AUTISM RECOVERY 101

How To Interpret The Organic Acids Test (OAT) From Great Plains Laboratory

Content Disclaimer

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AUTISM RECOVERY 101

Lecture Overview

- Organic Acids Testing (OAT)
- The role of the OAT in candida assessment
- The role of the OAT in clostridia assessment
- The role of the OAT in oxalate assessment
- Certain neurotransmitter imbalances
- Indicators of other problems – *vitamin deficiencies, fatty acid oxidation, etc*.
- Mitochondrial dysfunction assessment

Prioritization Based On Common Findings

- The OAT is a complicated test with many markers indicating a variety of *potential* problems.
- Not all markers on any given OAT indicate problems that demand immediate attention.
- The goal is to get proficient at reading the OAT with regards to your child's particular situation.

Support Documents for Module #3

- The Clinical Significance of the Organic Acids Test *(marker interpretation handout) - pdf*
- Sample OAT *(pdf)*
- OAT – Quick Assessment Guide of the Most Commonly Seen Markers in Autism *(pdf)*
- Mitochondrial Lab Assessment at a Glance *(pdf)*
- Mitochondrial Cocktail Options *(pdf)*
- Lecture slides *(pdf)*
- Lecture slides – *note taking (pdf)*

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The Clinical Significance of the Organic Acids Test

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The Organic Acids Test (OAT) offers 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 offers 74 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.

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Organic Acids Test (OAT) - *Quick Assessment Guide of the Most Commonly Seen Markers in Autism*

(The percentages and trends listed are approximations recognized by Dr. Woeller over many years in clinical practice evaluating the OAT.)

Page 1 of the OAT – *Yeast/Fungal Section*

1. Look at the Arabinose marker first. This will be the most common marker indicating the presence of candida. It is present in approximately 90% of OATs. Second to that is Tartaric Acid which can be seen with candida too. It tends to show up about 10 to 15% of the time. The level of Arabinose can be deceiving in some clinical situations. A high level doesn't always mean that a patient presents more symptomatically with yeast, or that a low level means a person is less affected. However, approximately 85 to 90% of the time the number matches up with a person's symptoms. Either way, any elevation suggests some invasiveness of candida and warrants some treatment.
2. Next evaluate the clostridia markers, i.e. HPHPA, 4-cresol. In the autism population these show up elevated approximately 60 to 70% of the time. The HPHPA is the most common marker for clostridia and appears elevated approximately 75% more frequently than 4-cresol. Both markers indicate

Page 1 – *Yeast & Fungal Markers*

Organic Acids Test - Nutritional and Metabolic Profile

	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient	Reference Population - Males Under Age 13
Intestinal Microbial Overgrowth					
Yeast and Fungal Markers					
1	Citramalic	≤ 5.0		4.4	4.4
2	5-Hydroxymethyl-2-furoic	≤ 28		1.6	1.6
3	3-Oxoglutaric	≤ 0.46		0	0.00
4	Furan-2,5-dicarboxylic	≤ 18		2.2	2.2
5	Furancarbonylglycine	≤ 3.1		0.15	0.15
6	Tartaric	≤ 6.5		1.3	1.3
7	Arabinose	≤ 50	H	93	93
8	Carboxycitric	≤ 25	H	68	68
9	Tricarballylic	≤ 1.3		0.08	0.08

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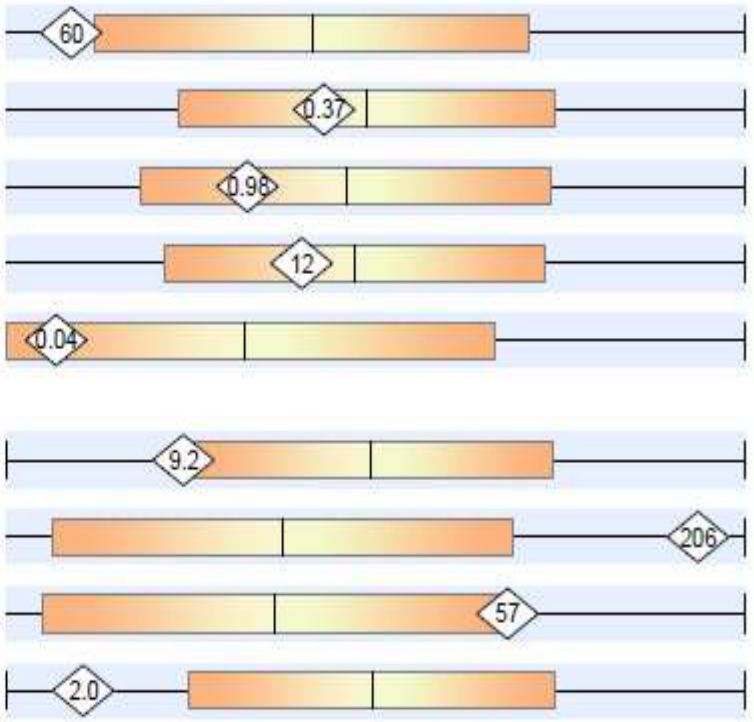
Page 1 – *Bacterial and Clostridia Markers*

Bacterial Markers					
10	Hippuric		≤ 680	60	
11	2-Hydroxyphenylacetic		≤ 0.86	0.37	
12	4-Hydroxybenzoic		≤ 3.0	0.98	
13	4-Hydroxyhippuric		≤ 30	12	
14	DHPPA (Beneficial Bacteria)		≤ 0.59	0.04	
Clostridia Bacterial Markers					
15	4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	2.0	- 32	9.2	
16	HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*		≤ 220	206	
17	4-Cresol *(C. difficile)*		≤ 84	57	
18	3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	0.60	- 14	2.0	



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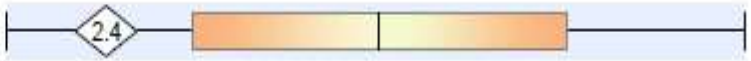
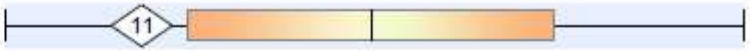
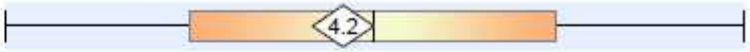
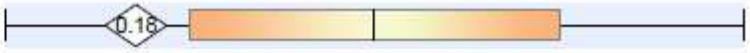
Page 2 – *Oxalate Metabolites*

Oxalate Metabolites					
19	Glyceric	0.74	- 13	2.4	
20	Glycolic	27	- 221	120	
21	Oxalic	35	- 185	110	

Page 2 – *Mitochondrial and Glycolytic Metabolites*

Glycolytic Cycle Metabolites							
22	Lactic	2.6	-	48		11	
23	Pyruvic	0.32	-	8.8		4.2	
Mitochondrial Markers - Krebs Cycle Metabolites							
24	Succinic		≤	23		5.2	
25	Fumaric		≤	1.8		0.25	
26	Malic		≤	2.3		1.1	
27	2-Oxoglutaric		≤	96		27	
28	Aconitic	9.8	-	39	L	5.6	
29	Citric		≤	597		335	
Mitochondrial Markers - Amino Acid Metabolites							
30	3-Methylglutaric	0.01	-	0.97		0.18	
31	3-Hydroxyglutaric		≤	16		0	
32	3-Methylglutaconic		≤	6.9		1.3	

Page 2 – *Neurotransmitter Metabolites*

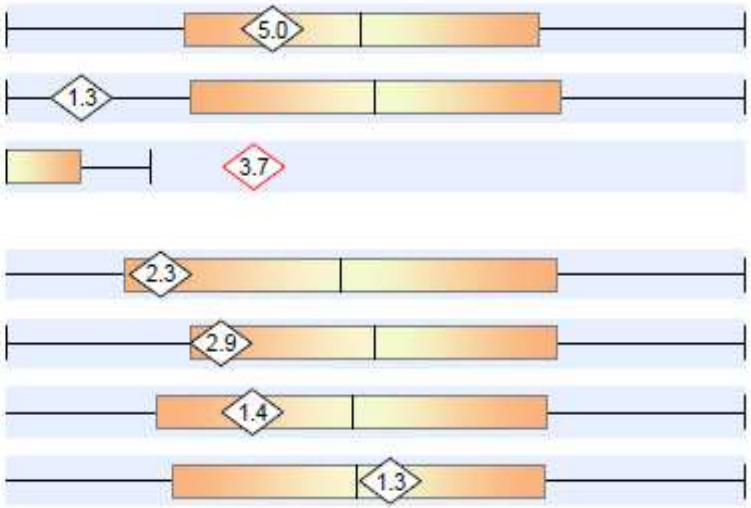
Neurotransmitter Metabolites

Phenylalanine and Tyrosine Metabolites

33	Homovanillic (HVA) *(dopamine)*	0.49	- 13		5.0	
34	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.72	- 6.4		1.3	
35	HVA / VMA Ratio	0.23	- 2.8	H	3.7	

Tryptophan Metabolites

36	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*		≤ 11		2.3	
37	Quinolinic	0.48	- 8.8		2.9	
38	Kynurenic		≤ 4.2		1.4	
39	Quinolinic / 5-HIAA Ratio		≤ 2.5		1.3	



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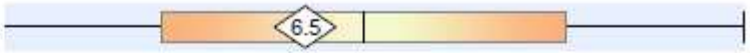
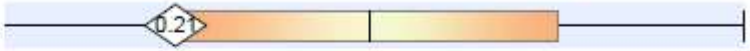
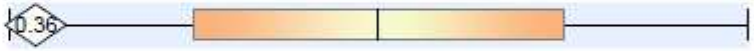
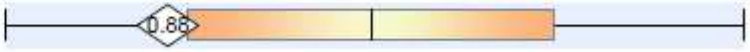
Page 3 – Pyrimidines and Fatty Acids

Pyrimidine Metabolites - Folate Metabolism					
40	Uracil		≤ 16	6.5	
41	Thymine		≤ 0.91	0.21	
Ketone and Fatty Acid Oxidation					
42	3-Hydroxybutyric		≤ 4.8	0.97	
43	Acetoacetic		≤ 10	0.36	
44	4-Hydroxybutyric		≤ 4.7	0.91	
45	Ethylmalonic	0.06 -	4.8	1.9	
46	Methylsuccinic		≤ 4.0	0.88	
47	Adipic	0.19 -	6.5	2.2	
48	Suberic		≤ 7.0	2.4	
49	Sebacic		≤ 0.61	0.16	

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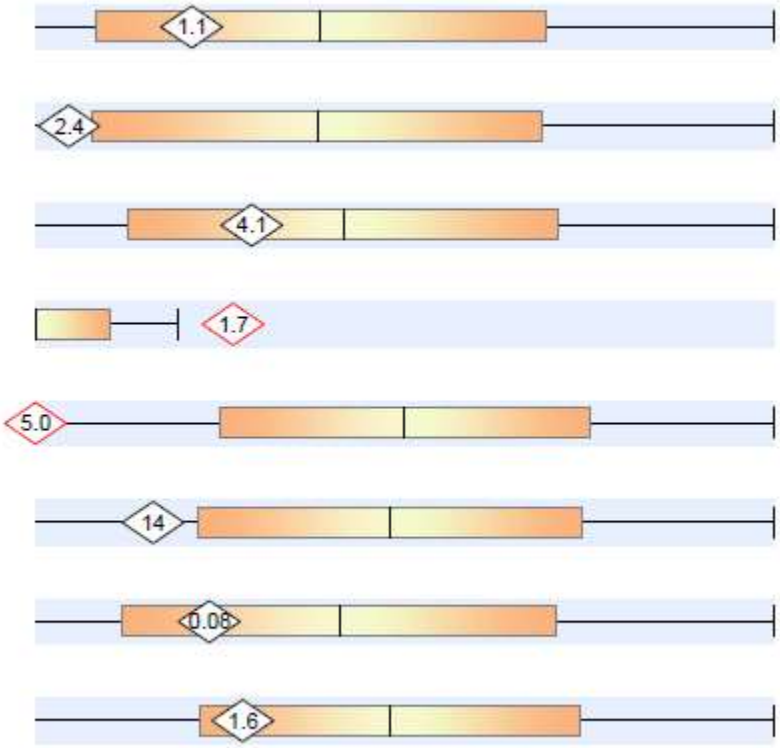
Page 3 – Nutritional Markers

Nutritional Markers

Vitamin B12						
50	Methylmalonic ✱		≤ 5.2		1.1	
Vitamin B6						
51	Pyridoxic (B6)		≤ 53		2.4	
Vitamin B5						
52	Pantothenic (B5)		≤ 14		4.1	
Vitamin B2 (Riboflavin)						
53	Glutaric ✱		≤ 1.4	H	1.7	
Vitamin C						
54	Ascorbic	10	- 200	L	5.0	
Vitamin Q10 (CoQ10)						
55	3-Hydroxy-3-methylglutaric ✱		≤ 88		14	
Glutathione Precursor and Chelating Agent						
56	N-Acetylcysteine (NAC)		≤ 0.34		0.08	
Biotin (Vitamin H)						
57	Methylcitric ✱		≤ 5.7		1.6	



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

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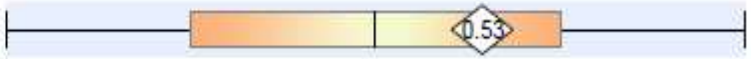
Page 4 – Indicators of Detoxification

Indicators of Detoxification

Glutathione					
58	Pyroglutamic ✸	13	- 62	22	
59	2-Hydroxybutyric ✸	0.19	- 2.0	1.3	
Ammonia Excess					
60	Orotic	0.04	- 0.80	0.53	
Aspartame, salicylates, or GI bacteria					
61	2-Hydroxyhippuric		≤ 1.2	0.31	

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

Page 4 – Amino Acid Metabolites and Mineral Metabolism

Amino Acid Metabolites

62	2-Hydroxyisovaleric		≤ 0.55	0	0.00
63	2-Oxoisovaleric		≤ 2.5	0	0.00
64	3-Methyl-2-oxovaleric		≤ 1.1	0	0.00
65	2-Hydroxyisocaproic		≤ 0.68	0.04	0.04
66	2-Oxoisocaproic		≤ 0.46	0.12	0.12
67	2-Oxo-4-methiolbutyric		≤ 0.33	0.01	0.01
68	Mandelic		≤ 0.30	0	0.00
69	Phenyllactic		≤ 0.19	0.02	0.02
70	Phenylpyruvic		≤ 4.0	0.07	0.07
71	Homogentisic		≤ 0.61	0.01	0.01
72	4-Hydroxyphenyllactic	0.05 -	1.1	0.26	0.26
73	N-Acetylaspartic		≤ 5.9	2.1	2.1
74	Malonic		≤ 18	12	12

Mineral Metabolism

75	Phosphoric	1 000 -	7 300	1 793	1793

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Indicator of Fluid Intake

77	*Creatinine	169	mg/dL

*The creatinine test is performed to adjust metabolic marker results for differences in fluid intake. Urinary creatinine has limited diagnostic value due to variability as a result of recent fluid intake. Samples are rejected if creatinine is below 20 mg/dL unless the client requests results knowing of our rejection criteria.

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.

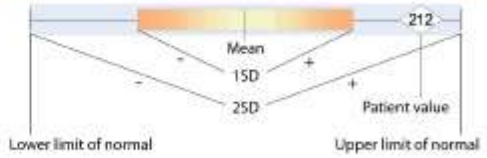
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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

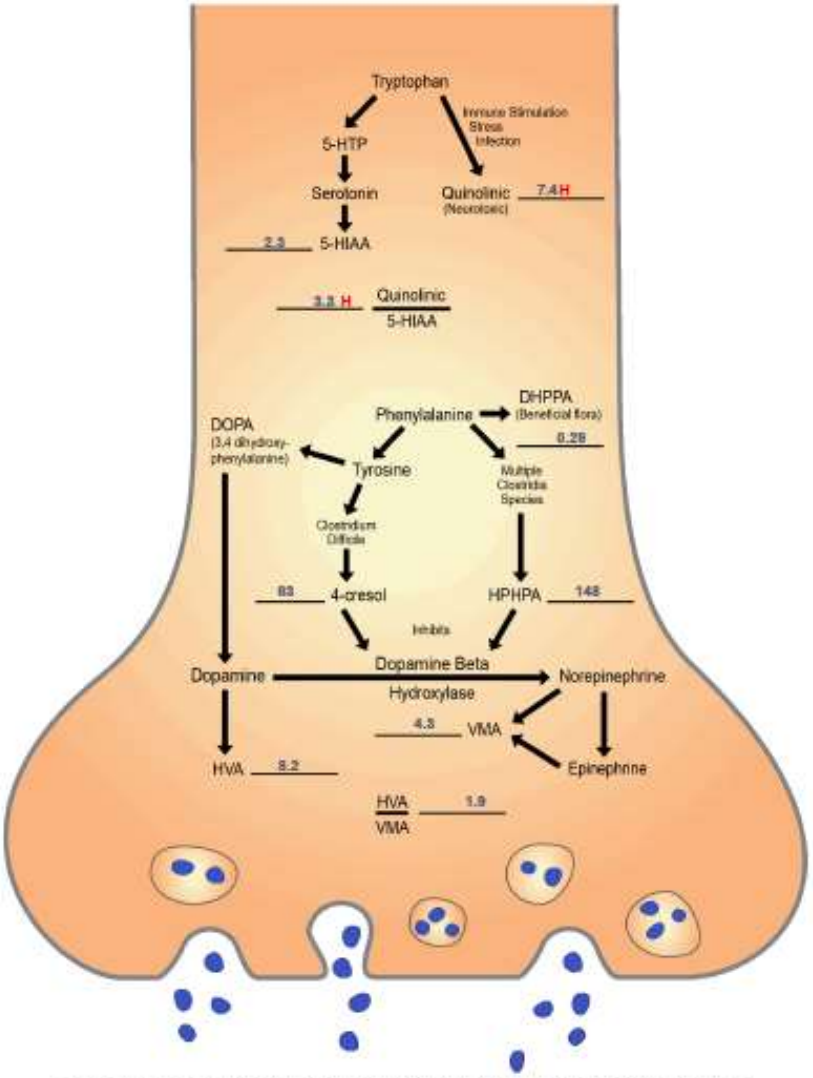
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Result	Reference Range - Males Age 13 and Under
Intestinal Microbial Overgrowth			
HPHPA (Clostridia marker)	< 219.9	212	



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	

Neurotransmitter Metabolism Markers



The diagram contains the patient's test results for neurotransmitter metabolites and shows their relationship with key biochemical pathways within the axon terminal of nerve cells. The effect of microbial byproducts on the blockage of the conversion of dopamine to norepinephrine is also indicated.

The Great Plains Laboratory, Inc.

Requisition #:	[redacted]	*Physician:*	KURT WOELLER DO
Patient Name:		*Date of Collection:*	3/16/2015

Interpretation

High yeast/fungal metabolites (Markers 1,2,3,4,5,6,7,8) indicate a yeast/fungal overgrowth of the gastrointestinal tract. Prescription or natural (botanical) anti-fungals, along with supplementation of high potency multi-strain probiotics (20-50 billion cfu's), may reduce yeast/fungal levels.

HVA levels below the mean (Marker 33) may indicate lower production of the neurotransmitter dopamine, perhaps due to low dietary intake of the amino acid precursors phenylalanine or tyrosine. Homovanillic acid is a metabolite of the neurotransmitter dopamine. Supplementation with phenylalanine or tyrosine may be beneficial. Enzyme cofactors magnesium, B6 (pyridoxine) or biopterin may also be deficient; neurotransmitter levels may increase with supplementation with these cofactors if these are deficient.

VMA levels below the mean (Marker 34) may indicate lower production of the neurotransmitter norepinephrine or the hormone adrenaline, perhaps due to low dietary intake of the amino acid precursors phenylalanine or tyrosine. Vanylmandelic acid (VMA) is a metabolite of norepinephrine or adrenaline. Low VMA may also result from blocked conversion of dopamine to norepinephrine by *Clostridia* metabolites. Supplementation with phenylalanine or tyrosine may be beneficial. Enzyme cofactors magnesium, B6 (pyridoxine) or biopterin may also be deficient and respond to supplementation.

High HVA/VMA ratio (Marker 35) The most common reason for an elevation of the HVA/VMA ratio is the decreased conversion of dopamine to norepinephrine and epinephrine. The enzyme responsible for this conversion, dopamine betahydroxylase, is copper and vitamin C dependent, so an elevated ratio could be due to deficiencies of these cofactors. Another common factor is inhibition of this enzyme by *Clostridia* byproducts. A high HPHPA, 4-Cresol, or other elevations of metabolites would be consistent with the latter explanation.

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The Great Plains Laboratory, Inc.

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

Requisition #:
Patient Name:
Patient Age:
Sex:
Physician Name:
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		2.9	2.9
2 5-Hydroxymethyl-2-furoic	≤ 30		4.3	4.3
3 3-Oxoglutaric	≤ 0.52	H	1.1	1.1
4 Furan-2,5-dicarboxylic	≤ 22		1.6	1.6
5 Furancarbonylglycine	≤ 3.6		0.74	0.74
6 Tartaric	≤ 3.9		1.4	1.4
7 Arabinose	≤ 56	H	73	73
8 Carboxycitric	≤ 34		1.1	1.1

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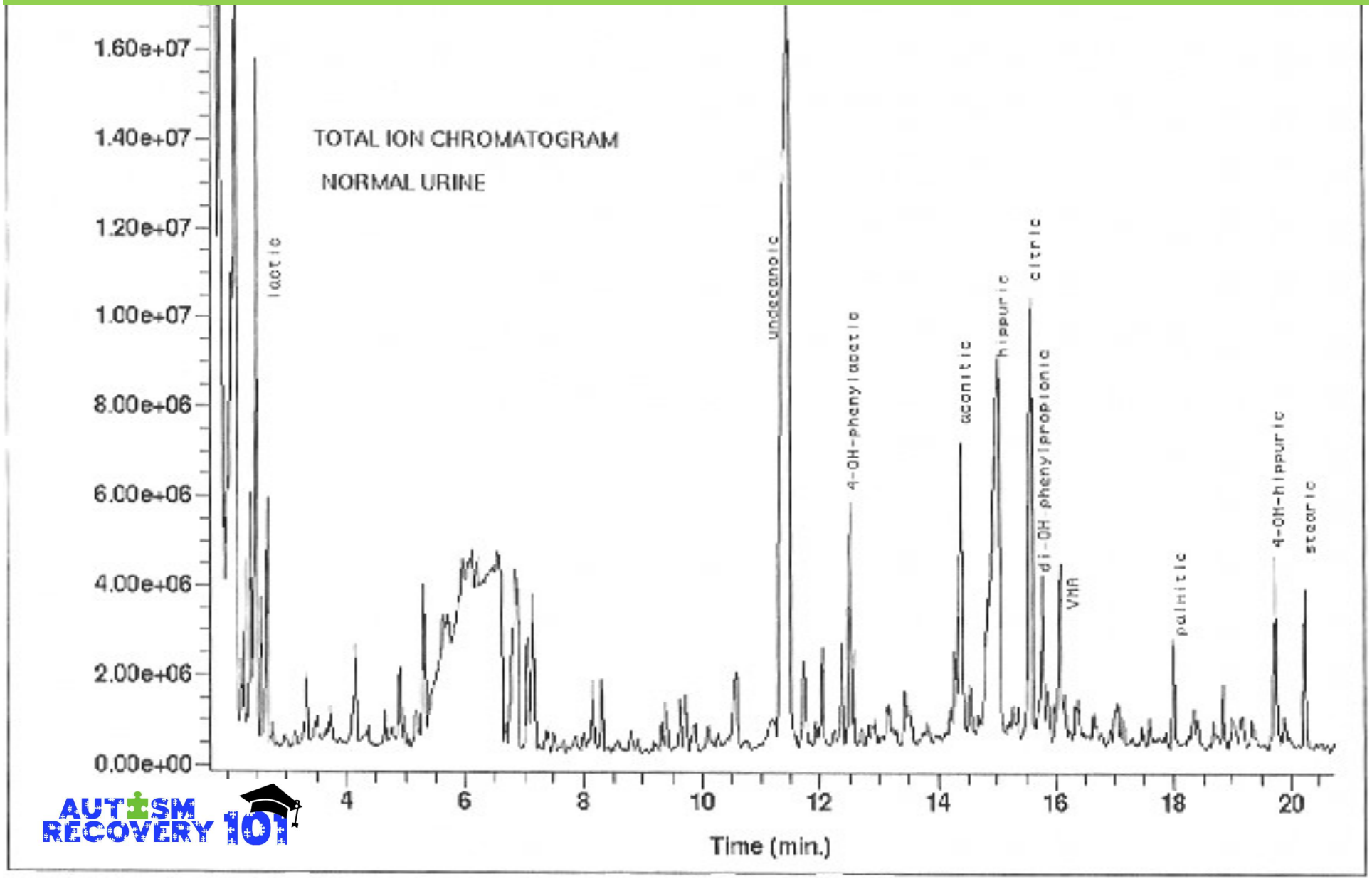
Shaw, W. Increased Urinary Excretion of Analogs of Krebs Cycle Metabolites and Arabinose in Two Brothers with Autistic Features. Clin Chem 41:1094-1104, 1995



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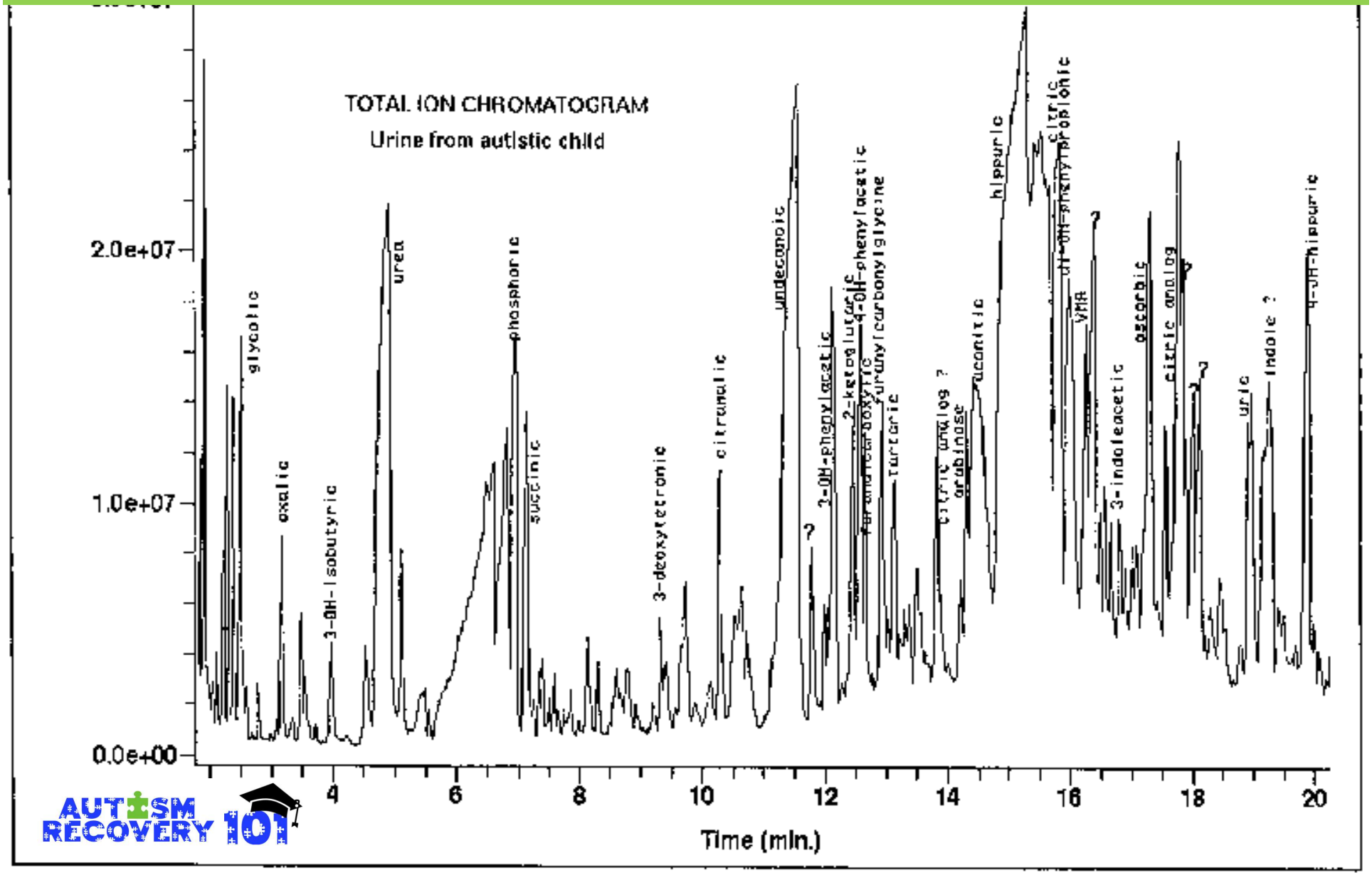
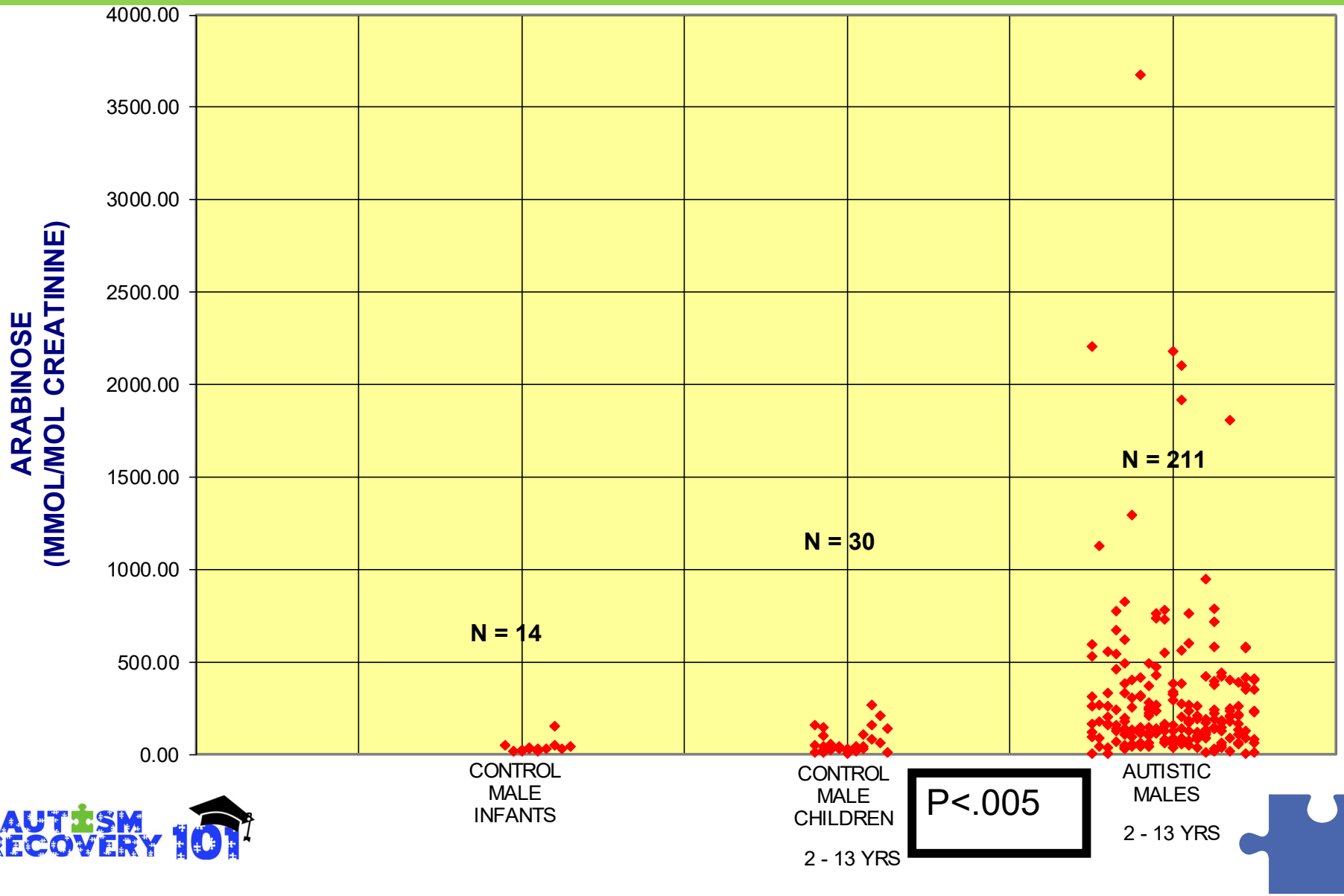


Shaw, W., et al Assessment of antifungal drug therapy in autism by measurement of suspected microbial metabolites in urine with GC/MS. Clinical Practice of Alternative Medicine: 15-26,2000.



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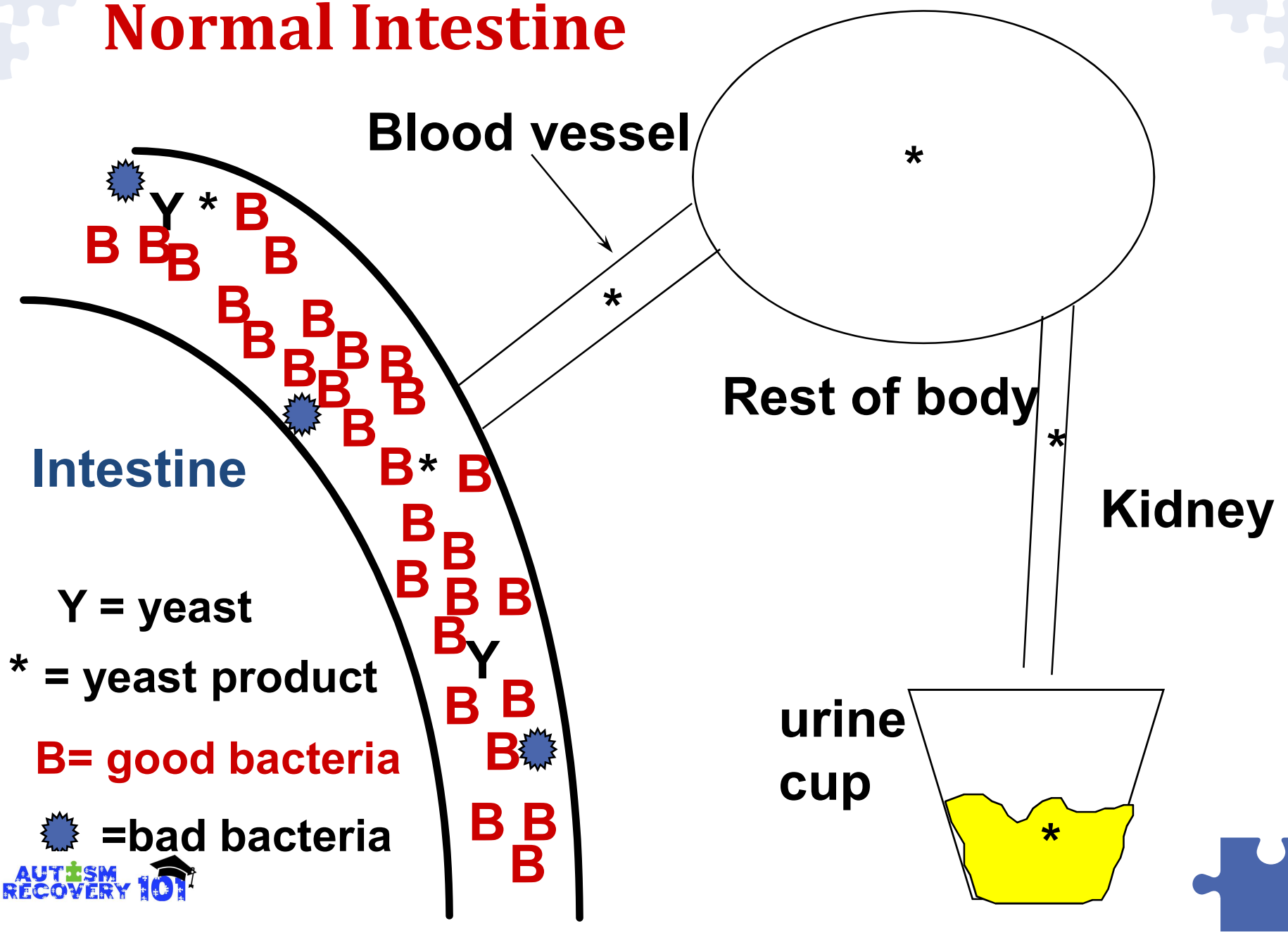
Normal Intestine



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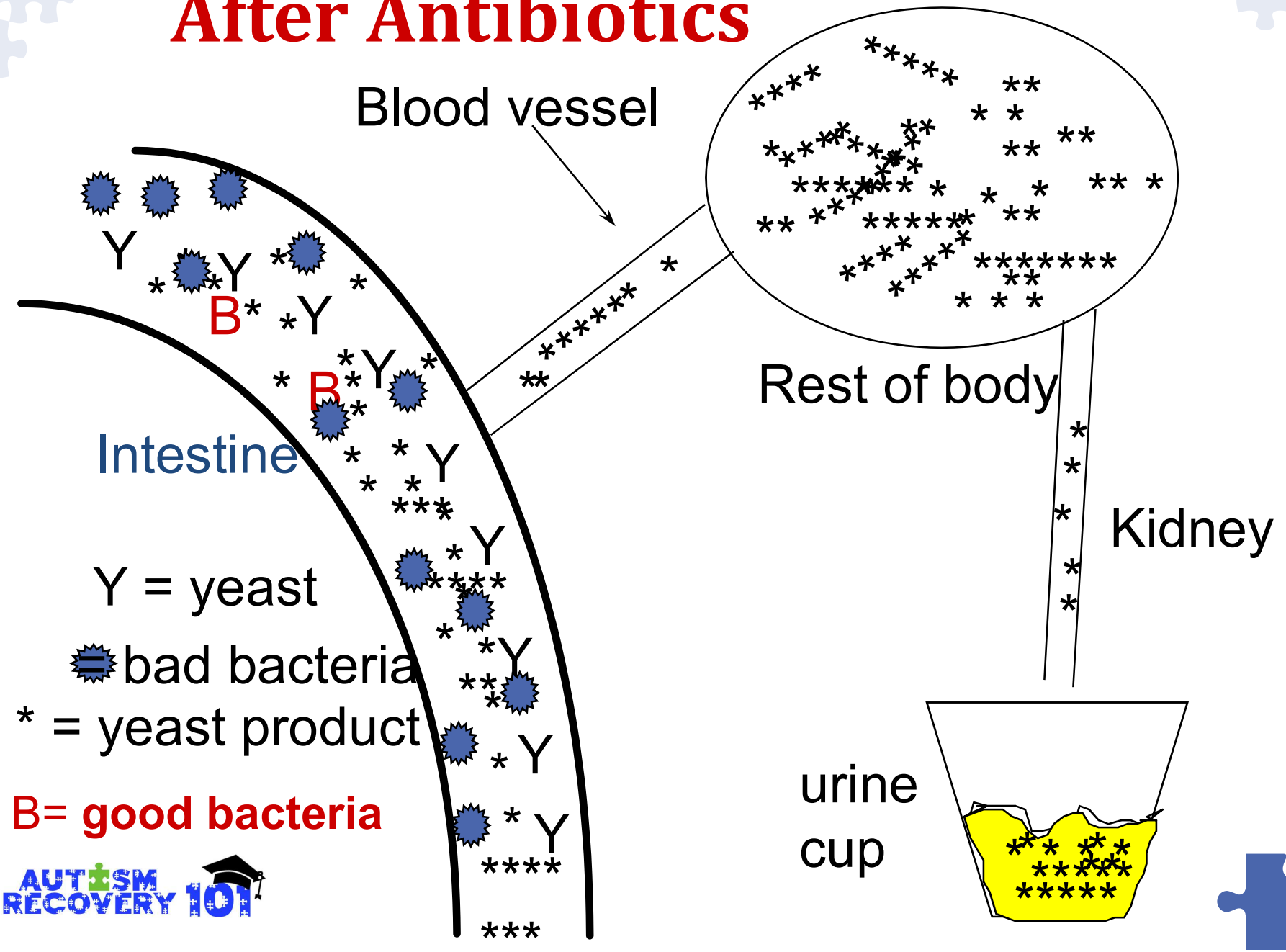
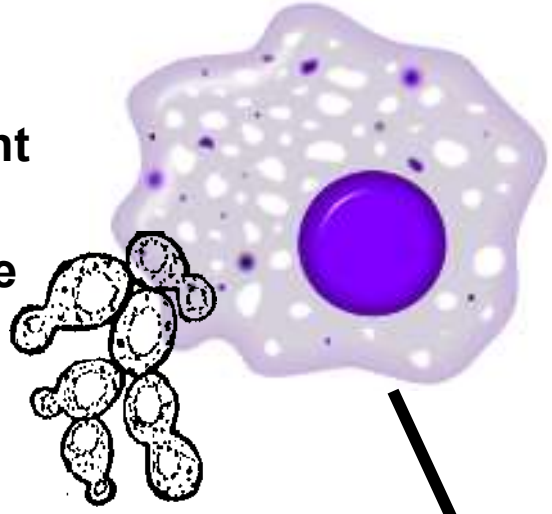
After Antibiotics



Production of arabinose, tartaric acids as indirect markers of invasive Candidiasis



Hyaluronic acid
Intercellular cement

hyaluronidase

Candida

Human macrophage

N-acetyl
Glucosamine,
Glucuronic acid

Kills Candida

ClO^-

Myeloperoxidase-WBC enzyme
response to Candida infection

Arabinose,
Tartaric acid

Hypochlorite ion-powerful oxidizing agent-tissue damage
Active ingredient of Clorox®

References

1. Jahn M, et al. Carbohydr Res. 1999, 321:228-34.
2. Shimizu MT et al. J Med Vet Mycol. 1995, 33:27-31

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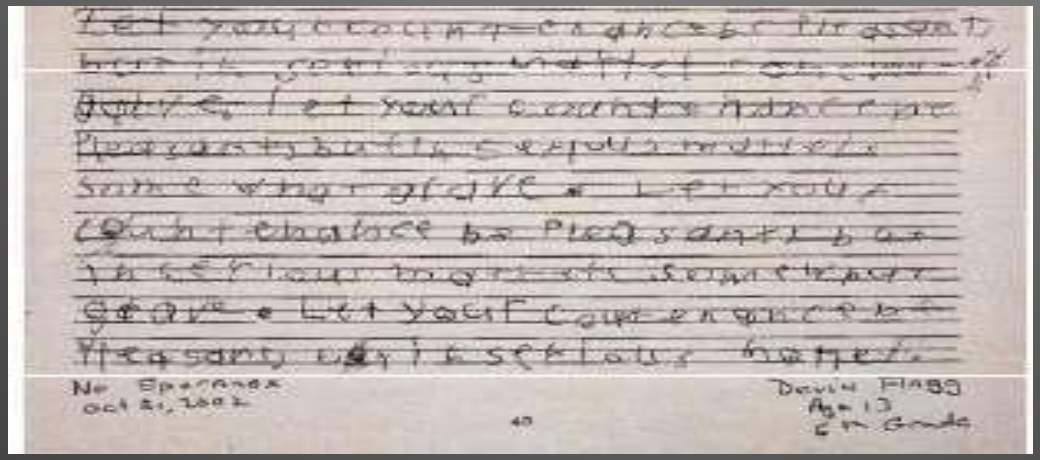
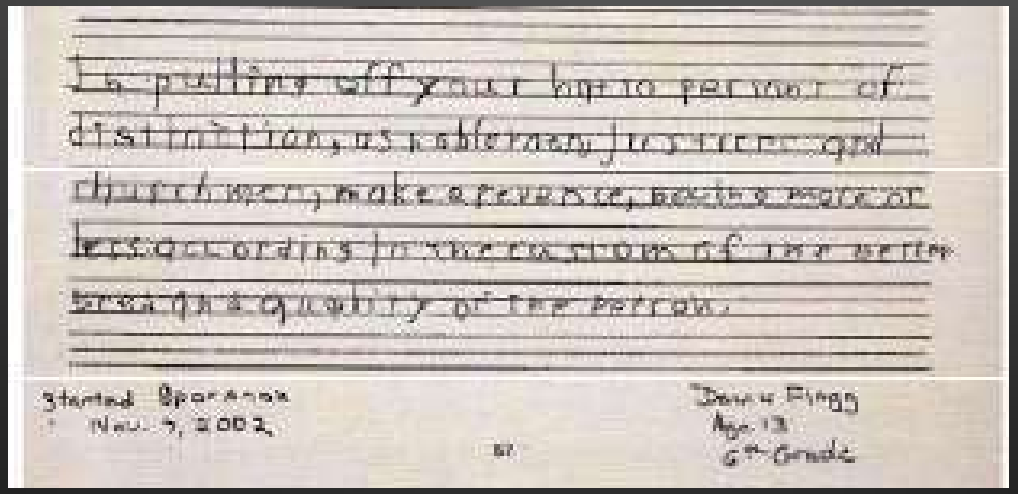
Handwriting improvement after antifungal therapy - *Discover Magazine*

Before Antifungal



After Antifungal - 1 month later



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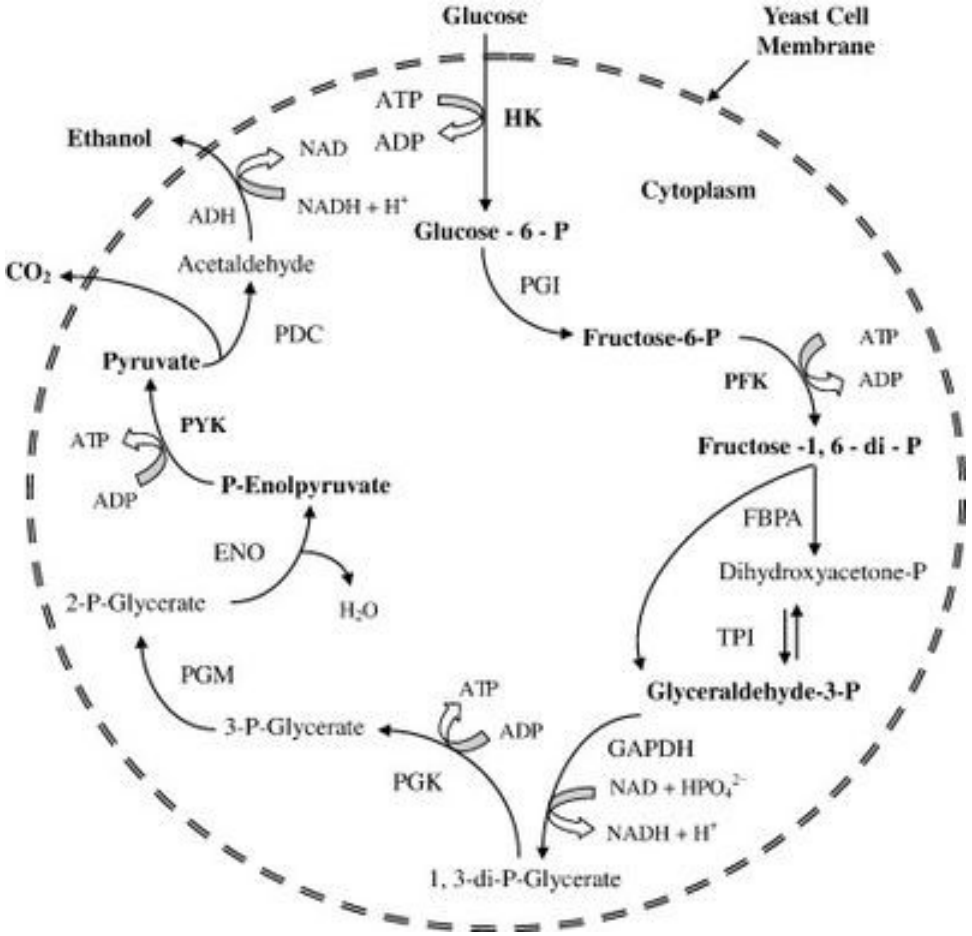
List of *Observations* Seen in Autism That Appear (in part) Related to Candida Overgrowth

- **Silly/goofy/giddy, inappropriate laughter – *"acts drunk."***
- Sugar and carbohydrate cravings intensified.
- Heightened sensory seeking behavior, anxiety, and emotional instability.
- Strange behavior such as seeking pressure, hanging upside down, heightened seeking of masturbation.

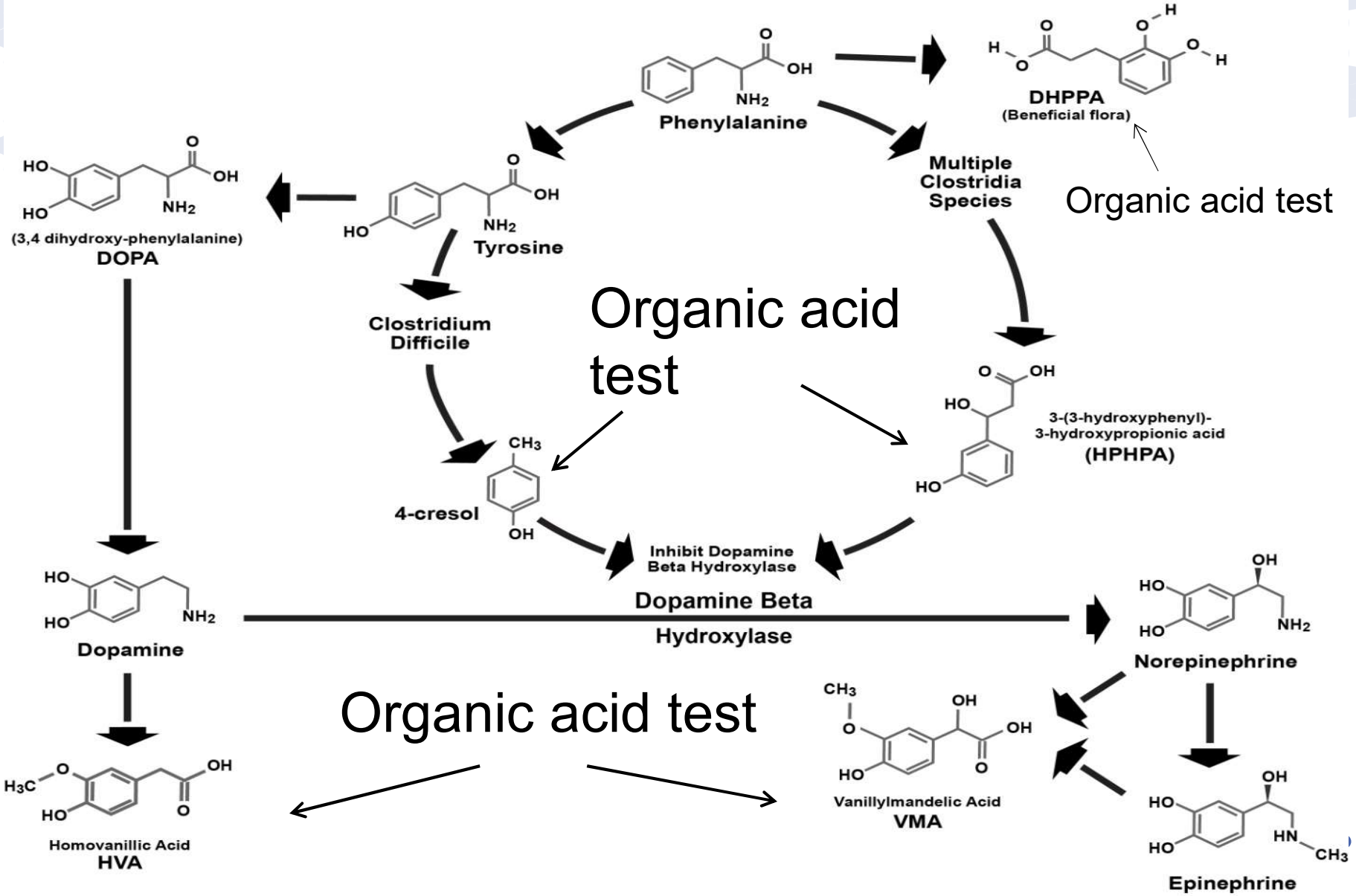
Alcohol-related symptoms have been observed



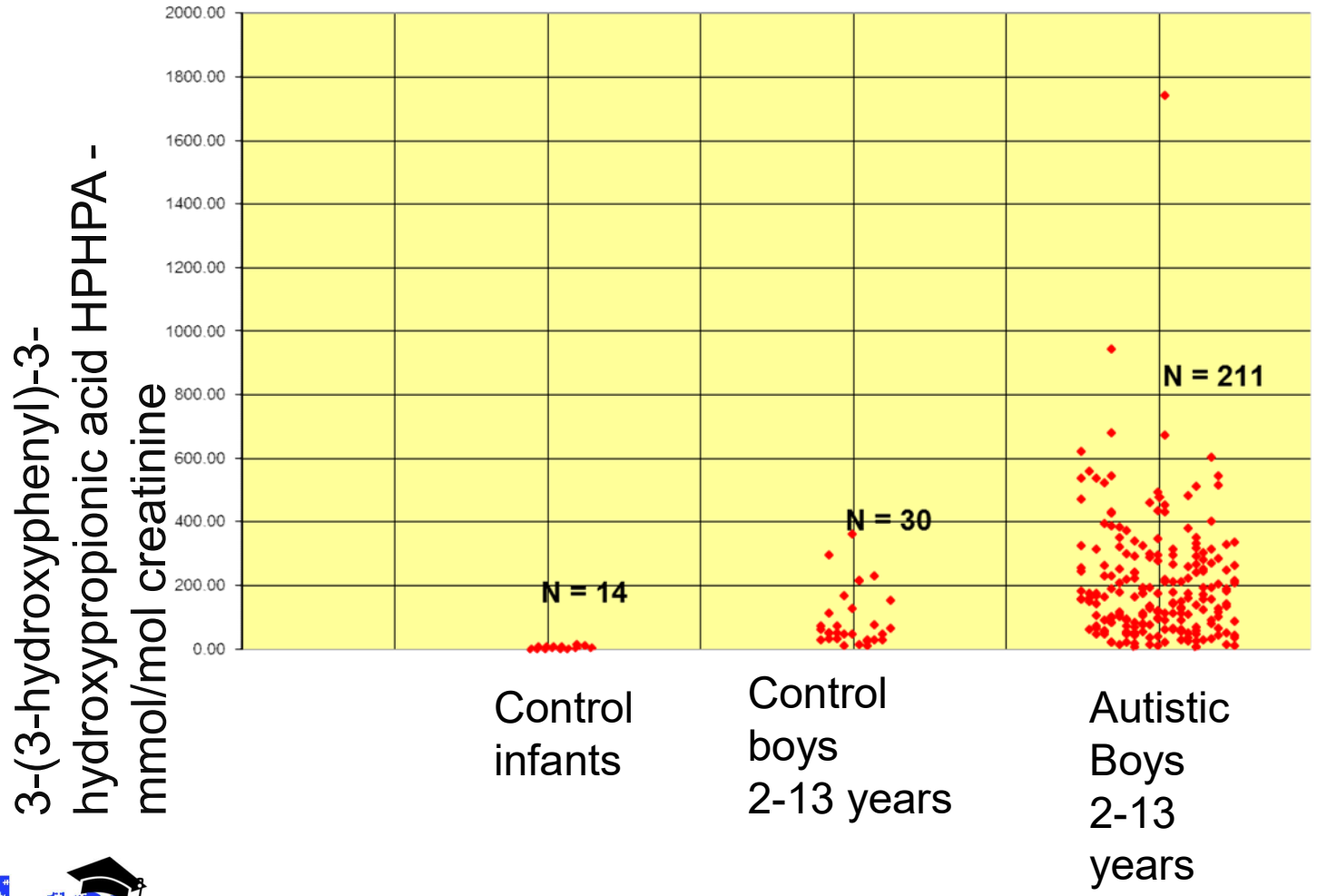
Plants, yeast and bacteria *– can ferment compounds (glucose) into acetylaldehyde and finally into alcohol.*

AUTISM RECOVERY 101

Critical effect of intestinal bacteria on certain brain and nervous system chemicals

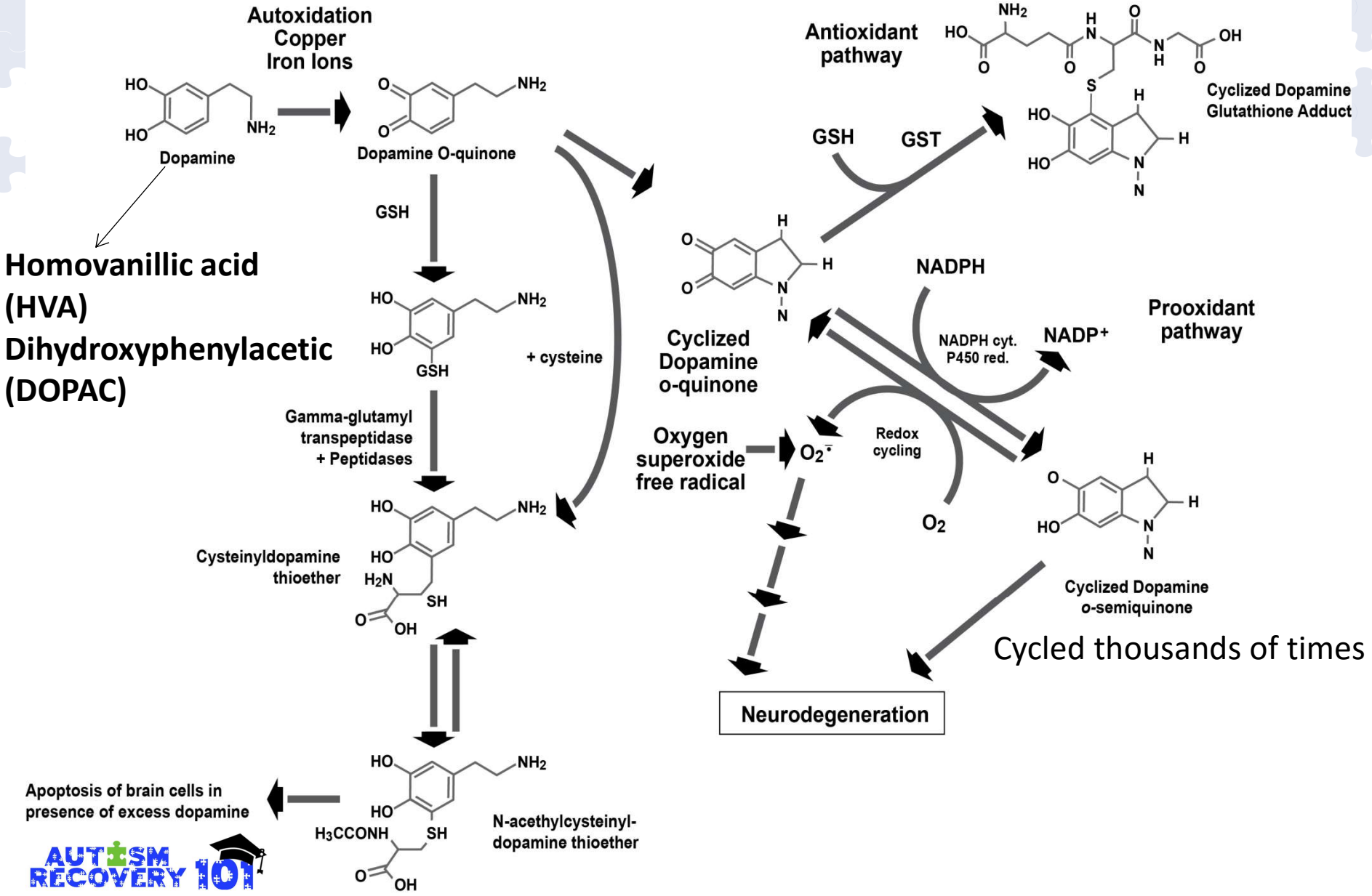


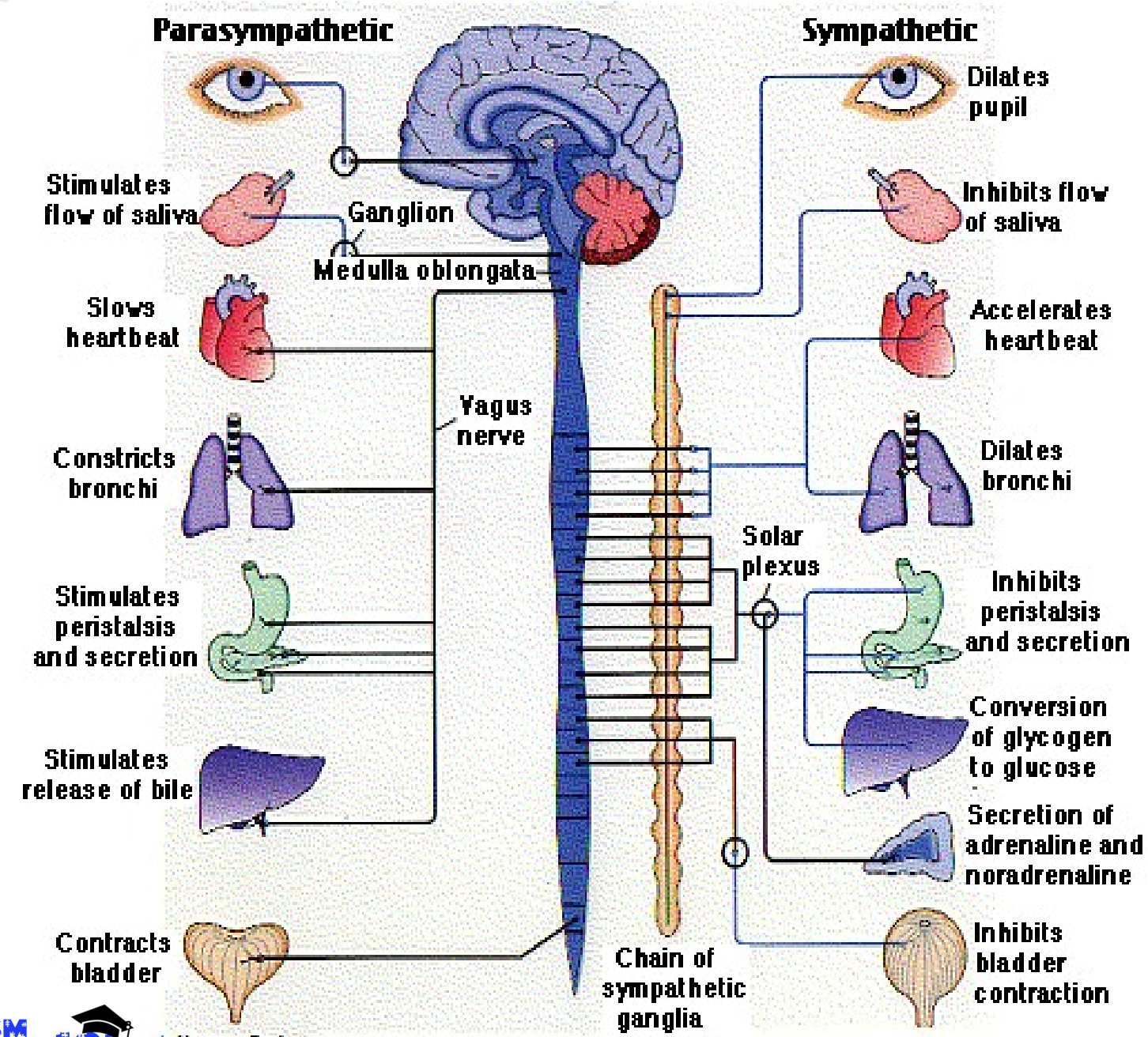
Distribution of values for HPHPA Clostridia metabolite in urine samples of male infants, control boys, and boys with autism.

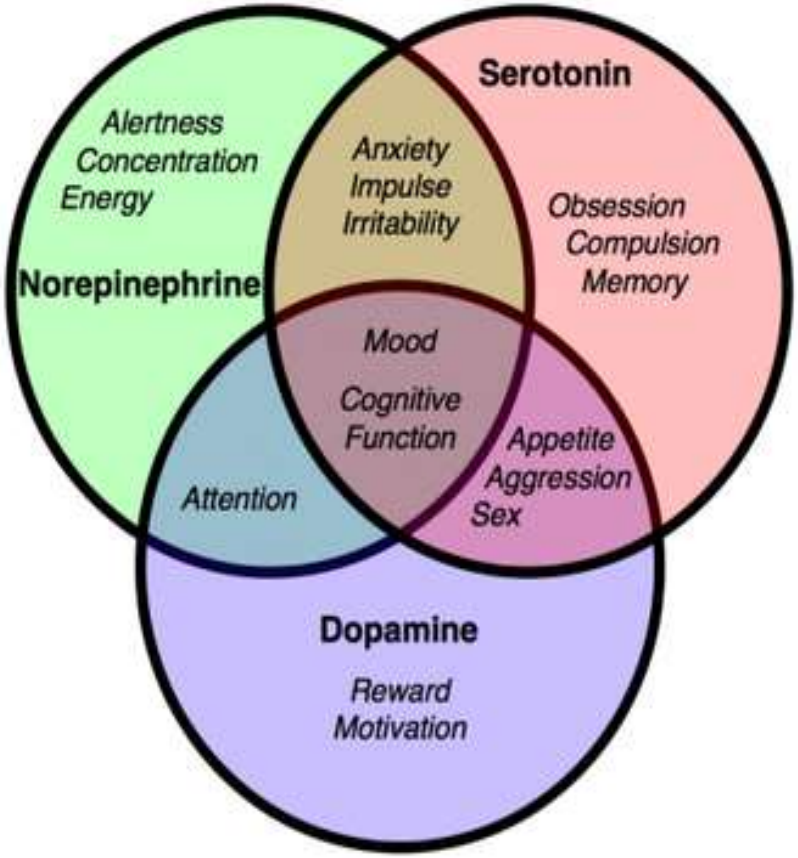


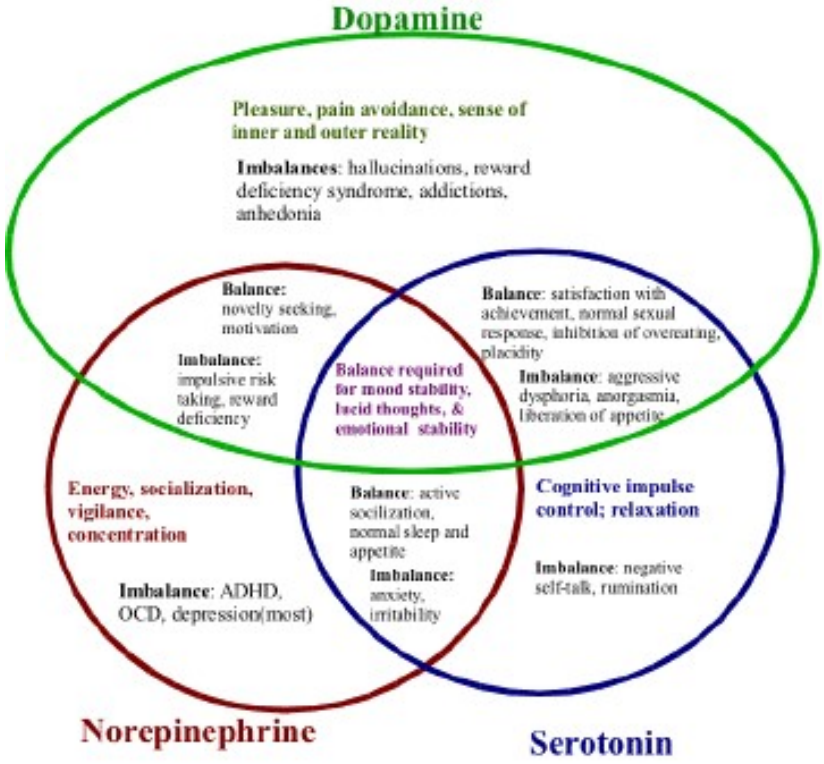
AUTISM RECOVERY 101

Toxicity of Excess Dopamine









Modified from Katz, N.B. 2005. Neurotransmitters: the bridges of the brain. Institute for Natural Resources, Health Update: Home-Study #1700, 27pp.


The Oxalate
problem

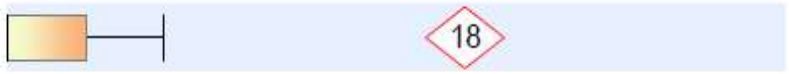
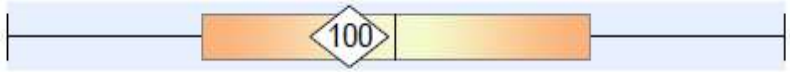
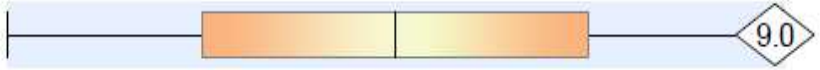
The Great Plains Laboratory, Inc.

Requisition #:

Physician Name:

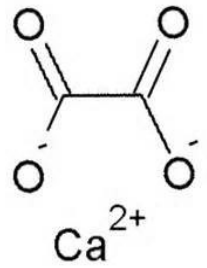
Patient Name:

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	
19 Glycolic	20 - 202	100	
20 Oxalic	15 - 174	H 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	

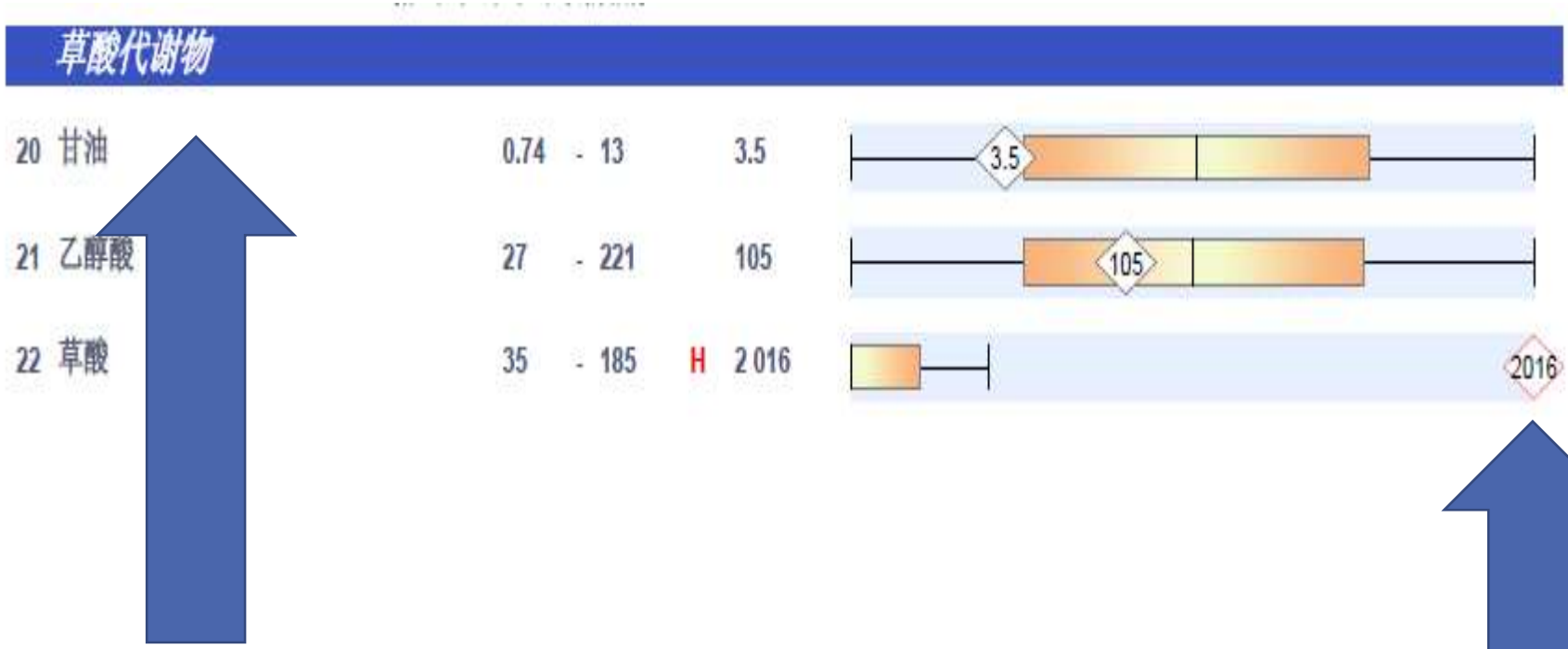
What Are Oxalates?

- Oxalate, and its acid form, are organic acids found from 3 primary sources:
  - *Diet*
  - *Fungus, such as mold and candida*
  - *Cell metabolism*



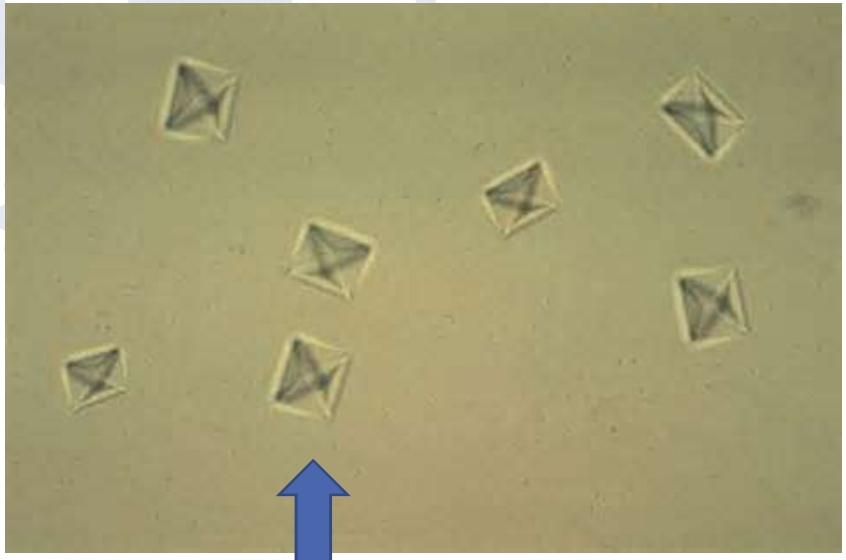
- Oxalic acid is the most acidic organic acid in body fluids.
- Ethylene glycol (antifreeze) - *primary toxicity effects are from oxalate crystal formation*.

Some Oxalate Levels Take Higher Priority Over Others

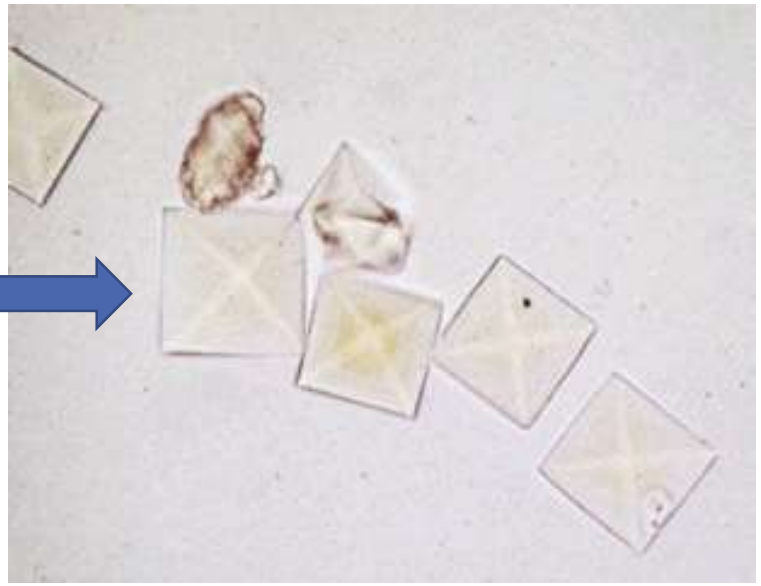


Likely Soy Consumption

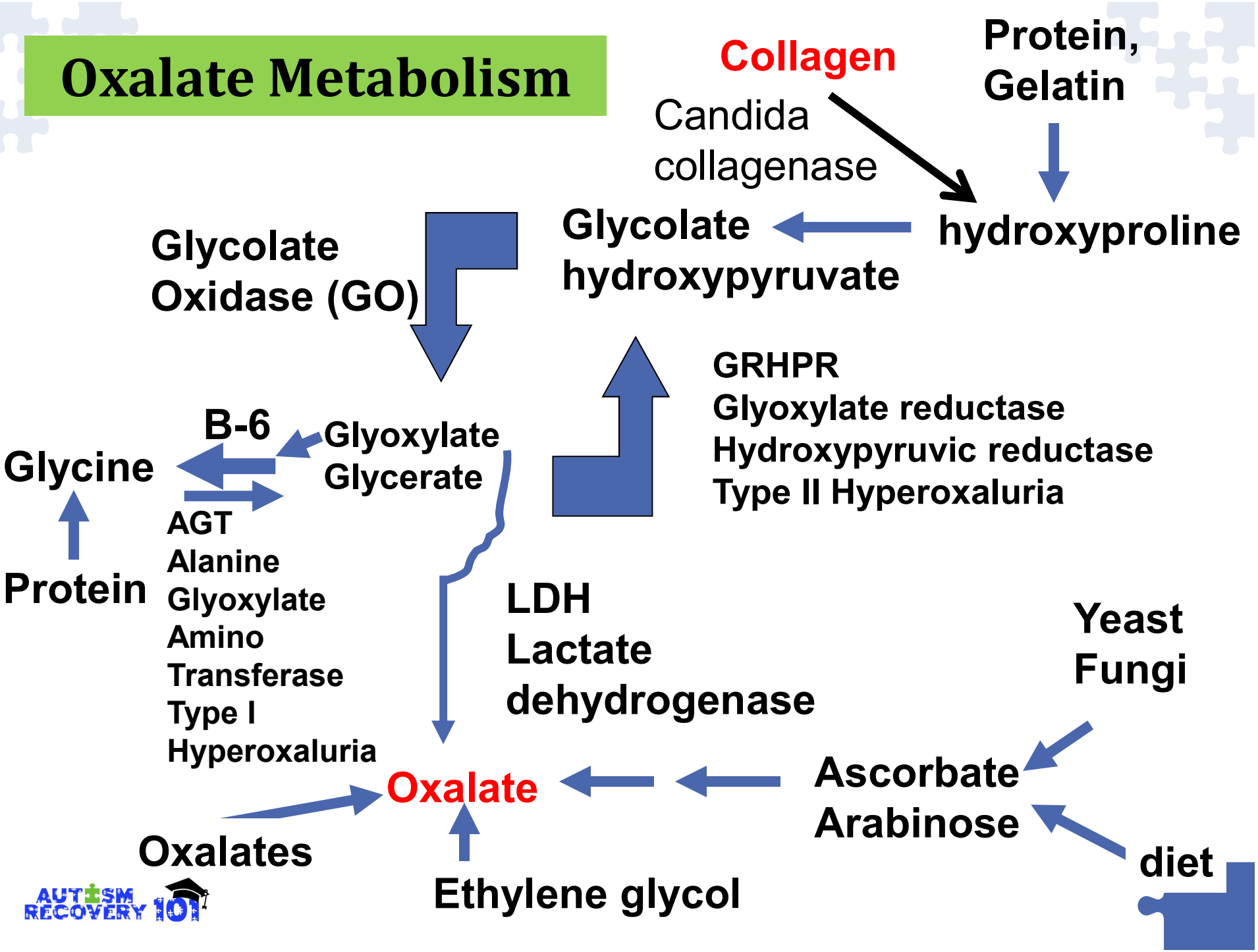
AUTISM RECOVERY 101



‘X’ Mark



AUTISM RECOVERY 101


Oxalate Metabolism
Collagen
Protein,
Gelatin
Candida
collagenase
hydroxyproline
Glycolate
hydroxypyruvate
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
Oxalate
Ascorbate
Arabinose
Oxalates
Ethylene glycol
diet
AUTISM RECOVERY 101

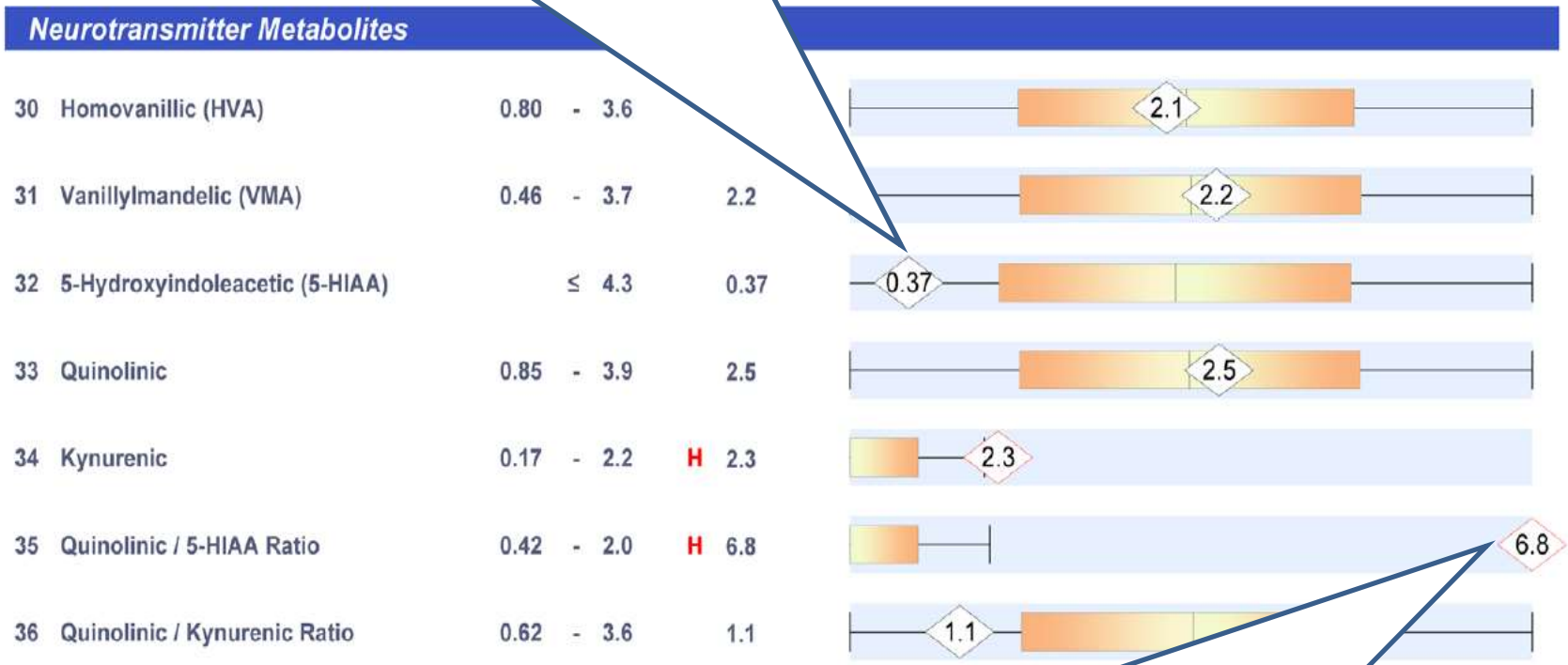
Common Complaints and Observations

- Sandy and grainy stools
- Bladder irritability
- **Pain on urination – *holding penis or groin region***
- **Eye pain (eye poking in children)**
- Body aches, burning feeling in muscles
- **Moodiness, irritability, and aggressive behavior – *often seen in autism.***
- **Generalized pain that likely manifests as aberrant behavior.**

AUTISM RECOVERY 101

Brain and Nervous System Chemical Imbalances

Low normal tryptophan metabolite 5-HIAA



Neurotransmitter Metabolites					
30	Homovanillic (HVA)	0.80 - 3.6		2.1	
31	Vanillylmandelic (VMA)	0.46 - 3.7		2.2	
32	5-Hydroxyindoleacetic (5-HIAA)	≤ 4.3		0.37	
33	Quinolinic	0.85 - 3.9		2.5	
34	Kynurenic	0.17 - 2.2	H	2.3	
35	Quinolinic / 5-HIAA Ratio	0.42 - 2.0	H	6.8	
36	Quinolinic / Kynurenic Ratio	0.62 - 3.6		1.1	

Normal quinolinic acid, but very high ratio indicates excessive conversion of tryptophan to quinolinic acid.

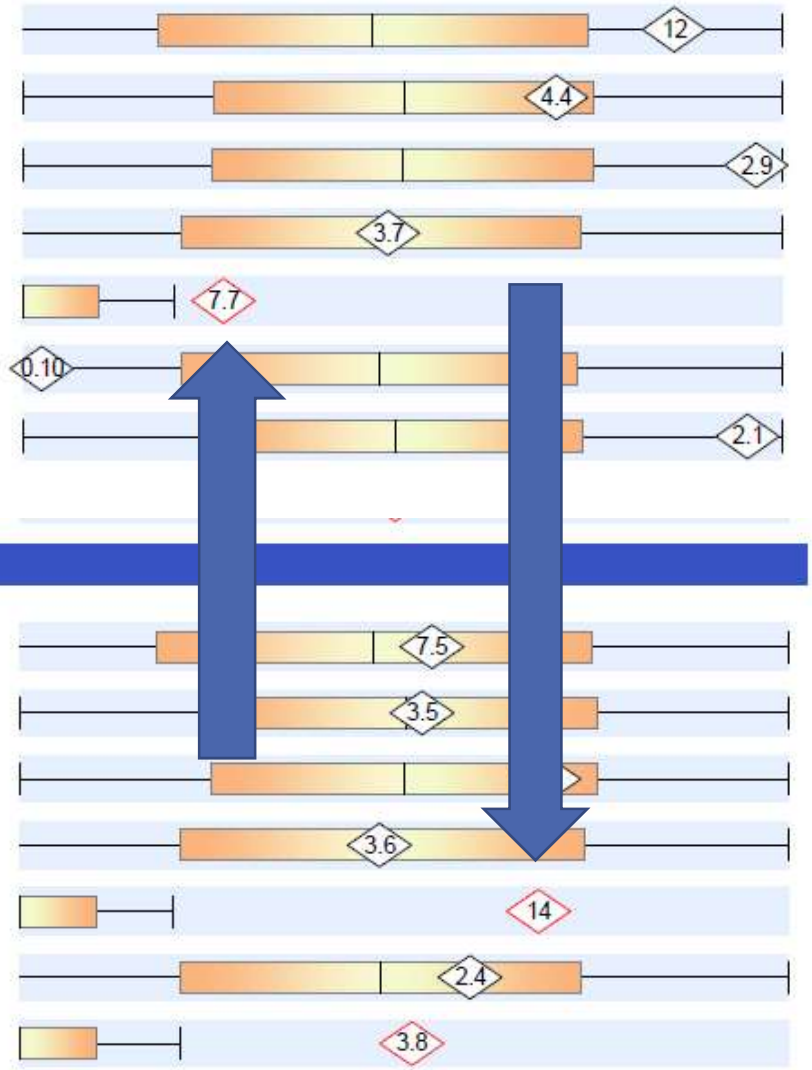
AUTISM RECOVERY 101

Neurotransmitter Metabolites

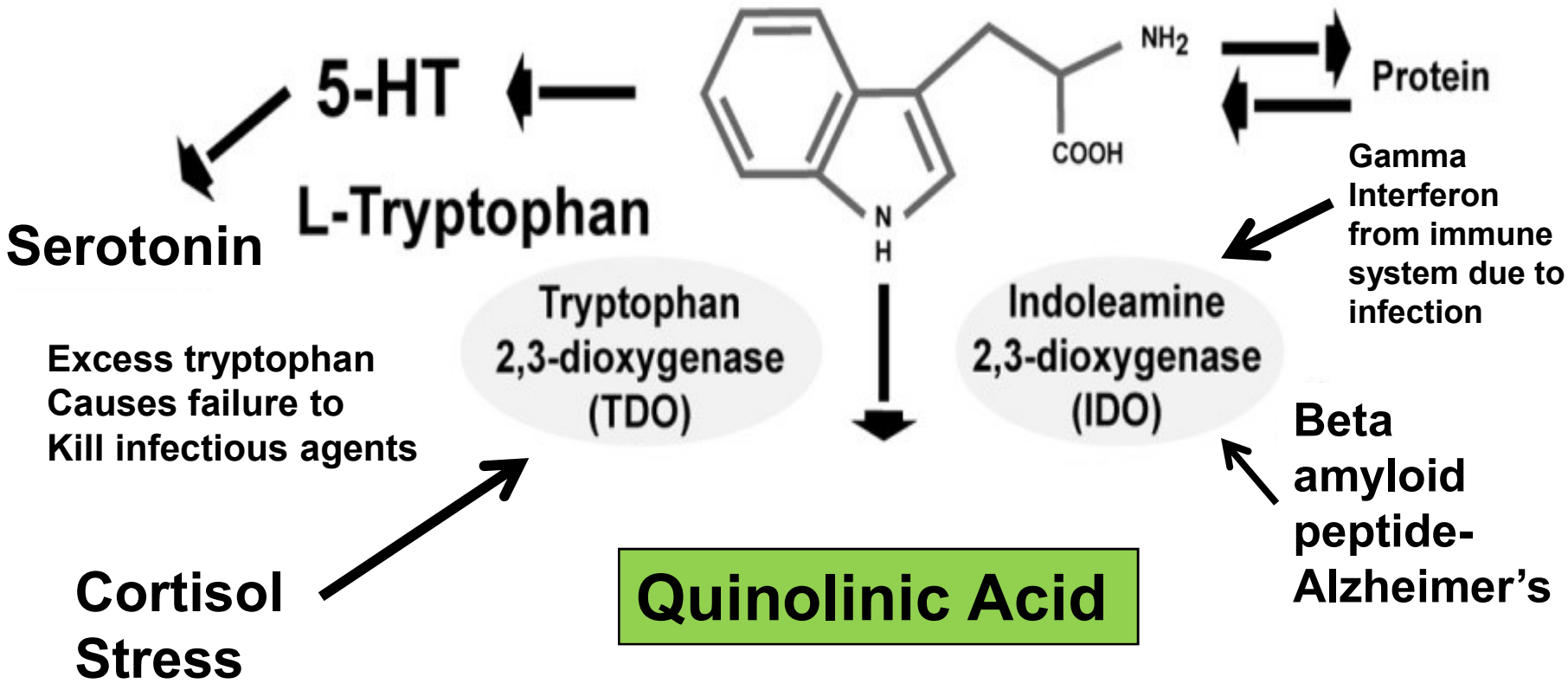
32	Homovanillic (HVA) *(dopamine)*		≤ 14		12	12
33	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.87	- 5.9		4.4	4.4
34	HVA / VMA Ratio	0.12	- 3.0		2.9	2.9
35	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*		≤ 7.7		3.7	3.7
36	Quinolinic	0.63	- 6.7	H	7.7	7.7
37	Kynurenic		≤ 4.1		0.10	0.10
38	Quinolinic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

Neurotransmitter Metabolites

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



AUTISM RECOVERY 101



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*.

AUTISM RECOVERY 101

Mitochondria Dysfunction

The Role of Mitochondrial Problems in Autism and the Association with Various Co-Morbid Conditions

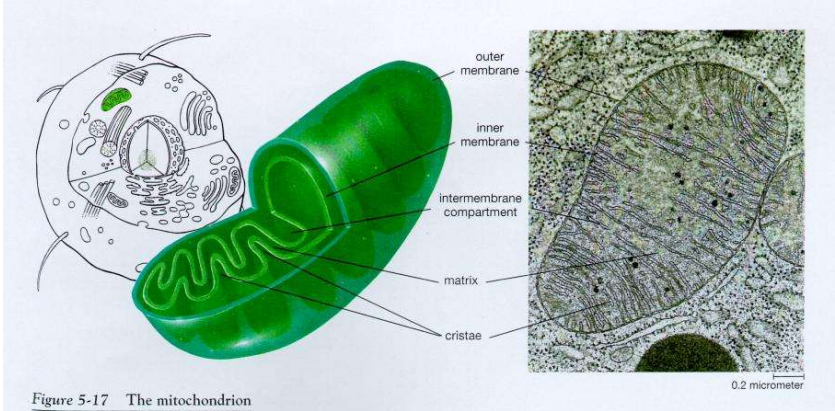
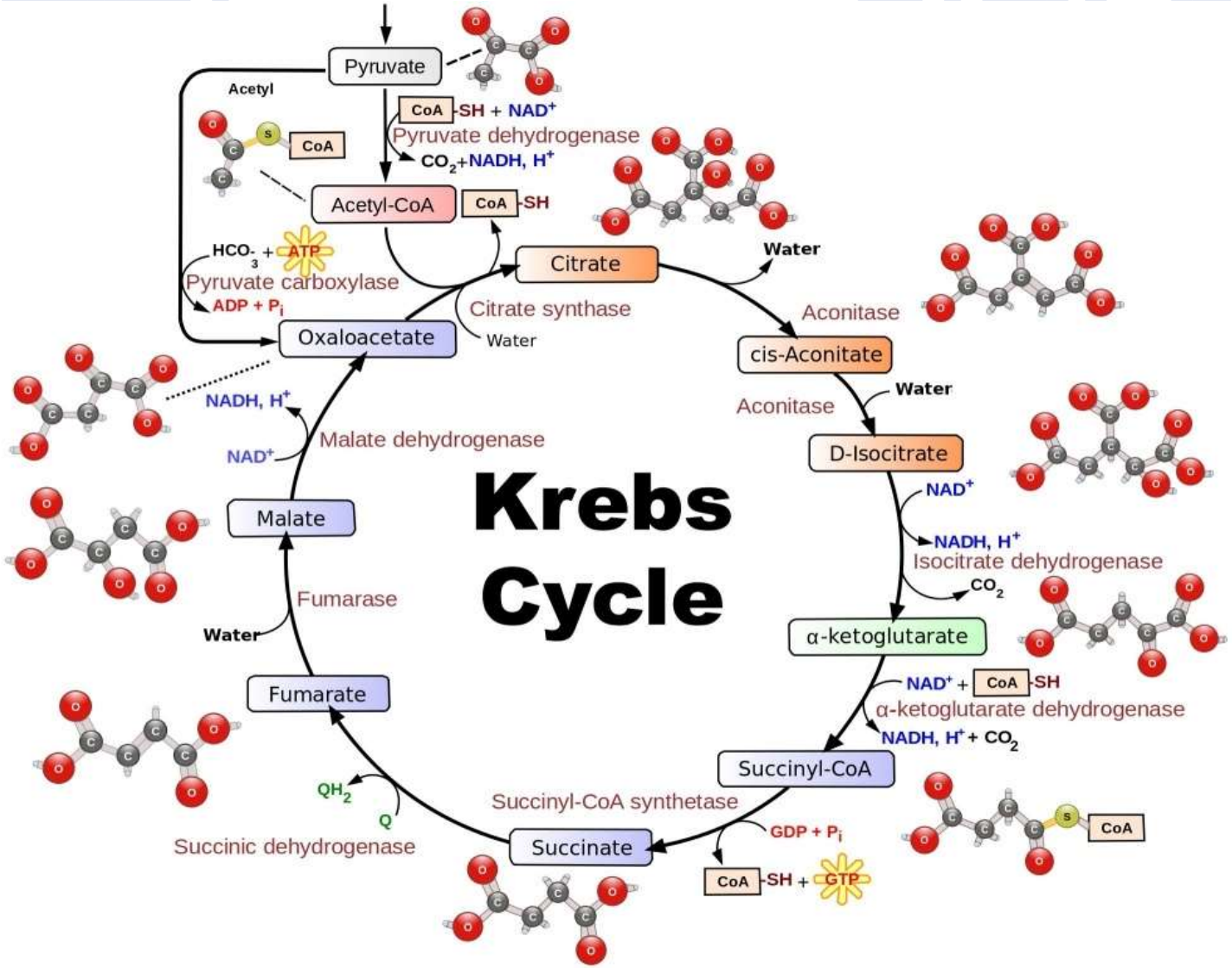


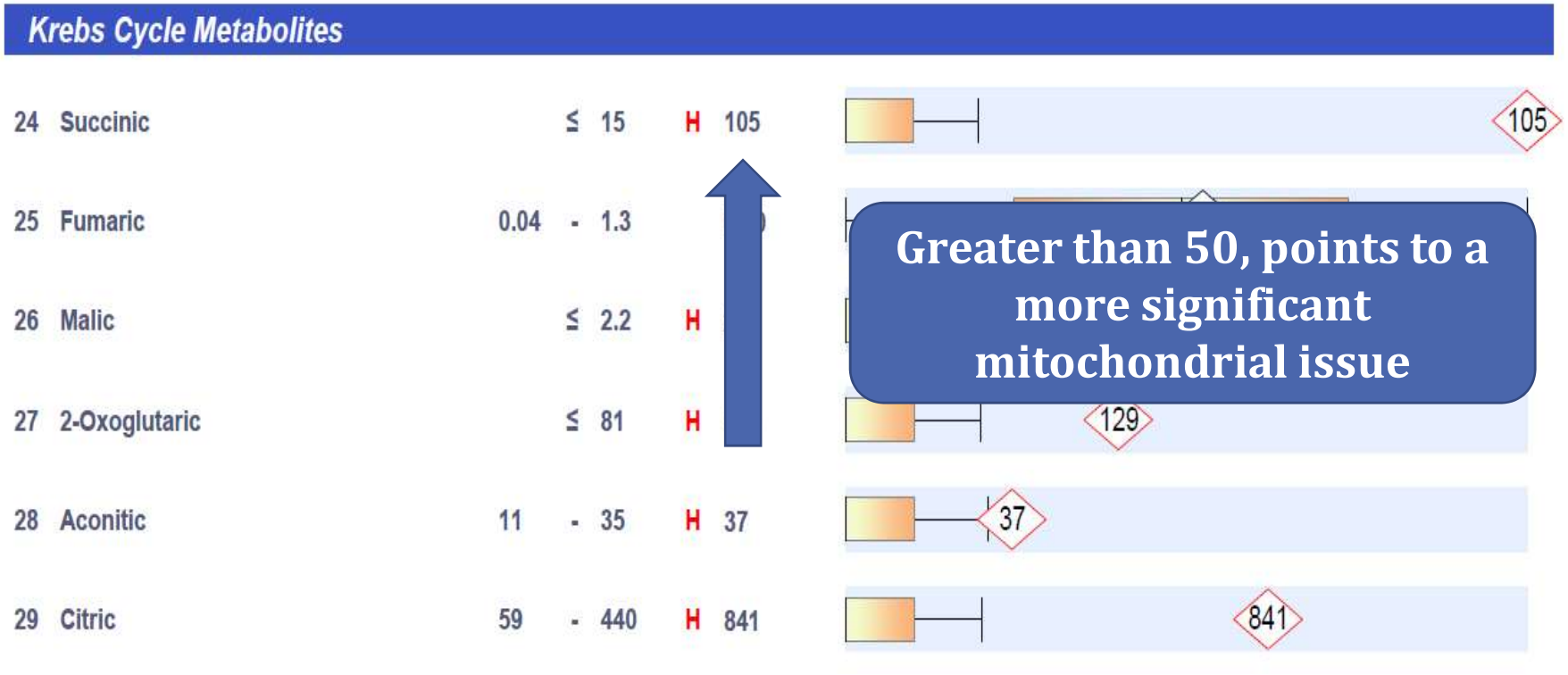
Figure 5-17 The mitochondrion

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.

AUTISM RECOVERY 101


Pyruvate
Acetyl
CoA
CoA-SH + NAD+
Pyruvate dehydrogenase
CO2+NADH, H+
Acetyl-CoA
CoA-SH
HCO-3 + ATP
Pyruvate carboxylase
ADP + Pi
Citrate
Water
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
QH2
Q
Succinic dehydrogenase
Fumarate
Water
Fumarase
Malate
NADH, H+
NAD+
Malate dehydrogenase
Krebs Cycle

Krebs Cycle Metabolites

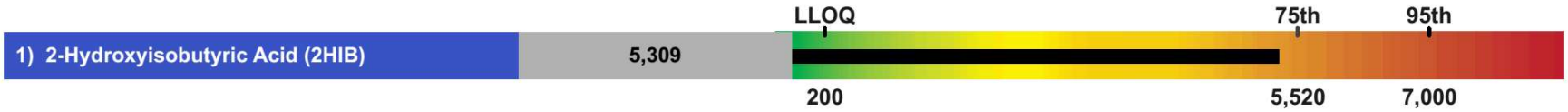


AUTISM RECOVERY 101

The Great Plains Laboratory, Inc.

GPL-TOX

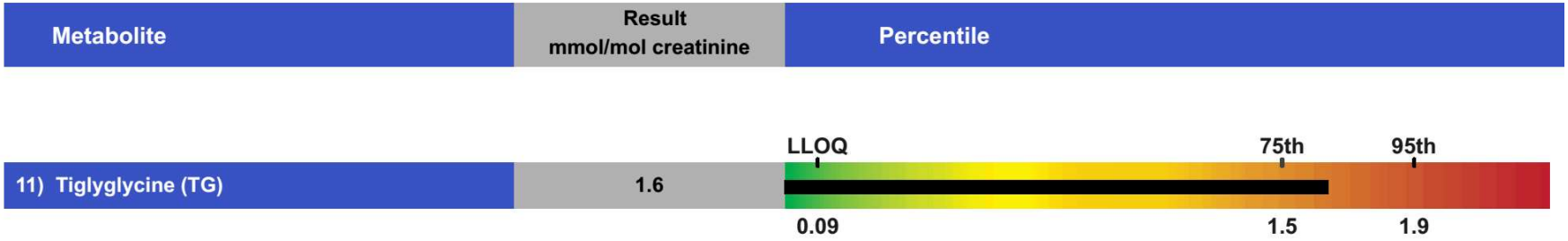
Toxic Organic Chemical Profile



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.

Marker for Mitochondria Function

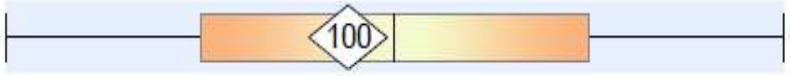
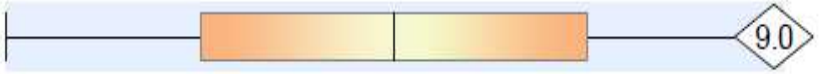


Tiglyglycine (TG) is a marker for mitochondrial disorders resulting from mutations of mitochondrial DNA, which can manifest from exposure to toxic chemicals, infections, inflammation, and nutritional deficiencies. TG indicates mitochondrial dysfunction by monitoring a metabolite that is elevated in mitochondrial deficiency of cofactors such as NAD+, flavin-containing coenzymes, and Disorders associated with mitochondrial dysfunction include autism, Parkinson's disease, and cancer.

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	
19 Glycolic	20 - 202	100	
20 Oxalic	15 - 174	H 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	

Mitochondrial Disease (Mde)

- Once thought to be rare, are now considered to be one of the most common metabolic problems in children.
- Some cases of Mde can occur in autism – *usually brought on by genetic mutations or abnormalities in the metabolic mechanism of mitochondrial function.*

AUTISM RECOVERY 101

Various Serious Health Problems

- **Heart defects** - *including electrical and contraction problems.*
- **Brain abnormalities** - *seizures, strokes*
- **Balance and coordination problems** - *including limb weakness and poor musculoskeletal development.*
- **Severe gastrointestinal problems** – *obstruction*

Autism = Mds (dysfunction - ***usually***)

In Autism, the majority of kids have a mitochondrial dysfunction (Mds) which indicates suboptimal functioning of mitochondria, but not definable as a specific mitochondrial disease (Mde).

Autism-Spectrum Children Can Have Similar Issues Related to Mito. Diseases

One study looking at over 20 autism-spectrum (ASD) kids showed no evidence of mitochondrial disease patterns via muscle biopsy testing, despite these kids having the following:

- *Attention, language, and behavior issues*
- *Seizures*
- *Poor muscle tone*
- *Gastrointestinal motility problems*

Mitochondrial Dysfunction in Autism

Mds versus Mde seems more common in autism as the majority of ASD kids overall presentation is *less severe* than kids with "classic" Mde.

Research and clinical speculation that many of the problems with Mds in Autism is environmentally induced.

1. Environmental chemicals, i.e. PCB, pesticides
2. Heavy metal toxicity, i.e. lead, nickel, cadmium, mercury.
3. Vaccine reactions
4. Cell membrane dysfunction from poor methylation, i.e. leads to increased oxidative stress via glutathione depletion.
5. Nutritional imbalances leading to susceptibility for poor cellular function.
6. Endogenous toxins from gut pathogens, i.e. clostridia (*propionic acid*).

AUTISM RECOVERY 101

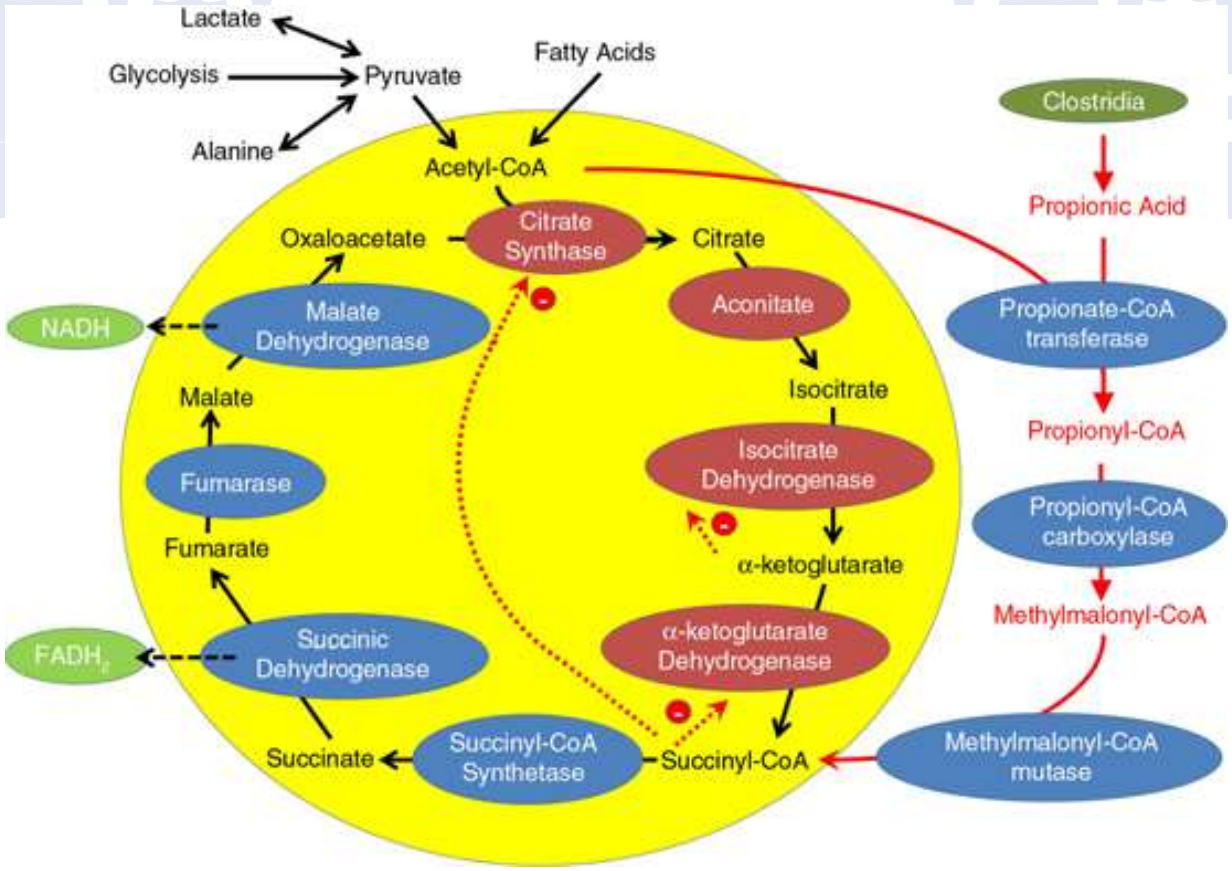


Fig. 2. The tricarboxylic acid cycle during high levels of propionic acid. Propionic acid, presumably derived from *Clostridia* spp., is metabolized to propionyl-CoA using acetyl-CoA. Propionyl-CoA is further metabolized into methylmalonyl-CoA, which enters the tricarboxylic acid cycle as succinyl-CoA. Succinyl-CoA inhibits the first and fourth enzyme in the tricarboxylic acid cycle. In this manner, propionic acid may 'short circuit' the tricarboxylic acid cycle, thereby reducing the production of nicotinamide adenine dinucleotide (NADH). This decrease in NADH is hypothesized to cause the decrease in complex I activity measured in the patients with consistent elevations in short and long acyl-carnitines (CESLAC)

Biomarkers For Mitochondrial Problems

Mitochondrial diseases are often associated with abnormal laboratory markers, including:

- *Elevated lactic acid, ammonia, pyruvate, creatine kinase, and AST (aspartate aminotransferase).*
- *Low carnitine*

Many of these are also found in autism as well in association with mitochondrial dysfunction (Mds).

AUTISM RECOVERY 101

Mitochondrial Lab Assessment at a Glance

The Organic Acids Test (OAT) is an excellent first-line test for mitochondrial function for the autism population. The various markers listed on this test are highly specific to different levels of biochemistry involved in cellular metabolism.

Even though a large number of children with an autism-spectrum disorder manifest with imbalances in the mitochondrial sections of the OAT, many of these imbalances occur because of other complicating factors. The most common causes of mitochondrial imbalances come from endogenous toxins produced by yeast and bacteria. Oxalates also create stress in the mitochondrial along with various nutritional imbalances. Therefore, as a priority it is always important to address these issues first with a healthy diet and removal of offending foods (i.e. gluten, casein).

The foundational supplements such as a multivitamin/mineral that include vitamin C, E, and, various B-vitamins, along with calcium and magnesium are all important for supporting cellular metabolism. You will often your child can achieve improvement in overall mitochondrial function through basic nutrient support. A follow test with the OAT will often show positive changes without the need for further testing or intervention. However, there are circumstances where additional nutritional supplementation is worthwhile and diagnostic testing

Mitochondrial Dysfunction in Autism – *Supplement Therapy*

Supplement support and antioxidant therapy can be helpful for mitochondrial issues.

Examples:

- **L-Carnitine** – helps with fatty acid transport
- **Thiamine (B1), Pyroxidine (B6), Riboflavin (B2)** - *all support mitochondrial function.*
- **Antioxidants** – *help to decrease oxidative stress*
- **'Mitochondrial Cocktail'** – *combination approach for balanced mitochondrial support.*

AUTISM RECOVERY 101

Mitochondrial Cocktail Options

In many situations you will be supporting mitochondrial function already through the foundational nutritional products, i.e. multivitamins and multi-minerals that contain vitamin E, C, and B-vitamins. However, there are certain supplements that have added benefit for cellular metabolism and can be useful to add to a supplement program.

See the handout document titled “Mitochondrial Lab Assessment at a Glance” for specifics on laboratory markers indicating problems in the mitochondria.

Clinical indicators that may suggest an underlying mitochondrial problem:

- *Poor physical energy and stamina*
- *Poor immunity*
- *Seizure disorder*
- *Low muscle tone and strength*
- *Poor gross and/or fine motor skills*
- *Cyclical vomiting*
- *Ongoing digestive problems not resolved by eradicating pathogens, dietary changes, and confirmation of no inflammation.*

Common Mitochondrial Support Supplements:

Mitochondrial 'Cocktail' Example

Example is for a 18 Kg (40lbs) child

- **L-Carnitine** – *40 to 50mg/kg per day (approx. 1000mg per day).*
- **(Ubiquinol – *active CoQ10*)** – *5 to 10 mg/kg (approx. 100mg to 200mg).*
- **NADH** – *5 mg+ daily*
- **Malic Acid** – *500mg to 1000mg daily*

NOTE: usually no more than 2000mg of L-carnitine or 400mg of CoQ10 are used daily for individuals with adult weights.

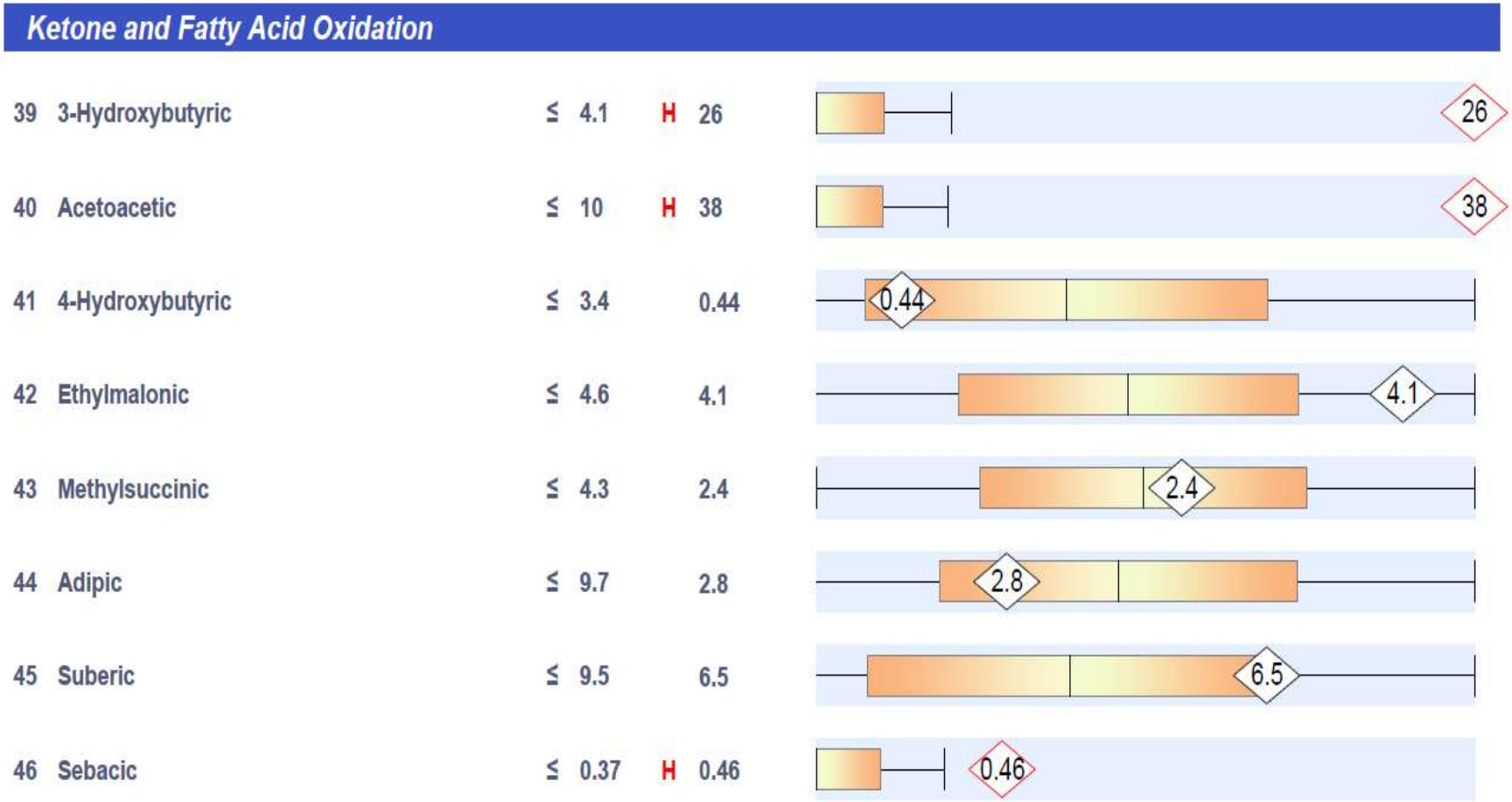
AUTISM RECOVERY 101

See handout "Mitochondrial Cocktail Options" for dosing recommendations

www.nbnus.com

AUTISM RECOVERY 101

Ketones and Fatty Acid Metabolism



AUTISM RECOVERY 101

2 year old girl from China

Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)		Patient	Reference Population - Females Under Age 13
Ketone and Fatty Acid Oxidation					
41	3-Hydroxybutyric	≤ 4.1	H	257	257
42	Acetoacetic	≤ 10	H	12	12
43	4-Hydroxybutyric	≤ 3.4		0.94	0.94
44	Ethylmalonic	≤ 4.6	H	5.5	5.5
45	Methylsuccinic	≤ 4.3	H	6.4	6.4
46	Adipic	≤ 9.7	H	187	187
47	Suberic	≤ 9.5	H	349	349
48	Sebacic	≤ 0.37	H	1 185	1185

High dose Medium Chain Triglycerides (MCT Oil)

AUTISM RECOVERY 101

Vitamin Indicators

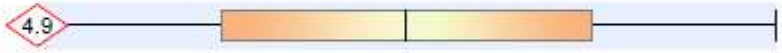
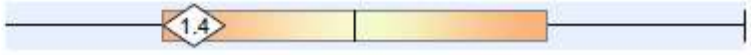
Indirect:

- Methylmalonic acid - *vitamin B-12*
- Methylcitric acid - *biotin*
- Glutaric and Succinic acid - *indicators of riboflavin and coenzyme Q-10 deficiency.*

Direct:

- Ascorbic acid - *vitamin C*
- Pantothenic acid - *B vitamin*
- Pyridoxic acid - *metabolite of vitamin B-6*

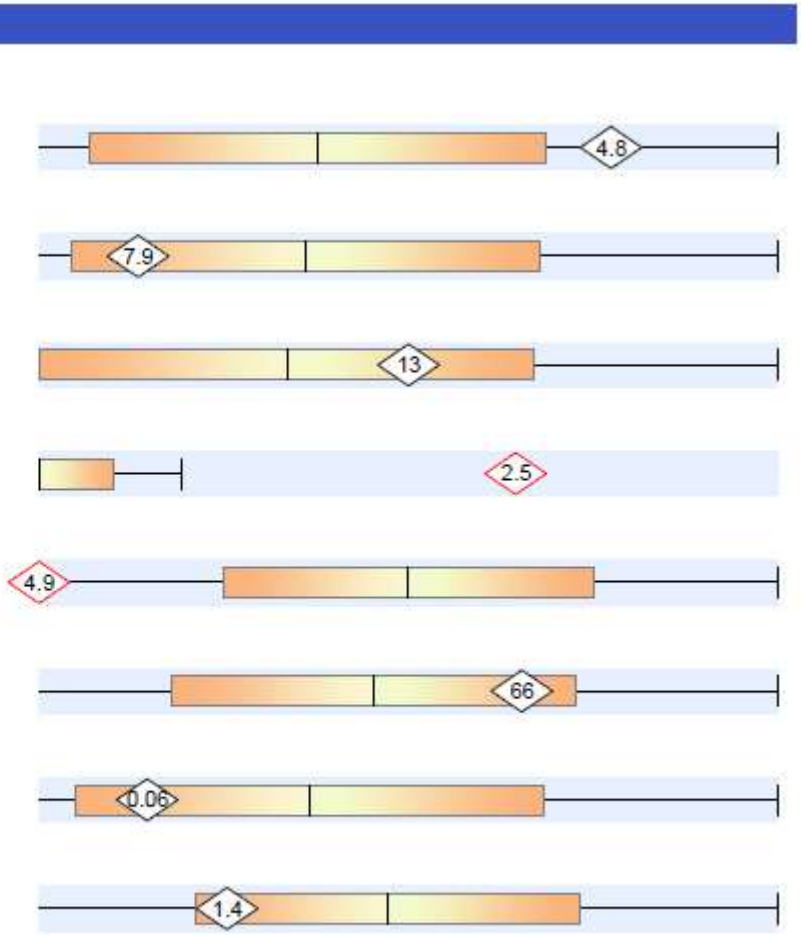
Nutritional Markers

Vitamin B12						
49	Methylmalonic ✱		≤ 6.2		4.8	
Vitamin B6						
50	Pyridoxic (B6)		≤ 59		7.9	
Vitamin B5						
51	Pantothenic (B5)		≤ 26		13	
Vitamin B2 (Riboflavin)						
52	Glutaric ✱		≤ 1.1	H	2.5	
Vitamin C						
53	Ascorbic	10	- 200	L	4.9	
Vitamin Q10 (CoQ10)						
54	3-Hydroxy-3-methylglutaric ✱		≤ 101		66	
Glutathione Precursor and Chelating Agent						
55	N-Acetylcysteine (NAC)		≤ 0.41		0.06	
Biotin (Vitamin H)						
56	Methylcitric ✱		≤ 5.5		1.4	

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

Nutritional Markers

Vitamin B12						
49	Methylmalonic ✱		≤ 6.2		4.8	
Vitamin B6						
50	Pyridoxic (B6)		≤ 59		7.9	
Vitamin B5						
51	Pantothenic (B5)		≤ 26		13	
Vitamin B2 (Riboflavin)						
52	Glutaric ✱		≤ 1.1	H	2.5	
Vitamin C						
53	Ascorbic	10	- 200	L	4.9	
Vitamin Q10 (CoQ10)						
54	3-Hydroxy-3-methylglutaric ✱		≤ 101		66	
Glutathione Precursor and Chelating Agent						
55	N-Acetylcysteine (NAC)		≤ 0.41		0.06	
Biotin (Vitamin H)						
56	Methylcitric ✱		≤ 5.5		1.4	



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

Most Common Nutritional Marker Imbalances

1. Low vitamin C (ascorbic acid)
2. Low or low normal vitamin B6 (pyridoxic acid)
3. High glutaric acid (vitamin B2)
4. High B5 (pantothenic acid)
5. Low to low normal N-acetyl-cysteine (NAC)
6. High CoQ10 marker
7. High B12 (methylmalonic acid) + High Methylcitric (biotin) – *rarely seen*

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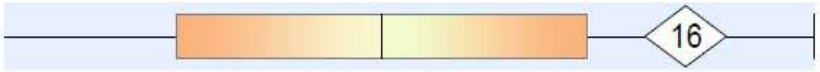
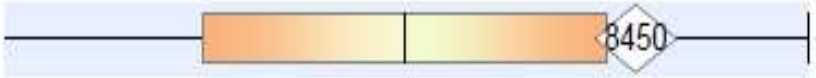
Requisition #: ***Physician Name:***

Patient Name: ***Date of Collection:***

Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*	Patient Value	Reference Population - Females Under Age 13
Pyrimidine Metabolites			
37 Uracil	≤ 19	16	
38 Thymine	0.02 - 0.88	0.44	
Bone Metabolites			
72 Phosphoric	≤ 10769	8450	

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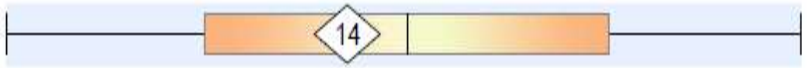
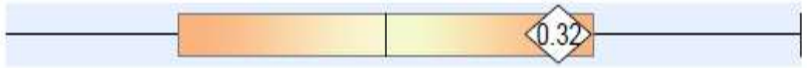
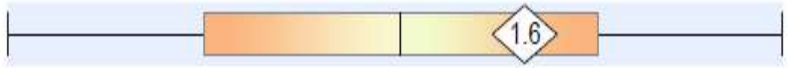
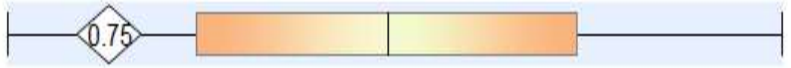
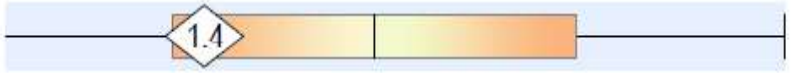
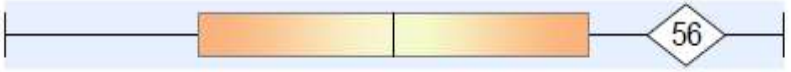
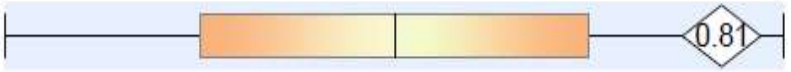
Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)				Patient	Reference Population - Males Age 13 and Over
Indicators of Detoxification							
57	Pyroglutamic	5.7	-	25		14	
58	Orotic		≤	0.46		0.32	
59	2-Hydroxyhippuric		≤	0.86	H	36	
Neurotransmitter Metabolites							
32	Homovanillic (HVA) *(dopamine)*	0.39	-	2.2			
33	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.53	-	2.2			
34	HVA / VMA Ratio	0.32	-	1.4	H		
17	HPHPA (Clostridia Marker)		≤	102		3.0	
18	4-Cresol (C. difficile)		≤	39		33	

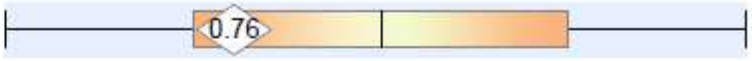
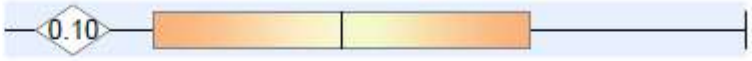
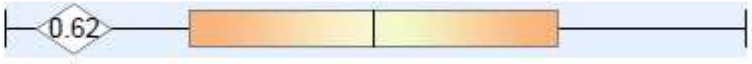
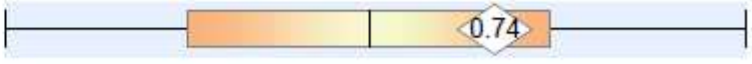
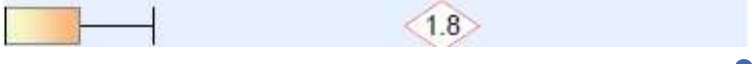
The Great Plains Laboratory, Inc.

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
Nutritional Markers				
Biotin (Vitamin H)				
54 Methylcitric	≤ 5.5		1.4	
Indicators of Detoxification				
55 Pyroglutamic	7.0 - 63		56	
56 Orotic	≤ 0.88		0.81	
57 2-Hydroxyhippuric	≤ 1.2	H	1.6	

Amino Acid Metabolites

58	2-Hydroxyisovaleric		≤ 1.2		0.85	
59	2-Oxoisovaleric	0.03	- 2.4		0.76	
60	3-Methyl-2-oxovaleric		≤ 1.1		0.10	
61	2-Hydroxyisocaproic		≤ 0.70		0.20	
62	2-Oxoisocaproic		≤ 0.54		0.09	
63	2-Oxo-4-methiolbutyric		≤ 0.30		0.11	
64	Mandelic		≤ 0.28		0.17	
65	Phenyllactic		≤ 0.27		0.02	
66	Phenylpyruvic	0.45	- 2.3		0.62	
67	Homogentisic		≤ 0.51		0.09	
68	4-Hydroxyphenyllactic	0.04	- 1.1		0.74	
69	N-Acetylaspartic		≤ 8.1		2.3	
70	Malonic		≤ 12		3.5	
71	3-Methylglutaric	0.07	- 0.95	H	1.8	

High values

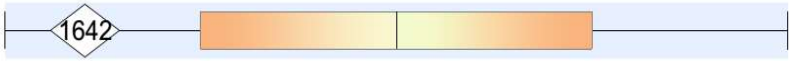
- High intake
- Hyperparathyroidism
- Vitamin D-resistant rickets
- Immobilization following paraplegia or fracture
- Vitamin D intoxication
- Renal tubular damage, heavy metal toxicity
- Familial hypophosphatemia
- **Metabolic acidosis**

Low values

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

AUTISM RECOVERY 101

骨质代谢

76 磷酸	1 000 - 7 300	1 642	

Phosphoric Acid

Vitamin D; blood spot

RESULTS			
	RESULT ng/mL	REFERENCE INTERVAL	OPTIMAL LOW | MOD- | MEAN | MOD+ | HIGH
25-Hydroxyvitamin D Total	**21**	40- 80	
25-Hydroxyvitamin D_2	**8**		
25-Hydroxyvitamin D_3	**13**		

AUTISM RECOVERY 101

Prioritization of OAT Findings
(general recommendations)

1. If any clostridia marker is high this takes priority regarding treatment.
2. If arabinose, or other yeast markers are high, need to correlate to clinical picture.
3. If oxalate is high need to correlate to clinical picture.

<u>NOTE</u>: remember, these 3 areas often greatly influence other markers on the OAT.

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Prioritization of OAT Findings
(general recommendations)

4. If one or more of the first 3 sections are positive *(yeast, clostridia, oxalate)* and other imbalances are seen then additional supplement therapy can be worthwhile:
   - *If one specific fatty acid marker is significantly high, or multiple are high using L-carnitine is worthwhile.*
   - *If multiple mitochondrial markers are high consider MitoSpectra or just L-Carnitine.*
   - *If HVA and/or HVA/VMA ratio are high cross check to clostridia markers.*

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Prioritization of OAT Findings (general recommendations)

4.*(continued):*

- If 5-HIAA is low to low normal consider 50mg to 100mg of 5-HTP daily for serotonin support.
- If Quinolinic Acid is high use at least 500mg of Niacinamide as a priority supplement.
- If HVA and/or HVA/VMA ratio high cross check to clostridia markers.
- If Uracil is high consider additional L-Methyl-Folate supplementation, i.e. 500mcg to 1000mcg daily.
- Address vitamin deficiencies individually as needed
- Low phosphoric – *consider Vitamin D testing or supplementation with Vitamin D3, i.e. 1000IU/25lbs body weight (approximately).*

Module #4

Topic

- Treating Yeast, Bacteria and Other Digestive Problems*:*
  - *Success strategies for treating common pathogens*
  - *Remedies for other digestive problems*
  - *Review of behaviors often linked to digestive problems.*

Thank You

Kurt N. Woeller, D.O.

www.AutismRecovery101.com

AutismRecovery101@gmail.com