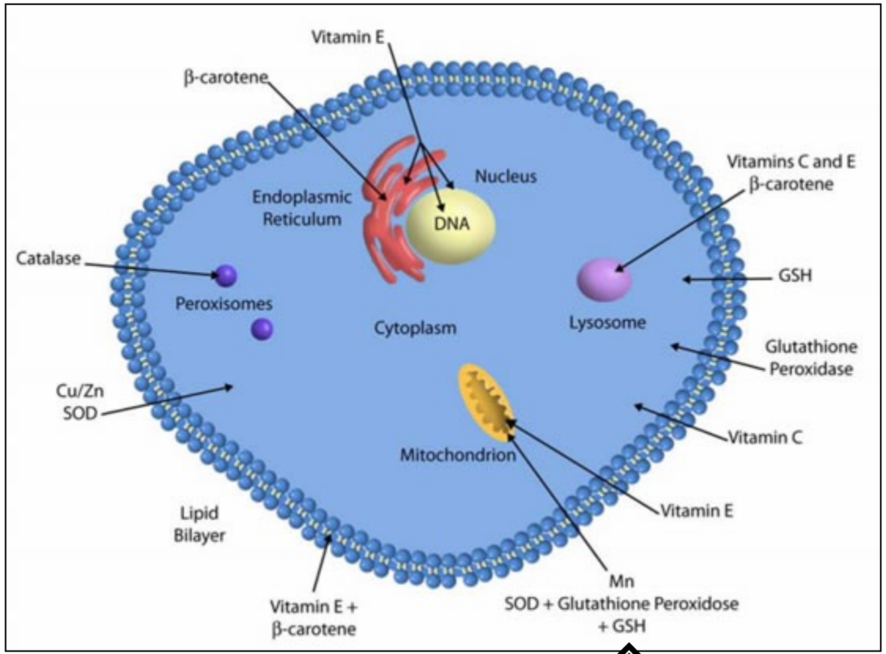


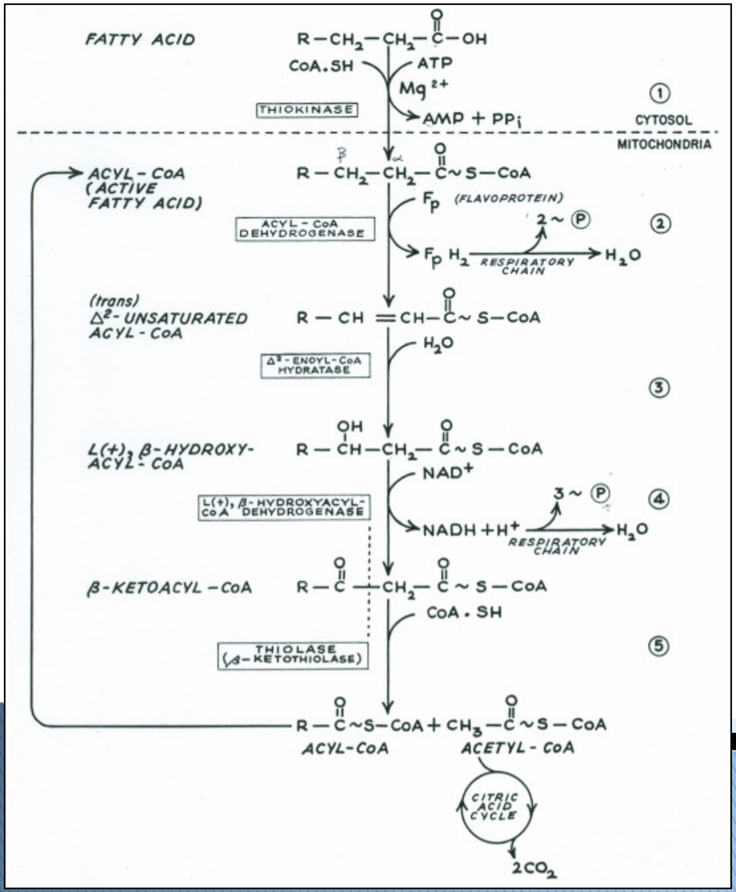
Table 1. Colony forming units (spores) per m^3

	CFU/ m3									
Plate#	*Cladosporium*	*Penicillium*	*Aspergillus*	*Alternaria*	*Fusarium*	*Epicoccum*	*Trichoderma*	*Yeast*	*Other*	*Total*
1.Main bedroom	40	20	0	0	80	0	0	0	60	200
2.Main bathroom	80	0	0	20	0	0	0	0	40	140
3.Bedroom 2 Maliyah	0	20	0	0	20	0	0	0	40	80
4.Bedroom 3 Milan	0	20	0	0	0	0	0	0	60	80
5.Bathroom 2	100	20	0	20	0	0	0	0	0	140
6.Kitchen	80	80	0	40	0	0	0	0	40	240
7.Scullery	120	40	0	40	0	20	0	0	40	260
8.Lounge	100	20	0	20	0	20	0	0	0	160
9.Dining room	60	60	40	40	0	0	0	0	40	240
10.Passage	60	60	0	20	40	0	0	0	40	220
11.Double garage	120	80	0	60	0	0	0	0	0	260
12.Outdoor 1	120	120	0	60	0	20	0	0	60	380
13.Outdoor 2	120	40	0	60	0	0	20	0	20	260

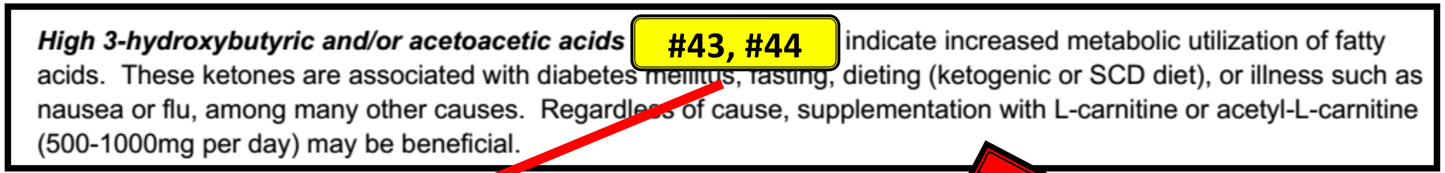


Glutathione – discussed in lecture #5

Fatty Acid Metabolites

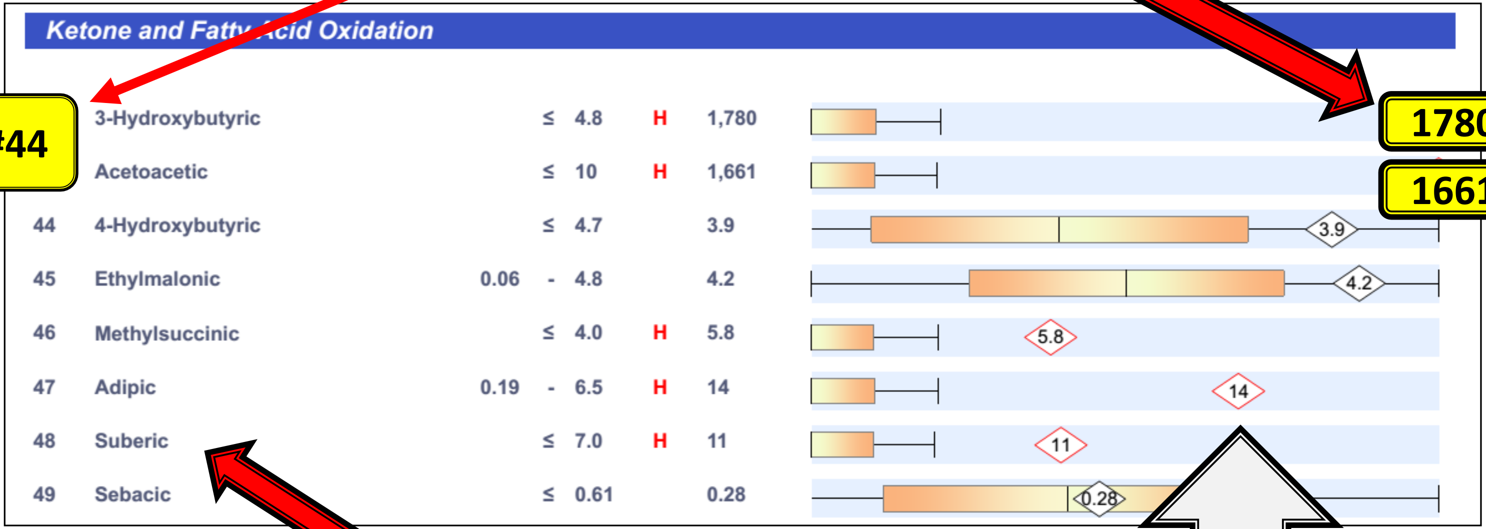


Beta-oxidation is the process by which fatty acid are broken down in the mitochondria to generate acetyl-CoA. The acetyl-CoA then enters citric acid cycle generating NADH which is used by the electron transport chain.



High 3-hydroxybutyric and/or acetoacetic acids indicate increased metabolic utilization of fatty acids. These ketones are associated with diabetes mellitus, fasting, dieting (ketogenic or SCD diet), or illness such as nausea or flu, among many other causes. Regardless of cause, supplementation with L-carnitine or acetyl-L-carnitine (500-1000mg per day) may be beneficial.

#43, #44



Ketone and Fatty Acid Oxidation

	3-Hydroxybutyric		≤	4.8	H	1,780
	Acetoacetic		≤	10	H	1,661
44	4-Hydroxybutyric		≤	4.7		3.9
45	Ethylmalonic	0.06	-	4.8		4.2
46	Methylsuccinic		≤	4.0	H	5.8
47	Adipic	0.19	-	6.5	H	14
48	Suberic		≤	7.0	H	11
49	Sebacic		≤	0.61		0.28

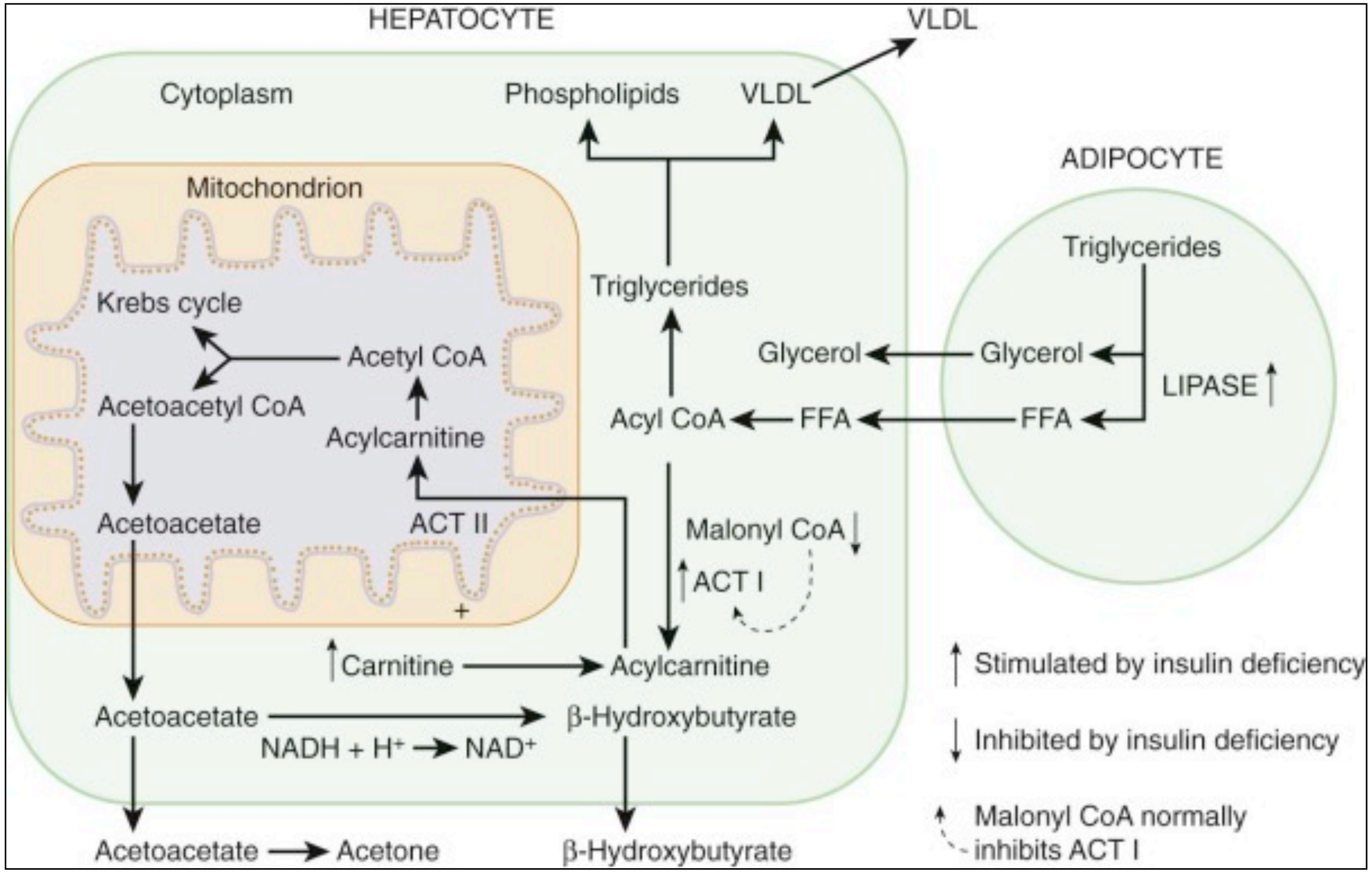
#43, #44

1780

1661

Suberic –
common with overnight fast

Adipic – *common with gelatin or “junk food” consumption*



High acetone can make breath smell like nail polish

Nutritional Markers & Remaining Sections

Nutritional Markers

Indirect:

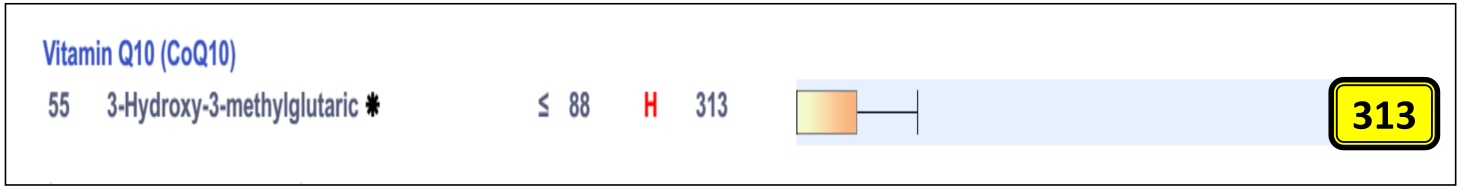
- Methylmalonic acid - *B-12 def.* →

Vitamin B12

50 Methylmalonic ✱ ≤ 2.3 H 3.0

3.0

- Methylcitric acid – *biotin deficiency*
- Glutaric and 3-hydroxy-3-methylglutaric - *indicators of riboflavin and coenzyme Q-10 deficiency, respectively.*



Vitamin Q10 (CoQ10)

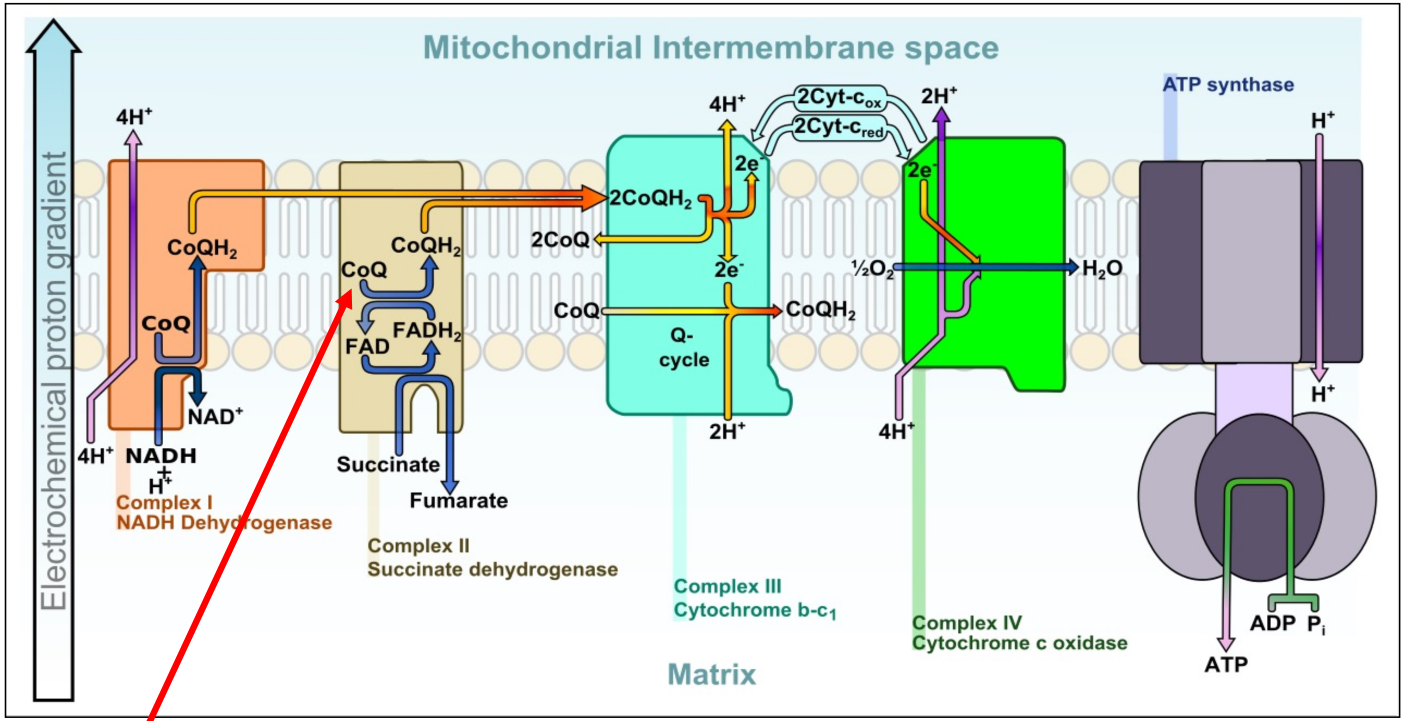
55 3-Hydroxy-3-methylglutaric ✱ ≤ 88 H 313

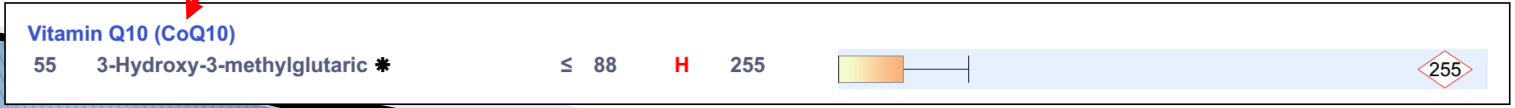
313

Direct:

- Ascorbic acid - *vitamin C*
- Pantothenic acid – *vitamin B5*
- Pyridoxic acid – *vitamin B6*

Electron Transport Chain
(aka Respiratory Chain)

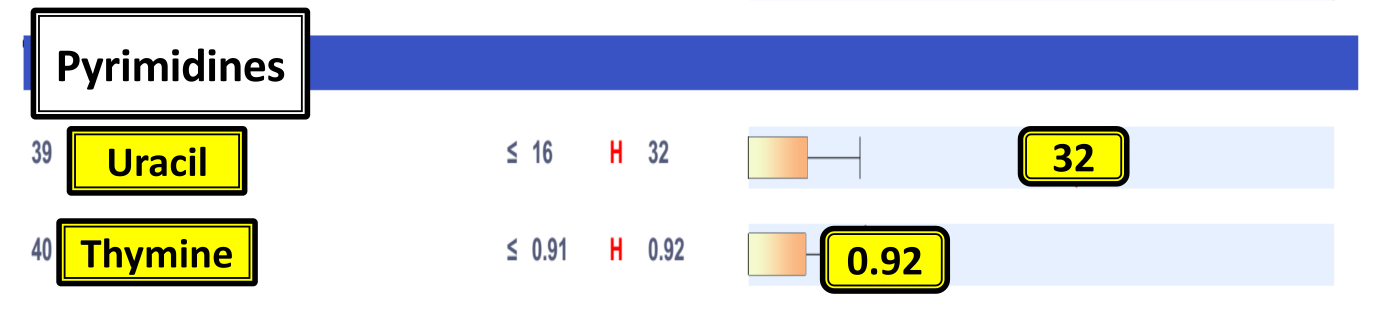



Vitamin Q10 (CoQ10)

55	3-Hydroxy-3-methylglutaric ✱	≤ 88	H	255	255

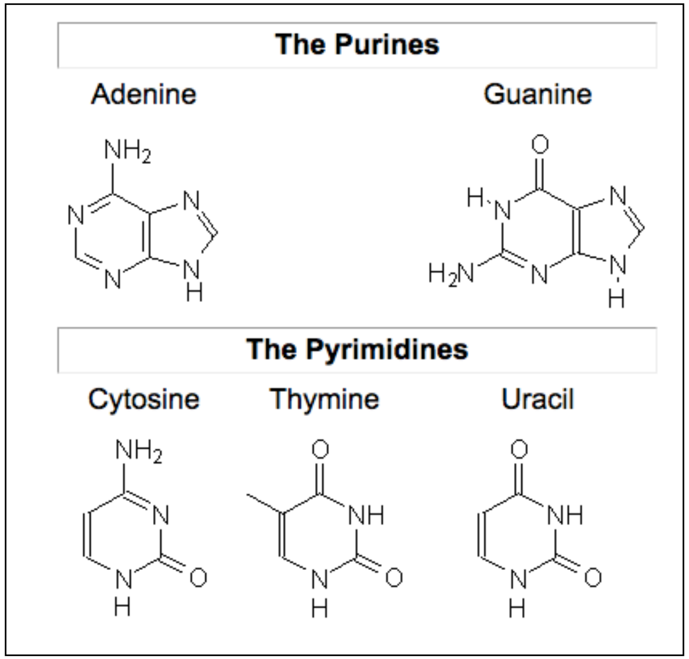
Pyrimidines

Elevated in cancer, genetic disease, folate issues.



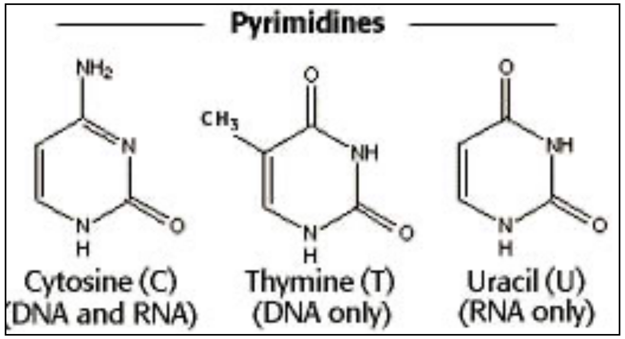
Pyrimidines

39	**Uracil**	≤ 16	H	32	**32**
40	**Thymine**	≤ 0.91	H	0.92	**0.92**



Two carbon nitrogen ring bases

One carbon nitrogen ring bases



Source: *Diff.com*

Bone Metabolites

72	Phosphoric	1 439 - 9 732	H	12 408		12408

...ated fat, trans fat, cholesterol, dietary fi... amin A, vitamin C, calcium and iron.
*Perc... aily Values are based on a 2,00... rie diet.
CARBONATED WATER, SUCROSE, CARAMEL COLOR, PHOSPHORIC ACID, NATURAL FLAVORS, CAFFEINE.
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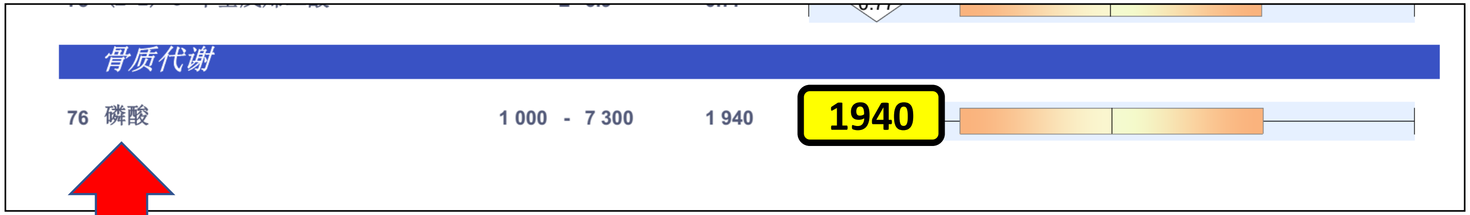
High values

- High intake
- Hyperparathyroidism
- Vitamin D-resistant rickets
- Immobilization following paraplegia or fracture
- Vitamin D intoxication
- Renal tubular damage, heavy metal toxicity
- Familial hypophosphatemia
- Metabolic acidosis

Low values

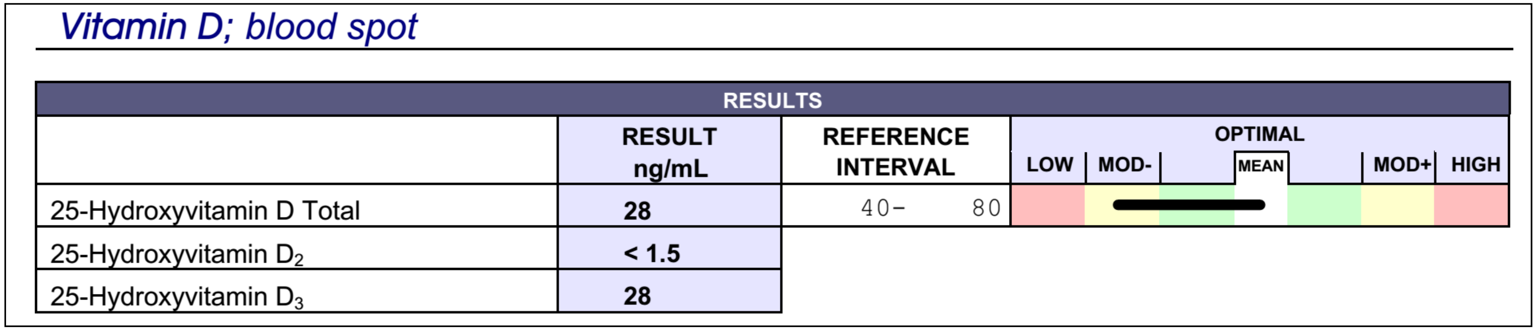
- Low intake
- Hypoparathyroidism
- Pseudohypoparathyroidism
- Parathyroidectomy
- **Vitamin D deficiency**



骨质代谢

76	磷酸	1 000 - 7 300	1 940	1940

Phosphoric (acid)

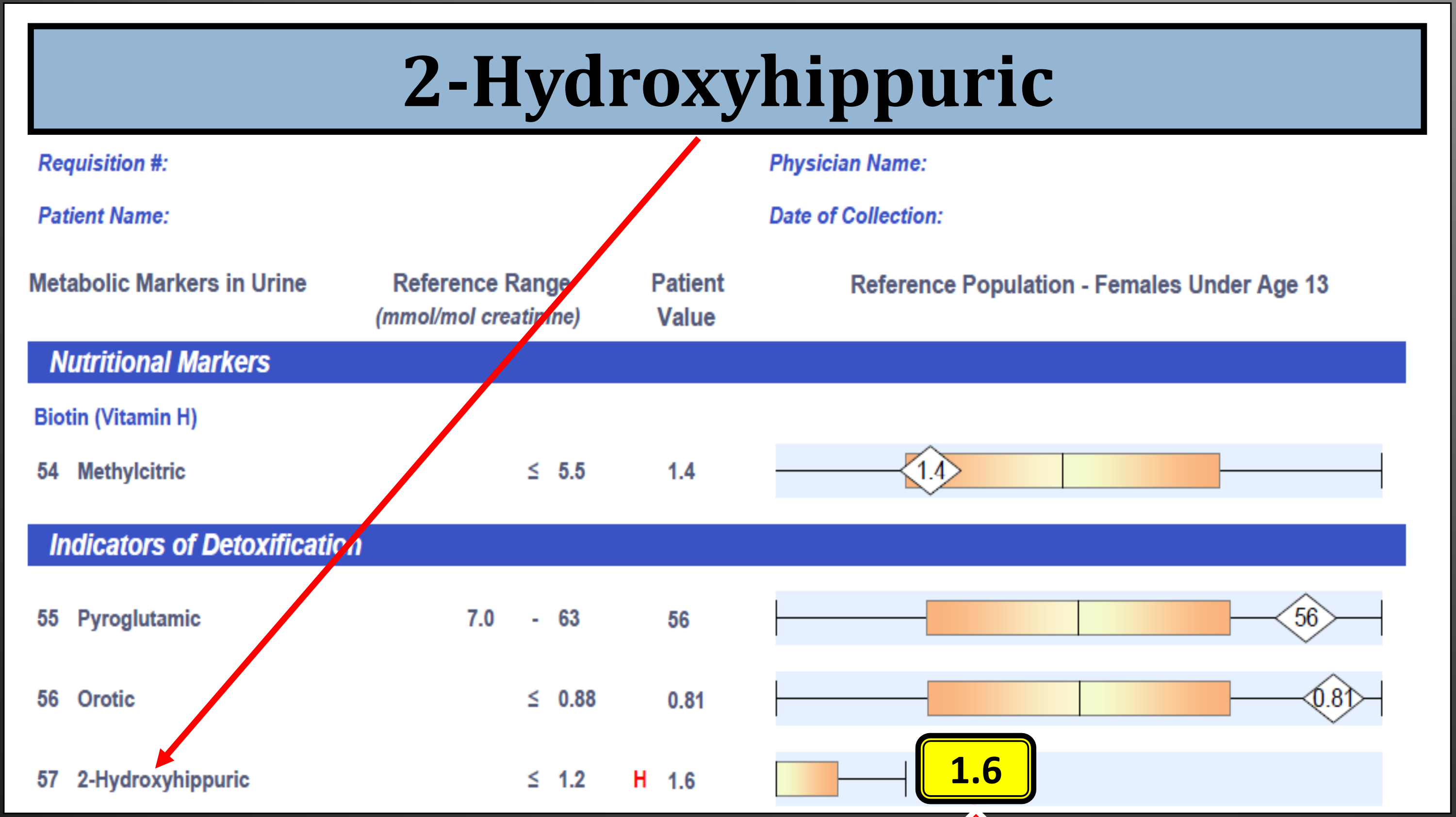


Vitamin D; blood spot

RESULTS

	RESULT ng/mL	REFERENCE INTERVAL	OPTIMAL				
			LOW	MOD-	MEAN	MOD+	HIGH
25-Hydroxyvitamin D Total	28	40- 80					
25-Hydroxyvitamin D_2	< 1.5						
25-Hydroxyvitamin D_3	28						

2-Hydroxyhippuric



Requisition #:

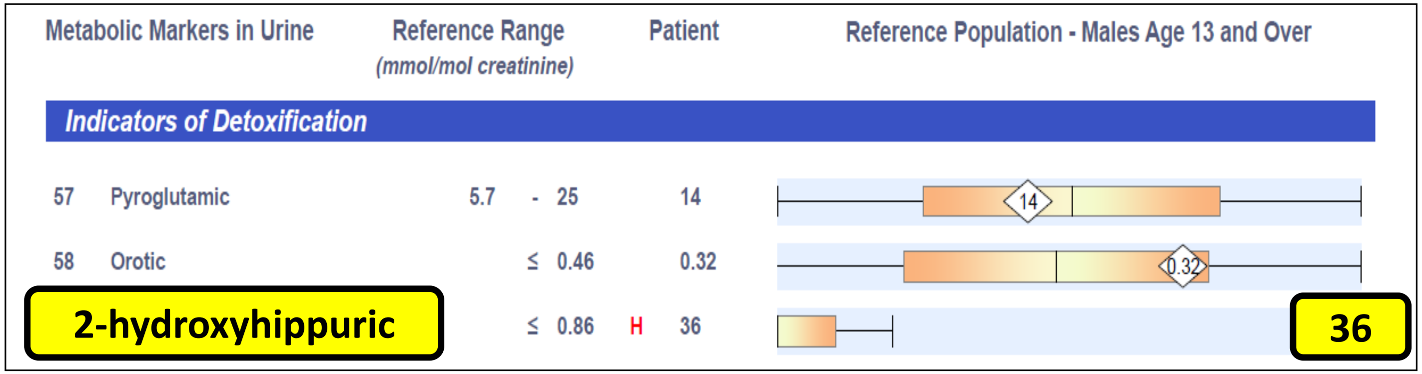
Physician Name:

Patient Name:

Date of Collection:

Metabolic Markers in Urine	Reference Range *(mmol/mol creatine)*		Patient Value	Reference Population - Females Under Age 13
Nutritional Markers				
Biotin (Vitamin H)				
54 Methylcitric	≤ 5.5		1.4	1.4
Indicators of Detoxification				
55 Pyroglutamic	7.0 - 63		56	56
56 Orotic	≤ 0.88		0.81	0.81
57 2-Hydroxyhippuric	≤ 1.2	H	1.6	1.6

2-Hydroxyhippuric



Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)		Patient	Reference Population - Males Age 13 and Over
Indicators of Detoxification					
57	Pyroglutamic	5.7 - 25		14	
58	Orotic	≤ 0.46		0.32	
	2-hydroxyhippuric	≤ 0.86	H	36	

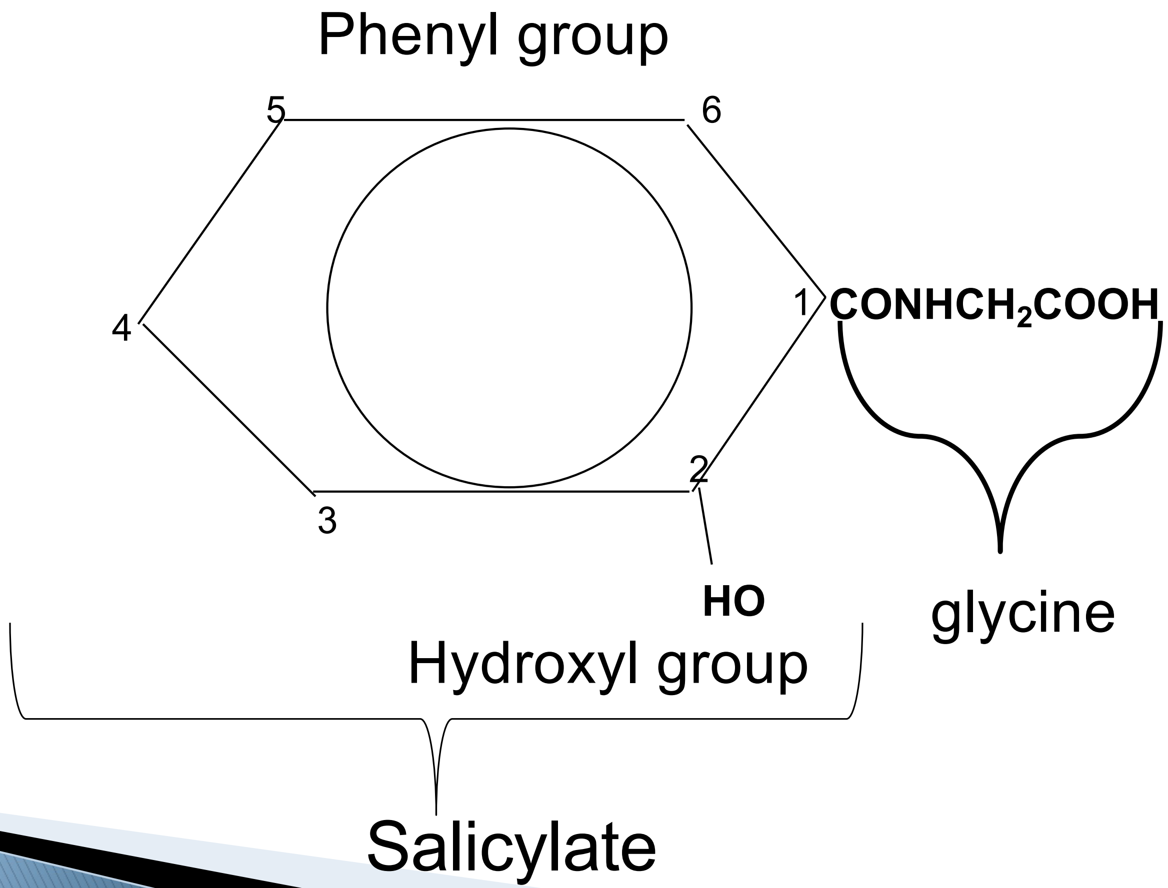
36

Aspartame

Aspartame, salicylates, or GI bacteria				
61	2-Hydroxyhippuric	≤ 0.86	H	192

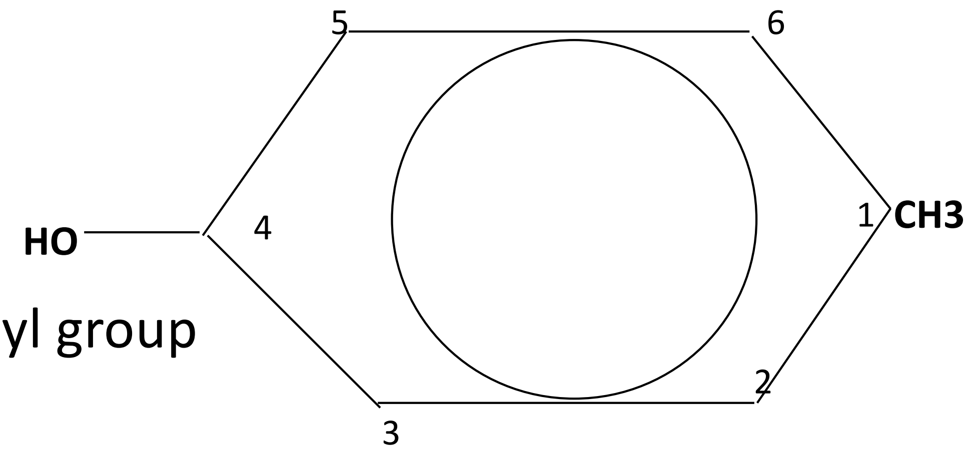
192

Structure of 2-Hydroxyhippuric Acid - *metabolite of aspartame (Nutrasweet®), aspirin, foods, additives*



Structure of 4-cresol *(methylphenol)*

Phenyl group

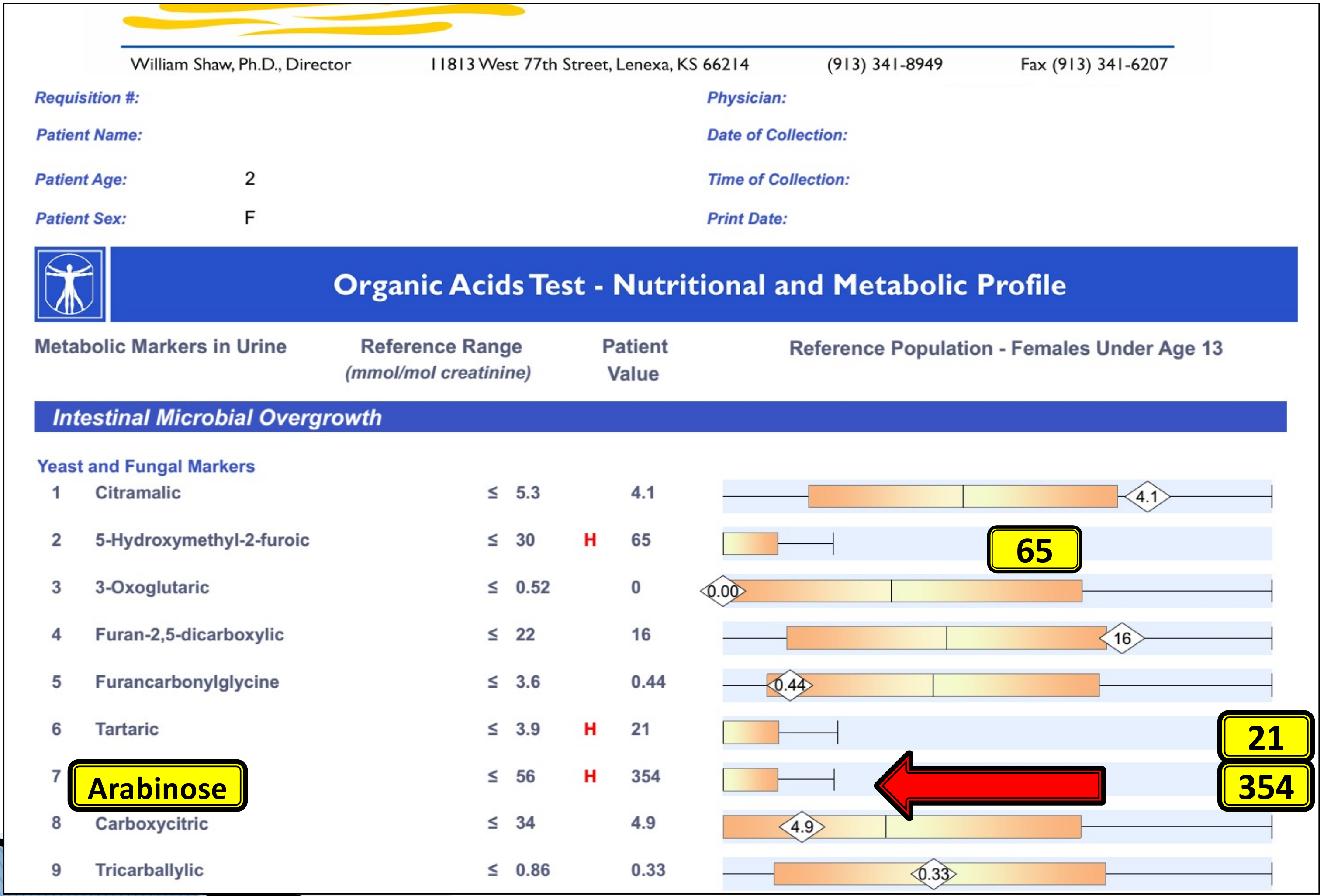


Hydroxyl group

Case Study: *2-year old child*

- 2-year old female
- Failure to thrive (suspected)
- Language delay

- Social inhibitions
- No behavioral issues
- Lives in S. Eastern United States



William Shaw, Ph.D., Director 11813 West 77th Street, Lenexa, KS 66214 (913) 341-8949 Fax (913) 341-6207

Requisition #:
Patient Name:
Patient Age: 2
Patient Sex: F

Physician:
Date of Collection:
Time of Collection:
Print Date:

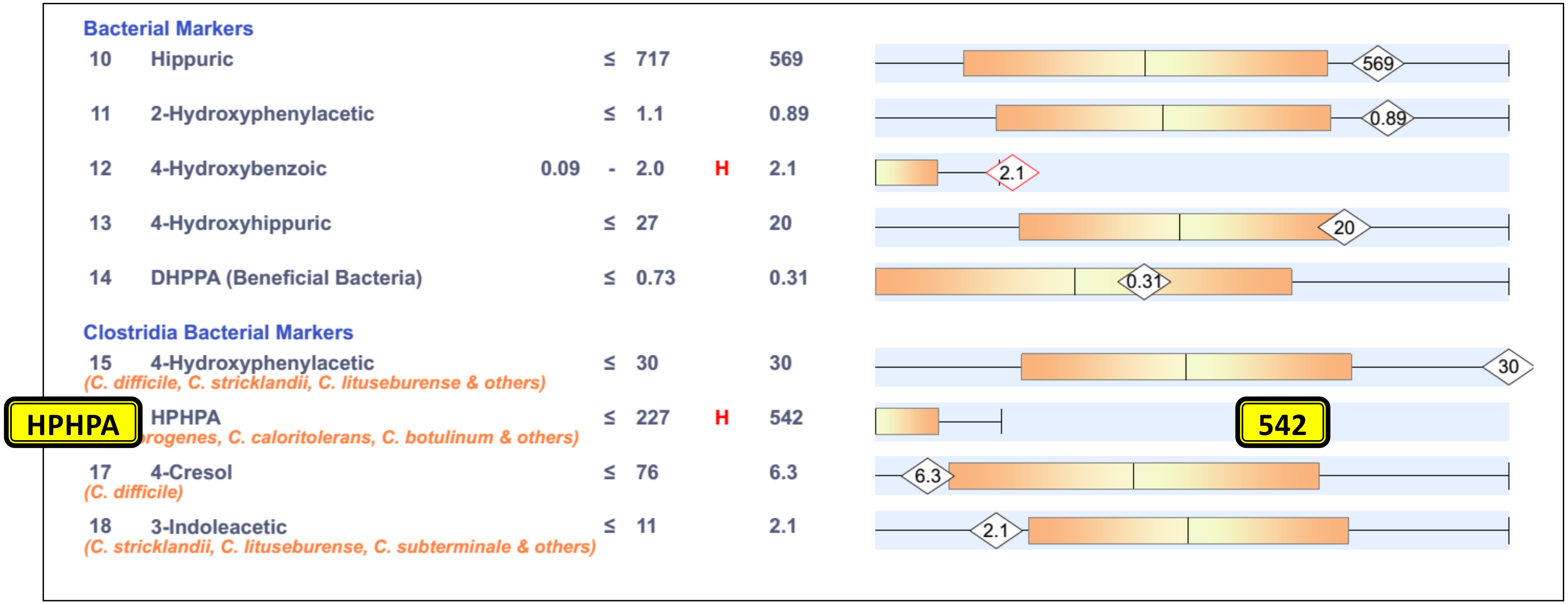
Organic Acids Test - Nutritional and Metabolic Profile

	Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*		Patient Value	Reference Population - Females Under Age 13

Intestinal Microbial Overgrowth

Yeast and Fungal Markers

1	Citramalic	≤ 5.3		4.1	4.1
2	5-Hydroxymethyl-2-furoic	≤ 30	H	65	65
3	3-Oxoglutaric	≤ 0.52		0	0.00
4	Furan-2,5-dicarboxylic	≤ 22		16	16
5	Furancarbonylglycine	≤ 3.6		0.44	0.44
6	Tartaric	≤ 3.9	H	21	21
7	Arabinose	≤ 56	H	354	354
8	Carboxycitric	≤ 34		4.9	4.9
9	Tricarballylic	≤ 0.86		0.33	0.33



Bacterial Markers

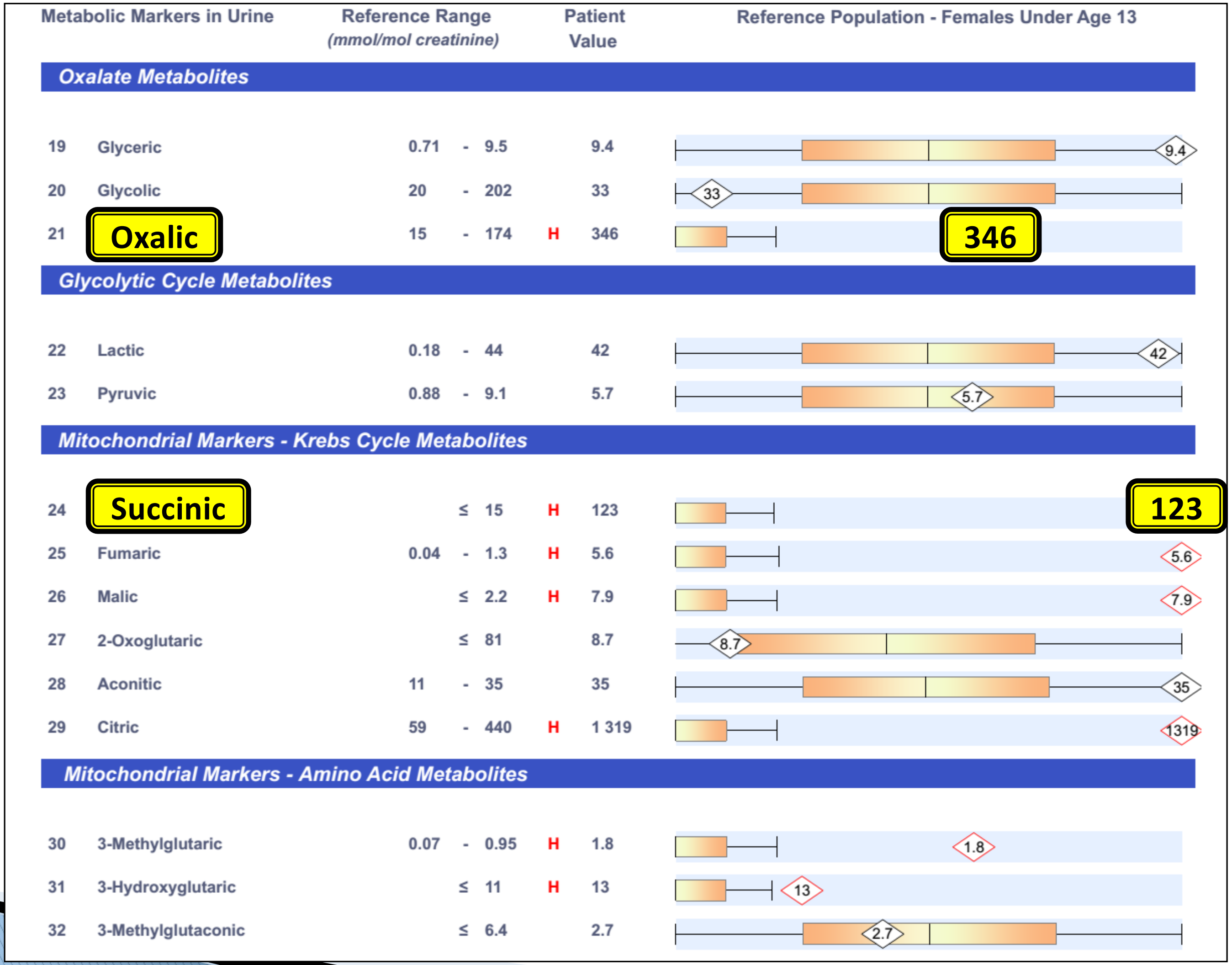
10	Hippuric		≤	717		569
11	2-Hydroxyphenylacetic		≤	1.1		0.89
12	4-Hydroxybenzoic	0.09	-	2.0	H	2.1
13	4-Hydroxyhippuric		≤	27		20
14	DHPPA (Beneficial Bacteria)		≤	0.73		0.31

Clostridia Bacterial Markers

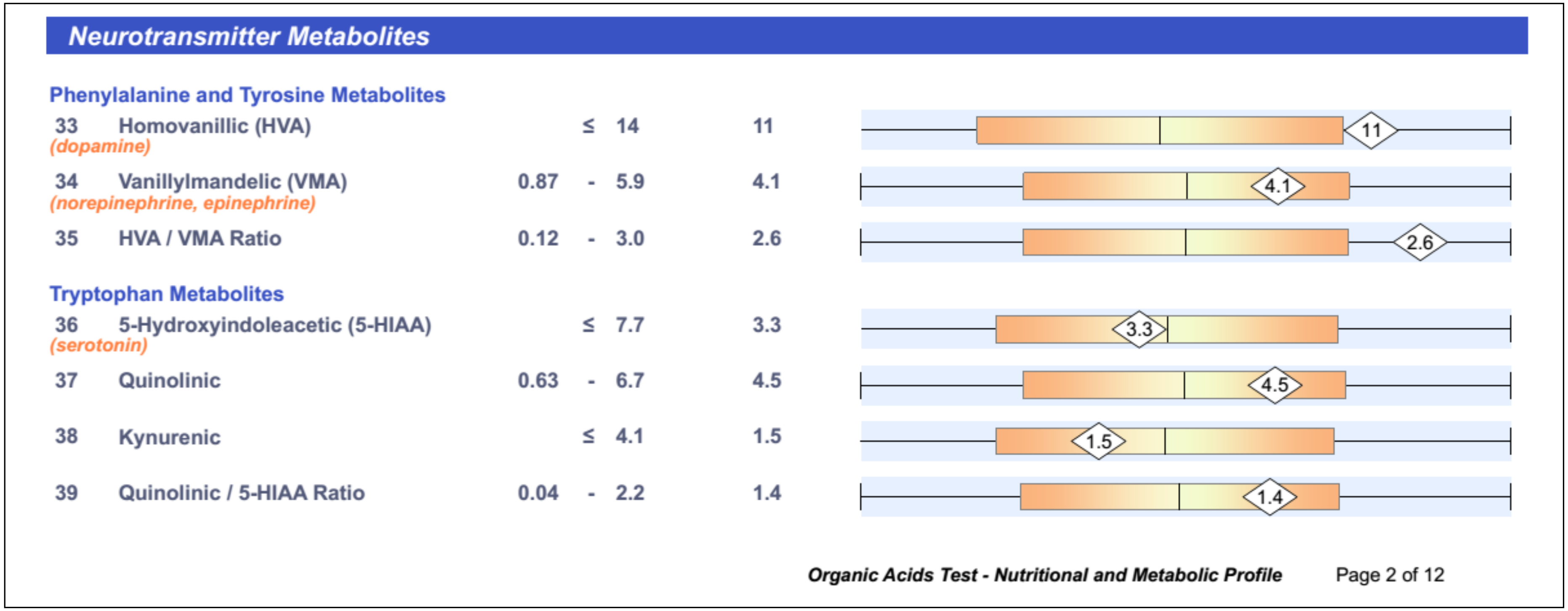
15	4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*		≤	30		30
	HPHPA *rogenes, C. caloritolerans, C. botulinum & others)*		≤	227	H	542
17	4-Cresol *(C. difficile)*		≤	76		6.3
18	3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*		≤	11		2.1

HPHPA

542



	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value
	Oxalate Metabolites			
19	Glyceric	0.71 - 9.5		9.4
20	Glycolic	20 - 202		33
21	Oxalic	15 - 174	H	346
	Glycolytic Cycle Metabolites			
22	Lactic	0.18 - 44		42
23	Pyruvic	0.88 - 9.1		5.7
	Mitochondrial Markers - Krebs Cycle Metabolites			
24	Succinic	≤ 15	H	123
25	Fumaric	0.04 - 1.3	H	5.6
26	Malic	≤ 2.2	H	7.9
27	2-Oxoglutaric	≤ 81		8.7
28	Aconitic	11 - 35		35
29	Citric	59 - 440	H	1 319
	Mitochondrial Markers - Amino Acid Metabolites			
30	3-Methylglutaric	0.07 - 0.95	H	1.8
31	3-Hydroxyglutaric	≤ 11	H	13
32	3-Methylglutaconic	≤ 6.4		2.7



Neurotransmitter Metabolites

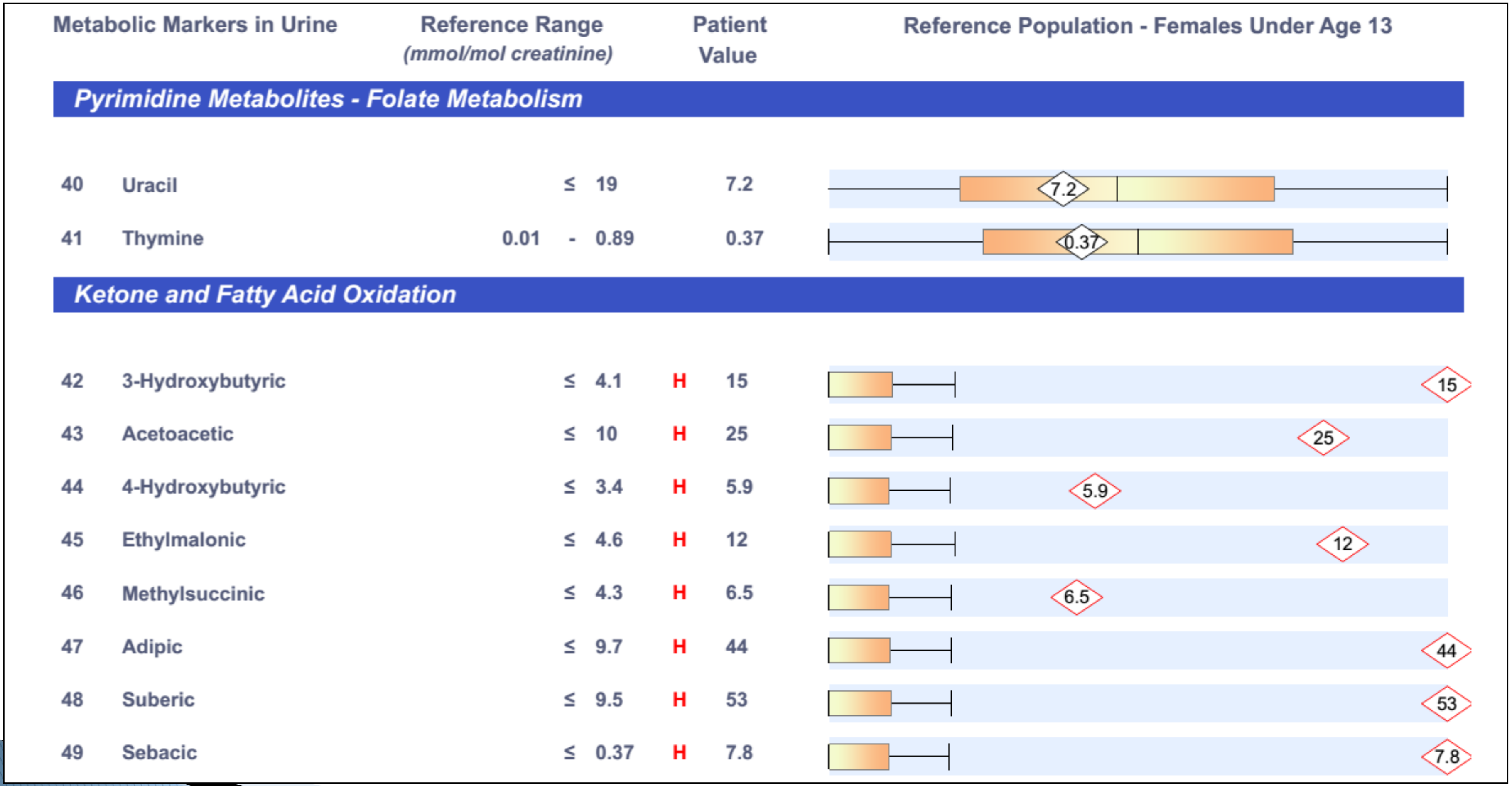
Phenylalanine and Tyrosine Metabolites

33	**Homovanillic (HVA)** *(dopamine)*	≤ 14	11
34	**Vanillylmandelic (VMA)** *(norepinephrine, epinephrine)*	0.87 - 5.9	4.1
35	**HVA / VMA Ratio**	0.12 - 3.0	2.6

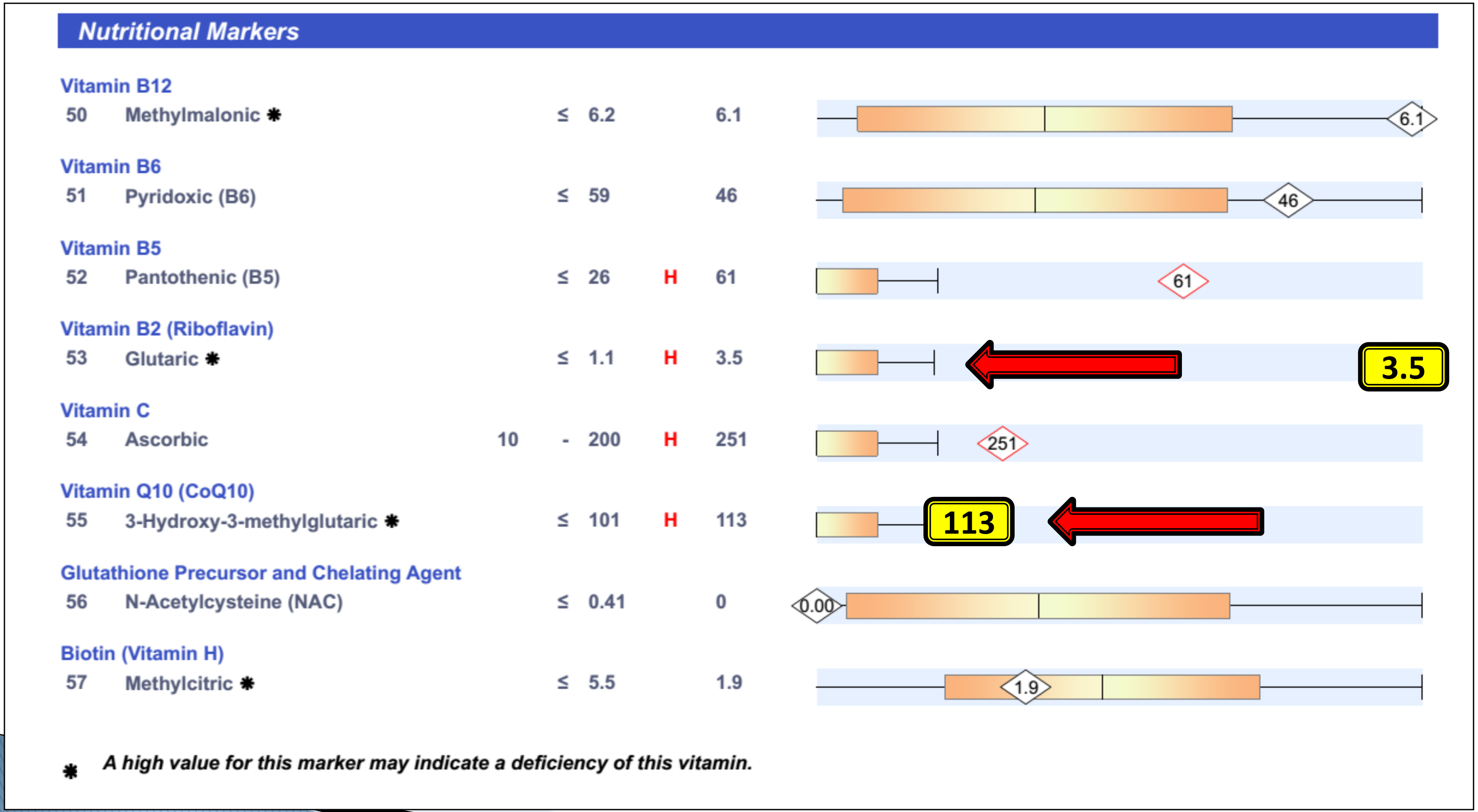
Tryptophan Metabolites

36	**5-Hydroxyindoleacetic (5-HIAA)** *(serotonin)*	≤ 7.7	3.3
37	**Quinolinic**	0.63 - 6.7	4.5
38	**Kynurenic**	≤ 4.1	1.5
39	**Quinolinic / 5-HIAA Ratio**	0.04 - 2.2	1.4

Organic Acids Test - Nutritional and Metabolic Profile Page 2 of 12



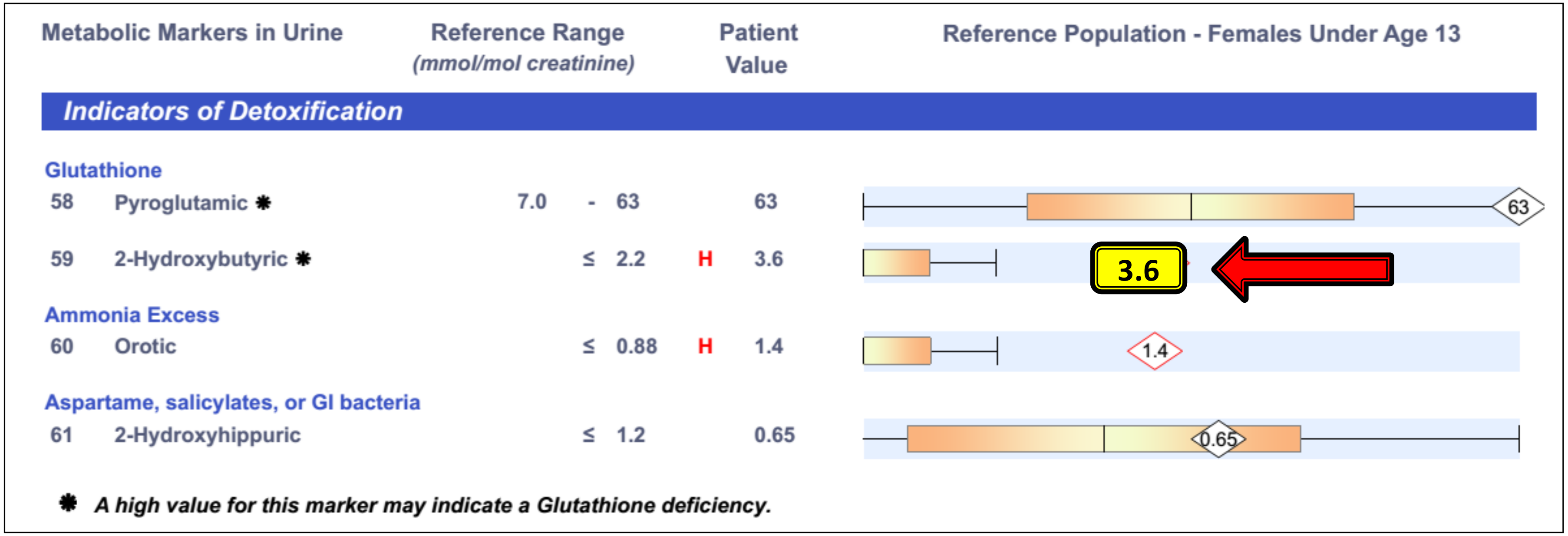
	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value
Pyrimidine Metabolites - Folate Metabolism				
40	Uracil	≤ 19		7.2
41	Thymine	0.01 - 0.89		0.37
Ketone and Fatty Acid Oxidation				
42	3-Hydroxybutyric	≤ 4.1	H	15
43	Acetoacetic	≤ 10	H	25
44	4-Hydroxybutyric	≤ 3.4	H	5.9
45	Ethylmalonic	≤ 4.6	H	12
46	Methylsuccinic	≤ 4.3	H	6.5
47	Adipic	≤ 9.7	H	44
48	Suberic	≤ 9.5	H	53
49	Sebacic	≤ 0.37	H	7.8



Nutritional Markers

Vitamin B12						
50	Methylmalonic ✱		≤	6.2		6.1
Vitamin B6						
51	Pyridoxic (B6)		≤	59		46
Vitamin B5						
52	Pantothenic (B5)		≤	26	H	61
Vitamin B2 (Riboflavin)						
53	Glutaric ✱		≤	1.1	H	3.5
Vitamin C						
54	Ascorbic	10	-	200	H	251
Vitamin Q10 (CoQ10)						
55	3-Hydroxy-3-methylglutaric ✱		≤	101	H	113
Glutathione Precursor and Chelating Agent						
56	N-Acetylcysteine (NAC)		≤	0.41		0
Biotin (Vitamin H)						
57	Methylcitric ✱		≤	5.5		1.9

✱ *A high value for this marker may indicate a deficiency of this vitamin.*



Metabolic Markers in Urine		Reference Range *(mmol/mol creatinine)*		Patient Value	Reference Population - Females Under Age 13
Indicators of Detoxification					
Glutathione					
58	Pyroglutamic ✸	7.0 - 63		63	
59	2-Hydroxybutyric ✸	≤ 2.2	H	3.6	
Ammonia Excess					
60	Orotic	≤ 0.88	H	1.4	
Aspartame, salicylates, or GI bacteria					
61	2-Hydroxyhippuric	≤ 1.2		0.65	

✸ ***A high value for this marker may indicate a Glutathione deficiency.***

Action Step Suggestions

- Start performing Organic Acids Tests when appropriate on a wide variety of patients.
- Keep a copy of "The Clinical Significance of the Organic Acids Test" for easy reference for test marker descriptions.
- Keep searching for additional information about the clinical significance of the OAT.
- Contact Great Plains Laboratory directly for assistance with test interpretation.

The Great Plains Laboratory

GPL Academy

Practitioner Workshops

BEYOND THE BASICS:

ADVANCED ORGANIC ACIDS TESTING STRATEGIES

THANK YOU

Next Lecture

The OAT, Fungal Markers, and Chronic Candidiasis