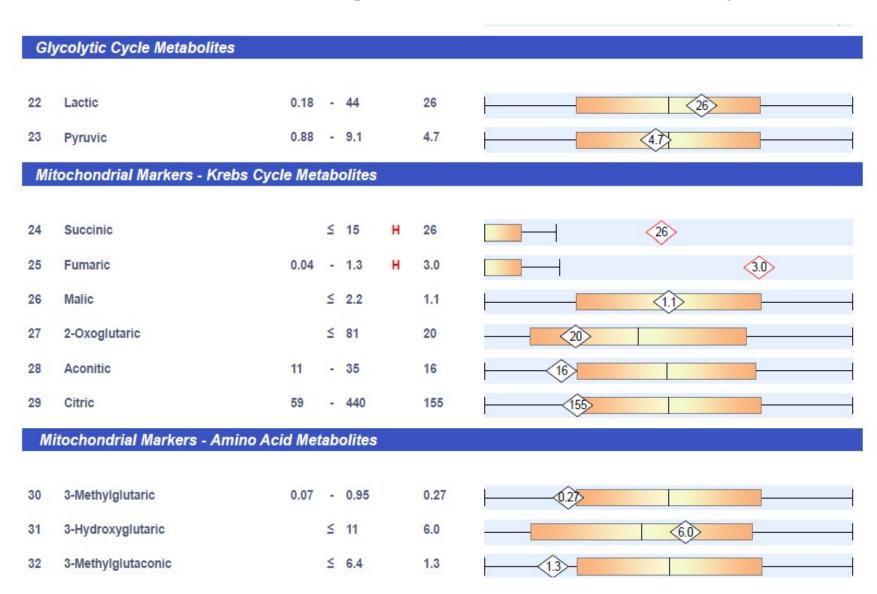
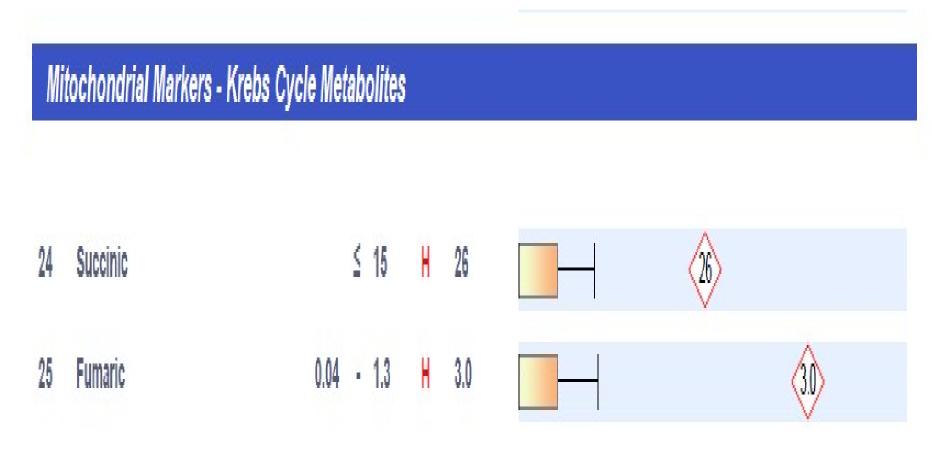
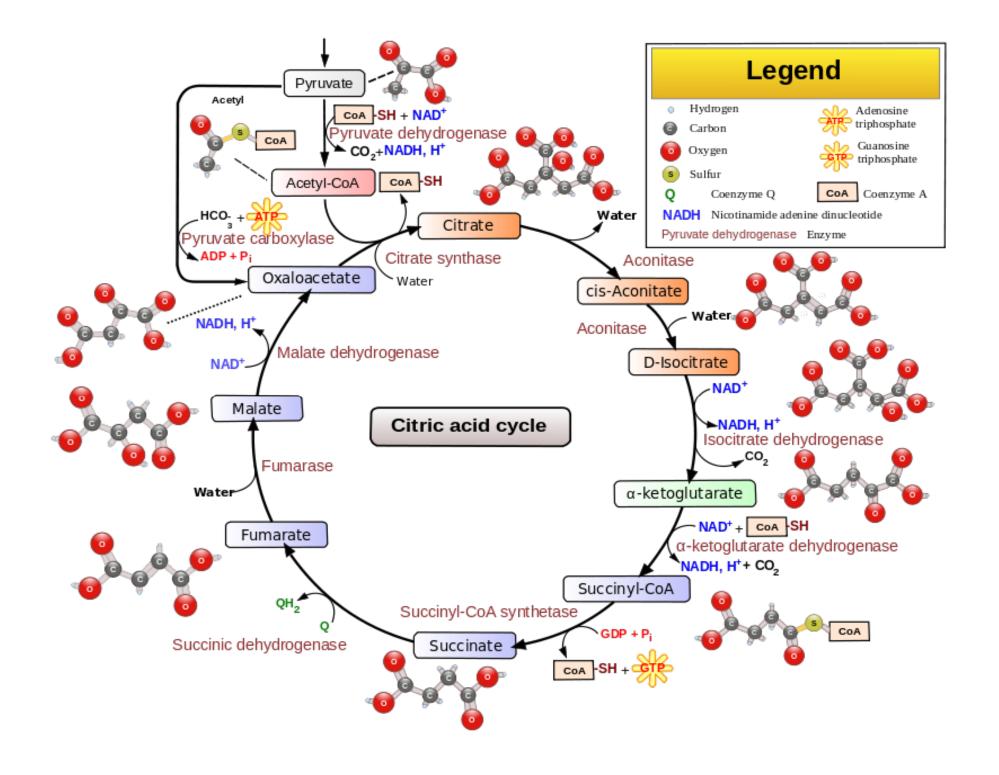


asi	t and Fungal Markers					
1	Citramalic	≤	5.3		0.99	0.99
2	5-Hydroxymethyl-2-furoic	≤	30		5.2	5.2
3	3-Oxoglutaric	≤	0.52		0.16	<b>1</b> 6
4	Furan-2,5-dicarboxylic	≤	22		3.3	3.3
5	Furancarbonylglycine	≤	3.6		2.0	2.0
6	Tartaric	≤	3.9		3.4	3.4
7	Arabinose	≤	56	Н	61	61
8	Carboxycitric	≤	34		3.7	3.7
9	Tricarballylic	≤	0.86		0.21	——————————————————————————————————————

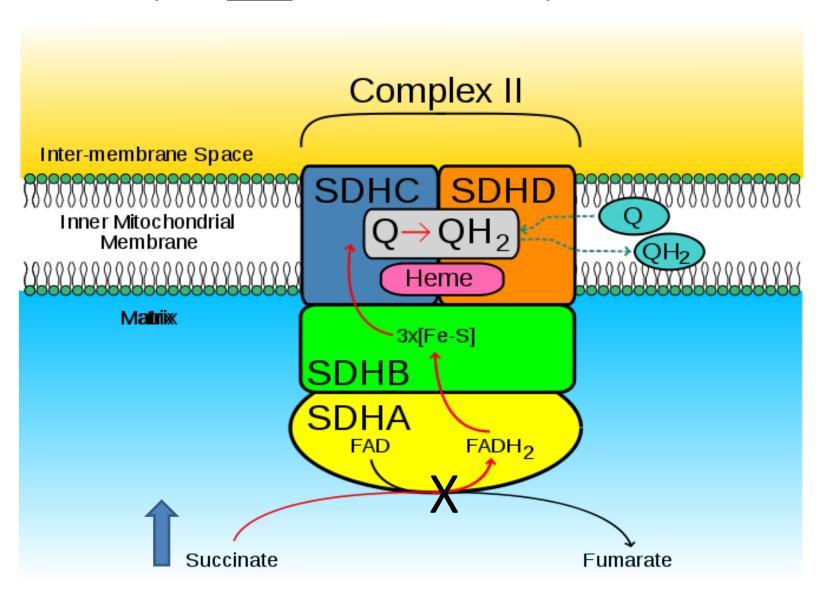
	O						•
Bacter	rial Markers						
10	Hippuric	<u> </u>	4	717		307	307
11	2-Hydroxyphenylacetic	≤	4	1.1		0.43	0.43
12	4-Hydroxybenzoic	0.09	-	2.0		1.8	
13	4-Hydroxyhippuric	2	4	27	Н	33	33
14	DHPPA (Beneficial Bacteria)	5	<	0.73		0.20	0.20
Clostr	idia Bacterial Markers						
15 (C. diff	4-Hydroxyphenylacetic icile, C. stricklandii, C. lituseburense & others)	\$	4	30		15	15
16 (C. spc	HPHPA progenes, C. caloritolerans, C. botulinum & other	ers)	4	227		77	77
17 (C. diff	4-Cresol licile)	5	4	76		17	17
18 (C. stri	3-Indoleacetic cklandii, C. lituseburense, C. subterminale & or		4	11		2.2	2.2



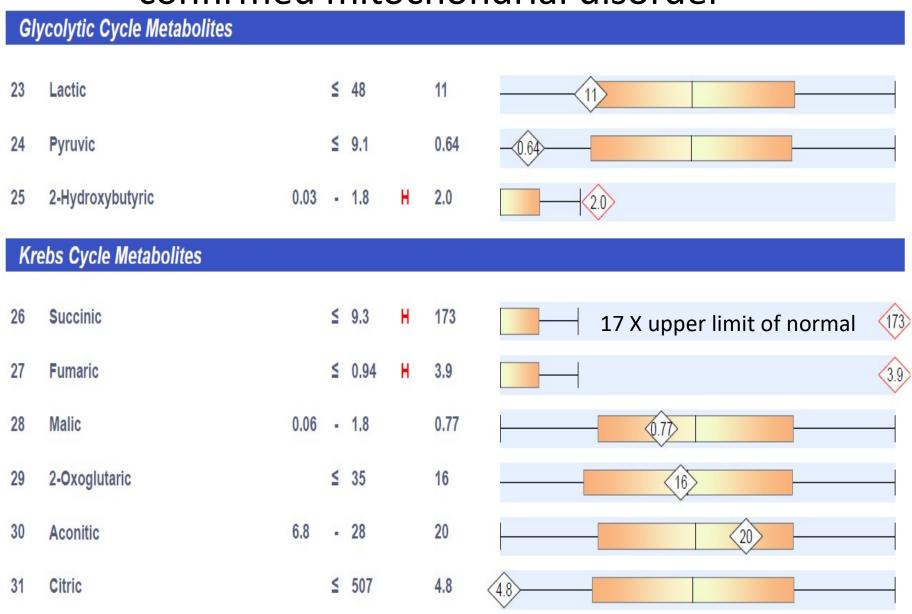


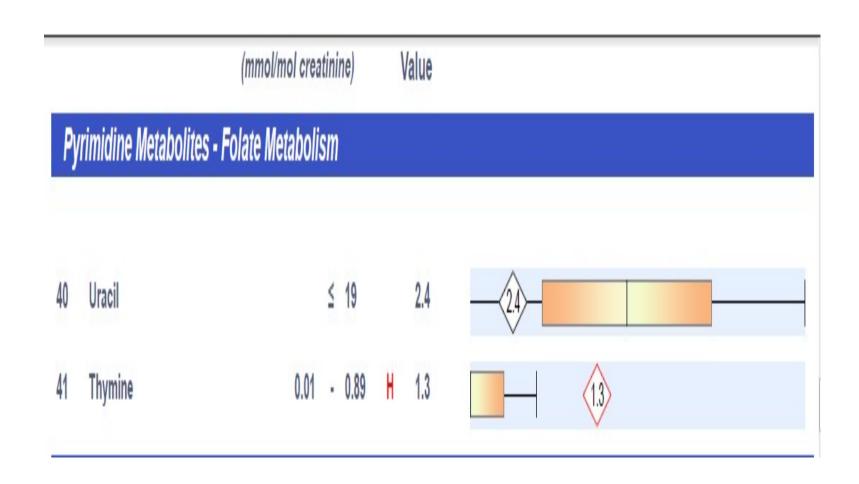


### Succinic dehydrogenase-only enzyme that is part of Krebs cycle and electron transport chain



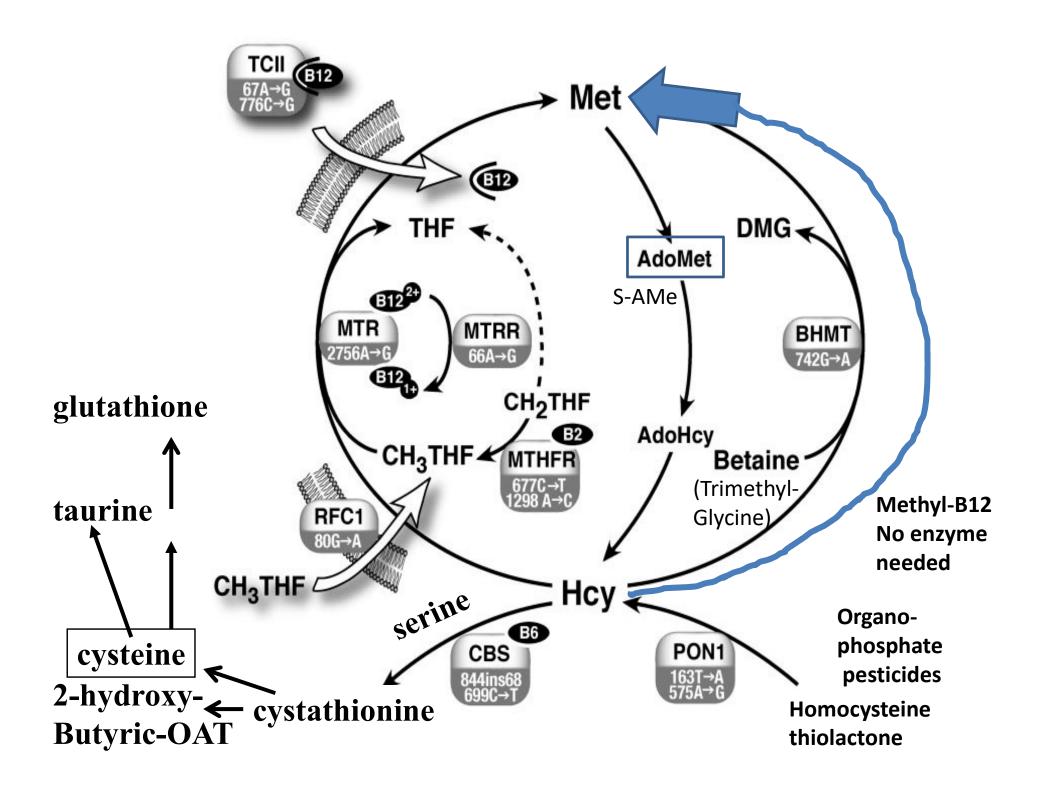
### Adult patient with Kearns Sayres syndrome-a confirmed mitochondrial disorder







Metabolic Markers in Urine Reference Range Patient Reference Population - Females Under Age 13 (mmol/mol creatinine) Value **Indicators of Detoxification** Glutathione Pyroglutamic \* ≤ 2.2 2.9 2-Hydroxybutyric \* Ammonia Excess 0.50 Orotic ≤ 0.88 (0.50) Aspartame, salicylates, or GI bacteria ≤ 1.2 3.3 2-Hydroxyhippuric (3.3) \* A high value for this marker may indicate a Glutathione deficiency.



### Production of 2-hydroxybutyric acid from cystathionine via cystathionase

#### Causes of excess 2-hydroxybutyric

- 1. There is increased need for glutathione to detoxify a host of toxic chemicals, resulting in increased shunting of homocysteine into the production of cysteine for glutathione. This is the most common reason. Pyroglutamic high.
- 2. There are genetic variants of the DNA such that methylation of homocysteine by betaine homocysteine methyl transferase or methionine synthase is impaired.
- 3. There are nutritional deficiencies of betaine, methylcobalamin, or methyltetrahydrofolate that reduce the enzyme activities of the enzymes in #2 above.
- 4. There is a genetic variant in cystathionine beta synthase (CBS) enzyme such that there is excessive shunting of homocysteine into cysteine production that results in excessive 2-hydroxybutyric acid formation.

#### Summary of abnormalities in girl with itching

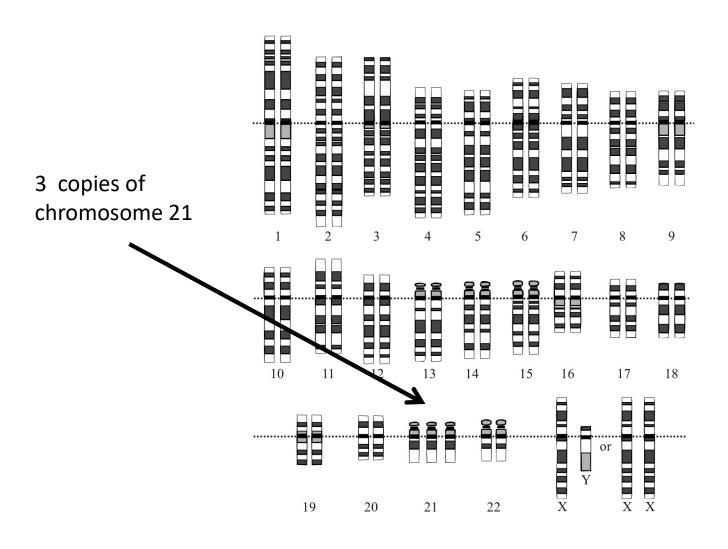
- Elevated Candida metabolites-antifungal treatment
- Elevated succinic acid-mitochondrial damage due to genetic damage or environmental exposure-hair metals test and GPLTOX test in urine
- B-vitamin deficiencies
- Elevated dopamine metabolite- elevated Clostridia, copper deficiency, or vitamin C deficiency. Clostridia not elevated, vitamin C not deficient so copper deficiency is possible
- Folate and B12 needed to improve methylation cycle
- High quinolinic acid and thymine indicate inflammation

hen	ylalanine and Tyrosine Metabolites							
33 lopa	Homovanillic (HVA) mine)		≤	14	Н	16	16	
34 norej	Vanillylmandelic (VMA) pinephrine, epinephrine)	0.87		5.9		2.2	22	
35	HVA / VMA Ratio	0.12		3.0	Н	7.4		7.4
rypt	ophan Metabolites							
6 serot	5-Hydroxyindoleacetic (5-HIAA)		≤	7.7		1.1	1.1	
37	Quinolinic	0.63		6.7	Н	9.4	9.4	
8	Kynurenic		<u> </u>	4.1		1.3	1.3	
39	Quinolinic / 5-HIAA Ratio	0.04		2.2	Н	8.7		

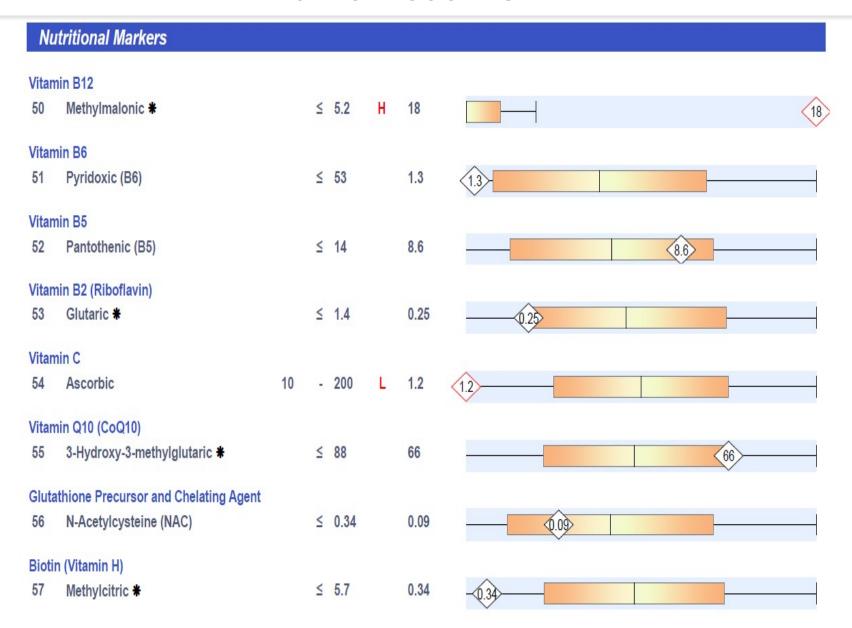
### Down syndrome



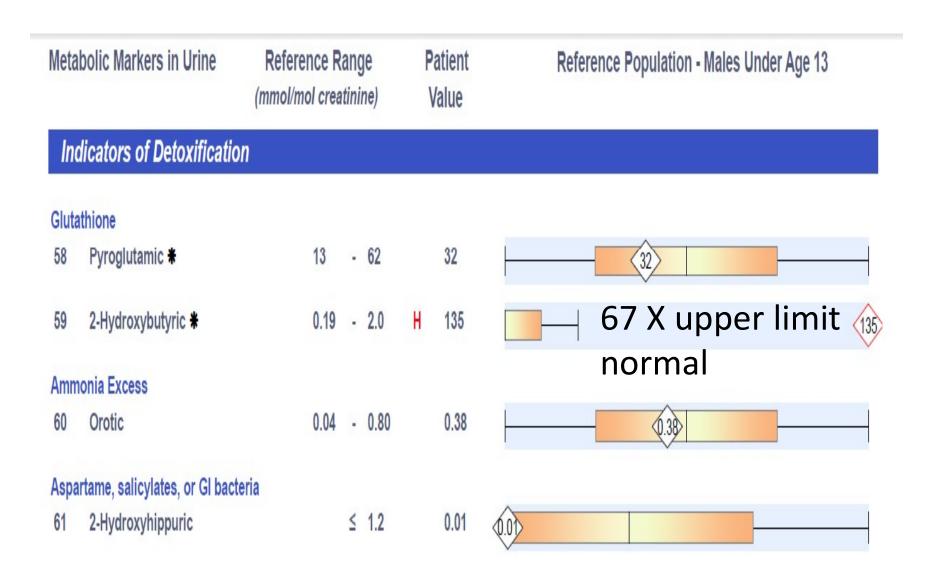
#### Down syndrome chromosomes (47)



### 3 yr old with Down syndrome-3 copies of chromosome 21



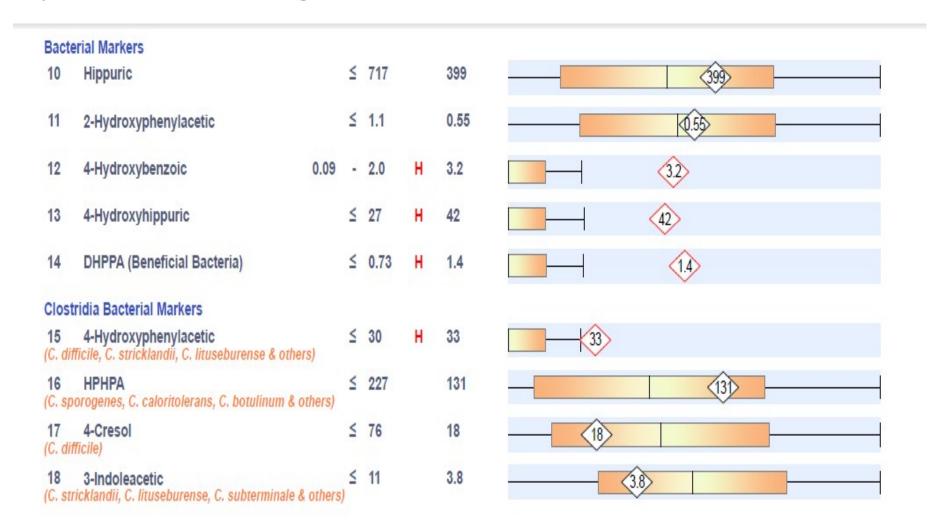
#### 3 yr old Down syndrome

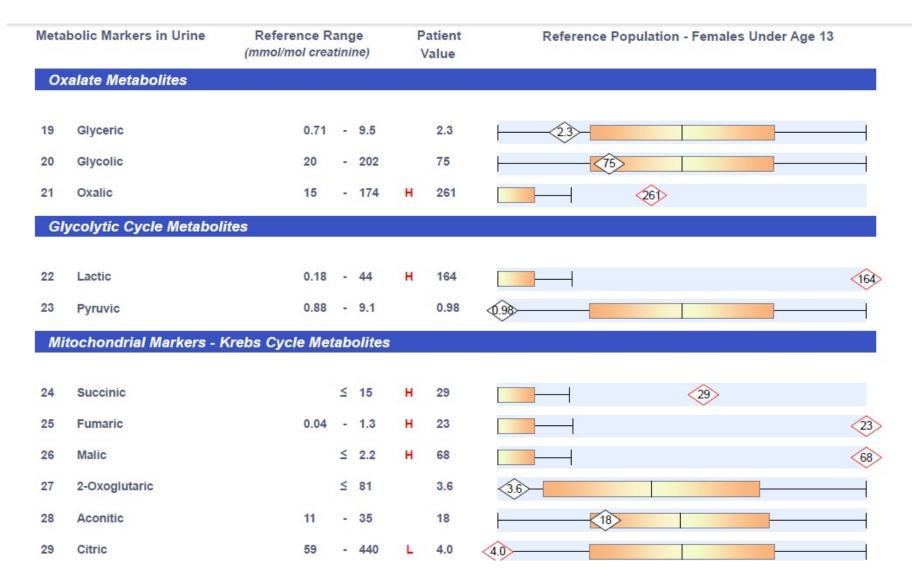


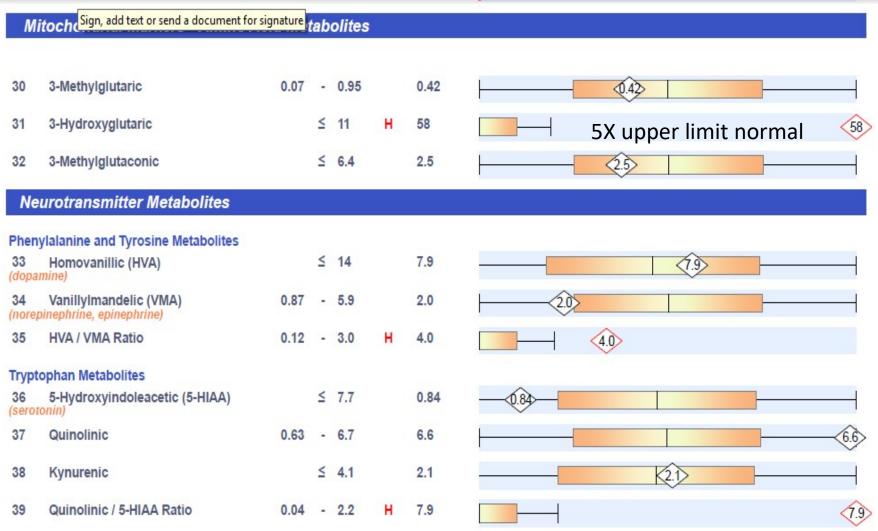
#### Consequences of CBS overdosage

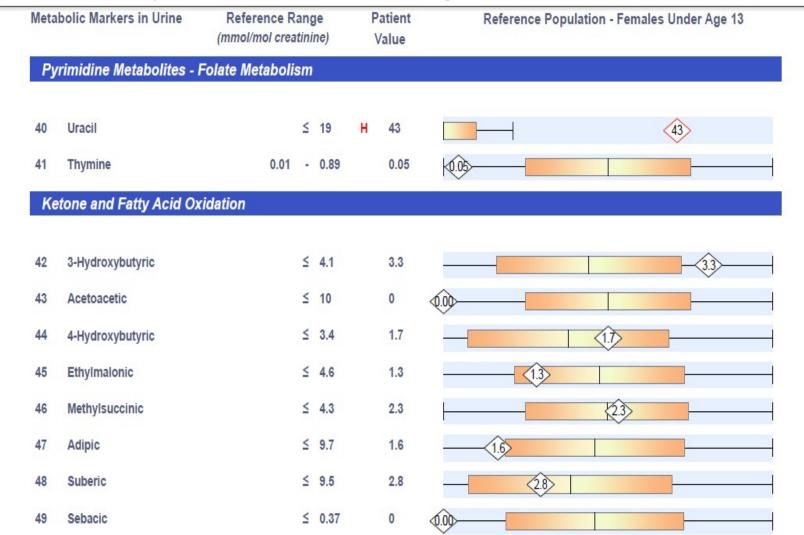
- Inadequate conversion of homocysteine back to methionine leading to overconversion of homocysteine to cysteine but inadequate production of methionine and s-adenosyl methionine (S-ame).
- Consequences: Inadequate methylation of neurotransmitters, DNA, many others
- Treatment: Supplementation with vitamin B12, methylcobalamin, methyl-tetrahydrofolate, and betaine
- Use homocysteine and 2-hydroxybutyric as indicators of need for methylation factors

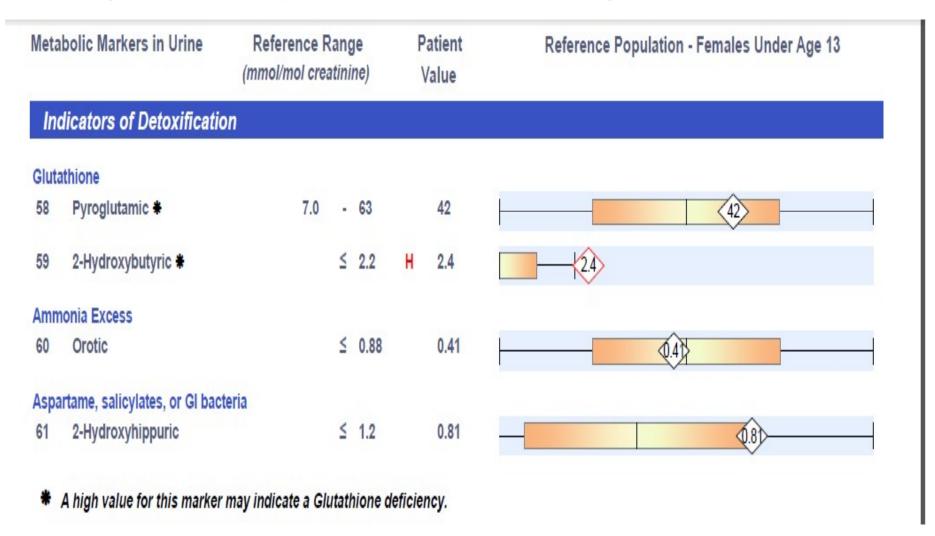
### 6 yr old girl with attention deficit, poor growth, peculiar rocking motion, unable to suck





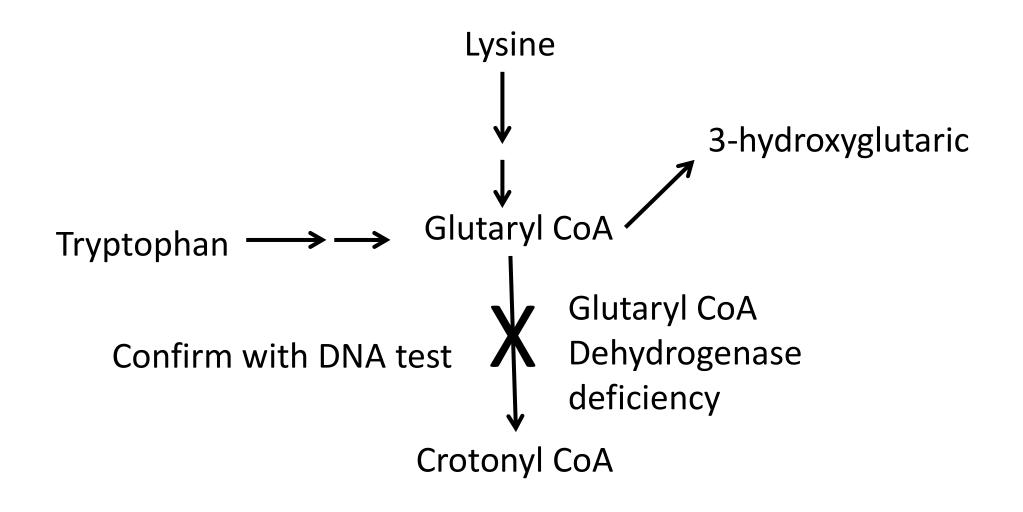






#### Symptoms of glutaryl CoA deficiency

- High 3-hydroxyglutaric acid in urine
- Macroencephaly (large head)
- Spasms, low muscle tone, jerking, poor sucking
- Peculiar movements
- Decreased mental attention
- Many times diagnosed as cerebral palsy
- Very common in groups that are more inbred such as Mennonites
- May cause bleeding into eyes or brain-parents may be wrongly convicted of child abuse



Treatment: Diet low in tryptophan and lysine, Intravenous carnitine, choline supplements

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

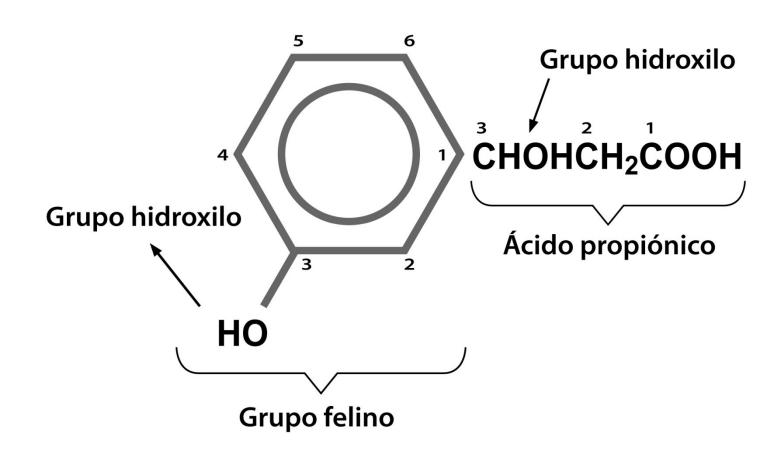
William Shaw ZO Nutrition Neuroscience 2010 Vol 13 No 3: 1-10

#### William Shaw

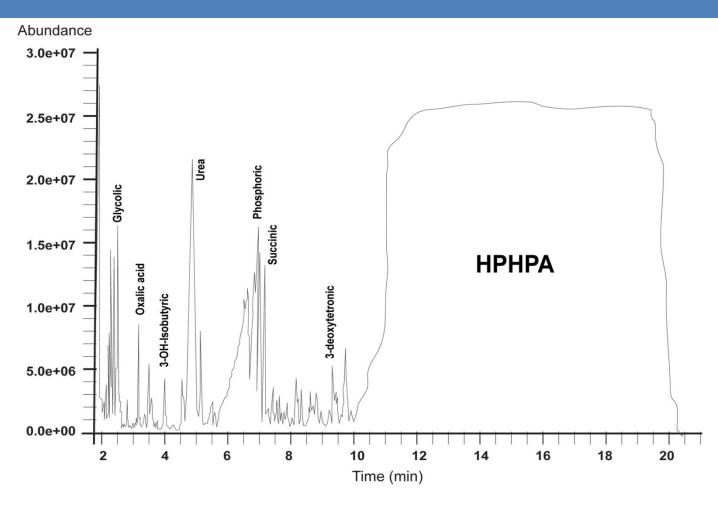
The Great Plains Laboratory, Inc., Lenexa, Kansas, USA

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 hyperreactivity) in experimental animals.

#### Estructura del ácido 3-(3-hidroxifenilo)-3-hidroxipropiónico



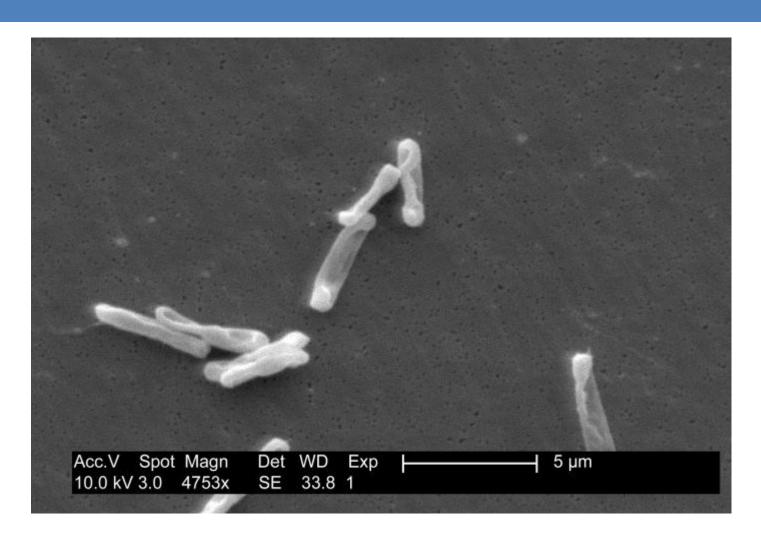
### Psicosis del niño durante hospitalización (simulado desde la memoria)



#### Colitis pseudomembranosa

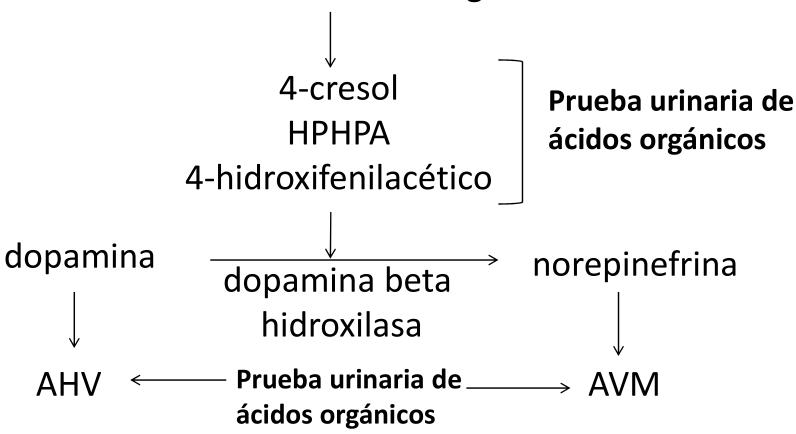


#### Clostridia por microscopía de electrones

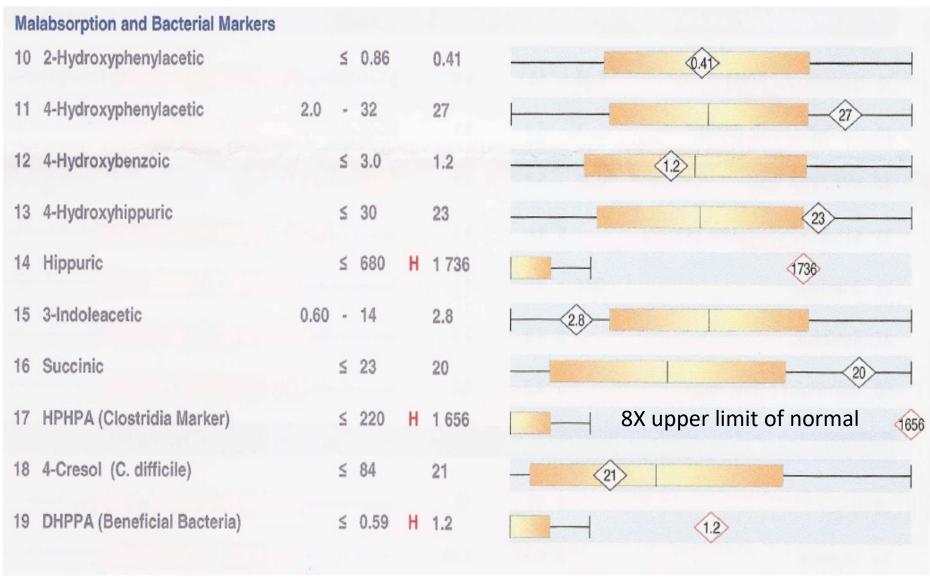


### Efecto crítico de la bacteria intestinal en los neurotransmisores cerebrales

Bacteria Clostridium-tracto gastrointestinal



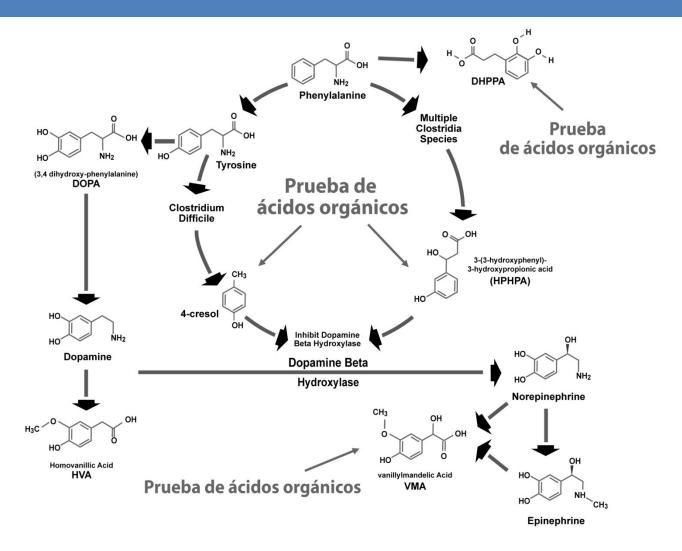
### 8 yr old autism severe clostridia baseline



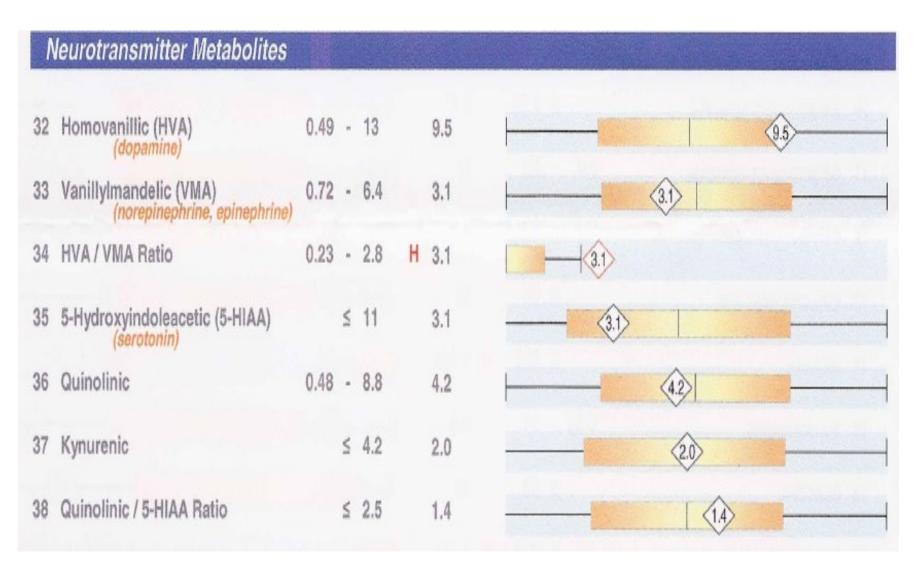
### Linan Chen, et al(2008) La dopamina citosólica no regulada causa neurodegeneración relacionada al estrés oxidativo en ratones. J. Neurosci. 28, 425–433

- La dopamina es una molécula muy reactiva comparada con otros neurotransmisores. Su degradación naturalmente produce especies oxidativas.
- Más del 90% de la dopamina en las neuronas de dopamina se almacena en abundantes vesículas terminales, protegidas de la degradación.
- Sin embargo, una pequeña fracción es citosólica, siendo la principal fuente del metabolismo de dopamina y supuesta toxicidad.
- La dopamina citosolica se degrada para formar el ácido 3,4dihidroxifenilacético (DOPAC) y AHV así como peróxido de hidrógeno por la vía de la monoaminooxidasa.

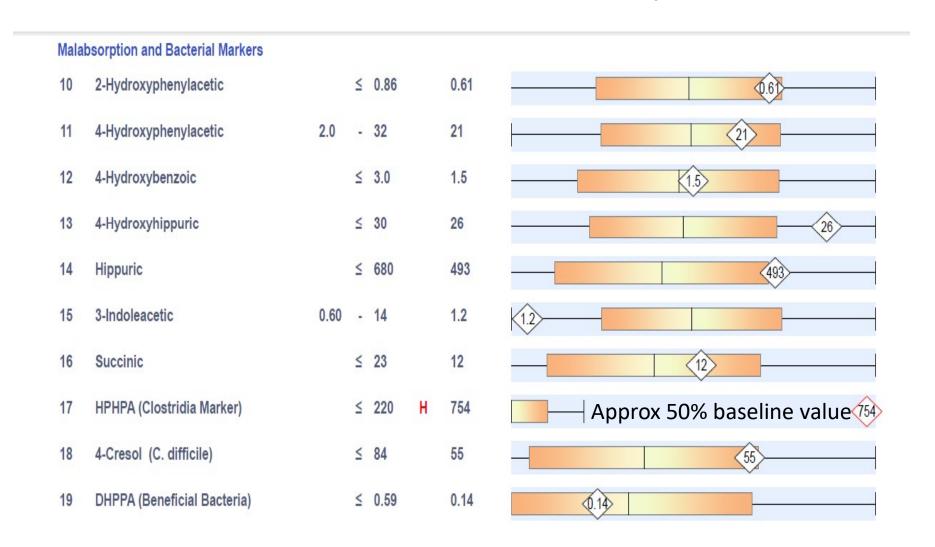
## Efecto crítico de las bacterias intestinales en los neurotransmisores cerebrales



# 8 yr old autism severe clostridia baseline



## 8 yr old autism severe clostridia after two consecutive rounds of oral vancomycin



## 8 yr old autism severe clostridia after two rounds of oral vancomycin

Mala	absorption and Bacterial Markers						
10	2-Hydroxyphenylacetic		<u> </u>	0.86		0.61	0.6
11	4-Hydroxyphenylacetic	2.0	-	32		21	21
12	4-Hydroxybenzoic		<u>&lt;</u>	3.0		1.5	1.5
13	4-Hydroxyhippuric		<b>\leq</b>	30		26	26
14	Hippuric		<	680		493	493
15	3-Indoleacetic	0.60	-	14		1.2	12
16	Succinic		<u>&lt;</u>	23		12	12
17	HPHPA (Clostridia Marker)		≤	220	Н	754	Approx 50% baseline (754)
18	4-Cresol (C. difficile)		<b>\leq</b>	84		55	55
19	DHPPA (Beneficial Bacteria)		<	0.59		0.14	0.14

## 8 yr old autism severe clostridia after use of Body Biotics Probiotics

#### **Malabsorption and Bacterial Markers**

	oor priori and Bastorial markets				
10	2-Hydroxyphenylacetic		≤ 0.86	0.32	0.32
11	4-Hydroxyphenylacetic	2.0	- 32	6.7	6.7
12	4-Hydroxybenzoic		≤ 3.0	0.32	0.32
13	4-Hydroxyhippuric		≤ 30	11	11
14	Hippuric		≤ 680	72	72
15	3-Indoleacetic	0.60	- 14	1.1	1.1
15 16	3-Indoleacetic Succinic	0.60	- 14 ≤ 23	1.1 5.4	5.4
		0.60			
16	Succinic	0.60	≤ 23	5.4	5.4
16 17	Succinic HPHPA (Clostridia Marker)	0.60	≤ 23 ≤ 220	5.4 74	5.4

## 8 yr old autism severe clostridia after use of Body Biotics Probiotics

Ne	urotransmitter Metabolites						
32	Homovanillic (HVA) (dopamine)	0.49	•	13		4.3	4.3
33	VanillyImandelic (VMA) (norepinephrine, epinephrine)	0.72	٠	6.4		1.8	1.8
34	HVA / VMA Ratio	0.23		2.8		2.4	2.4
35	5-Hydroxyindoleacetic (5-HIAA) (serotonin)		<	11		0.71	-0.7)
36	Quinolinic	0.48		8.8		2.4	2.4
37	Kynurenic		4	4.2		1.6	1.6
38	Quinolinic / 5-HIAA Ratio		<u>≤</u>	2.5	H	3.4	3.4

## Same child- 4 years later-nearly recovered from autism

sacte	erial Markers					
10	Hippuric	≤	680	Н	881	881
11	2-Hydroxyphenylacetic	≤	0.86		0.31	
12	4-Hydroxybenzoic	≤	3.0		0.54	0.54
13	4-Hydroxyhippuric	≤	30		5.9	5.9
14	DHPPA (Beneficial Bacteria)	<	0.59		0.56	0.50
Clost	ridia Bacterial Markers					
15 C. dit	4-Hydroxyphenylacetic 2.0 fficile, C. stricklandii, C. lituseburense & others)	-	32		17	17
16 C. sp	HPHPA orogenes, C. caloritolerans, C. botulinum & others)	<	220	Н	611	6X normal
17 C. dit	4-Cresol fficile)	≤	84		5.8	5.8
18	3-Indoleacetic 0.60 ricklandii, C. lituseburense, C. subterminale & others	-	14		1.3	1.3

### Normal sister of child with Clostridia

Bacte	rial Markers					
10	Hippuric	≤	717		610	610
11	2-Hydroxyphenylacetic	≤	1.1		0.16	0.16
12	4-Hydroxybenzoic 0.	09 -	2.0		0.59	0.59
13	4-Hydroxyhippuric	≤	27		4.2	4.2
14	DHPPA (Beneficial Bacteria)	≤	0.73		0.67	0.67
Closti	ridia Bacterial Markers					
15 (C. diff	4-Hydroxyphenylacetic ficile, C. stricklandii, C. lituseburense & others)	≤	30		3.8	3.8
16 (C. sp	HPHPA progenes, C. caloritolerans, C. botulinum & other	rs)	227	Н	356	356
17 (C. diff	4-Cresol Ficile)	≤	76		21	21
18 (C. str	3-Indoleacetic icklandii, C. lituseburense, C. subterminale & oth	≤ ners)	11		0.65	0.65

## The flush toilet-the most dangerous object in the house?



### Flushing Lidless Toilet Sends Spray Of Diarrhea-Causing Bacteria Into The Air: Study

① 01/06/2012 01:09 pm ET





It may be common sense, but we all need the reminder -- flush the toilet with the lid down, lest you send a <u>spray of diarrhea-causing bacteria</u> up into the air, according to a new study.

The study, published in the *Journal of Hospital Infection*, shows that the bacteria Clostridium difficile, which is known to cause diarrhea, is sprayed 25 centimeters, or nearly 10 inches, <u>above the toilet seat</u> when you flush without putting the lid down, ABC News reported. The most bacteria was found right after the toilet was flushed, with the number of bacteria declining as time passed on.



#### C. difficile Prevention

#### Infection Rates Are Higher than Previously Thought

The CDC's most recent figure for C. difficile-associated deaths in the U.S. is considerably higher than that of any previous survey. According to the CDC:\*



Nearly 500,000 C. diff infections estimated per year in the U.S., with more than 29,000 deaths

Up to \$4.8 billion in excess health care costs for acute care facilities

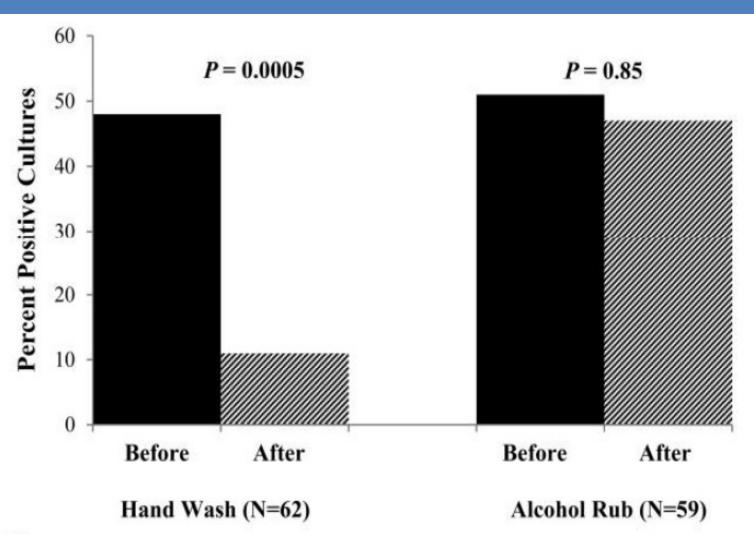


#### Learn More About CDC Study →

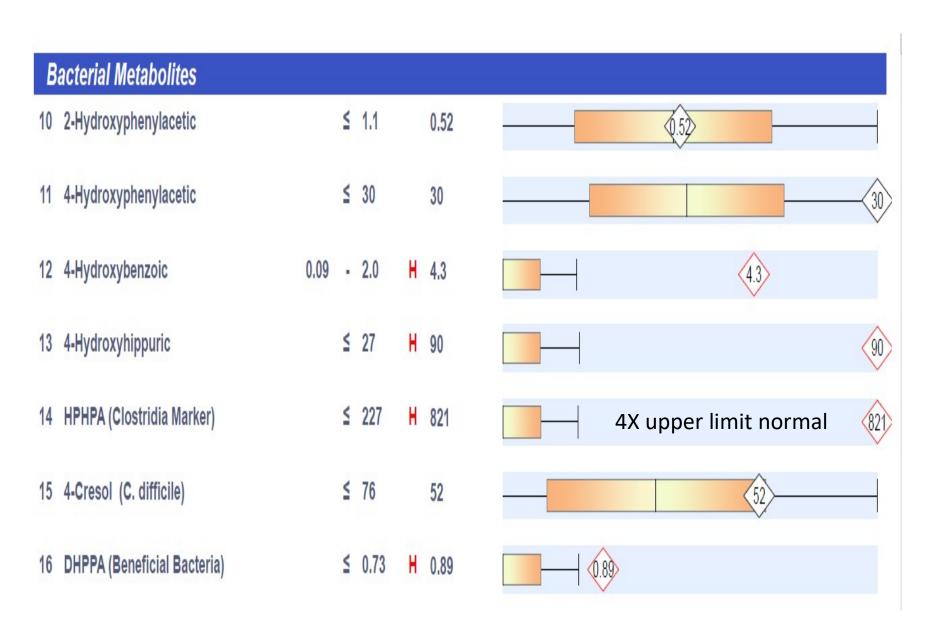
\*"Nearly Half a Million Americans Suffered from Clostridium difficile Infections in a Single Year" (press release), Feb. 25, 2015. http://www.cdc.gov/media/releases/2015/p0225-clostridium-difficile.html.

## A Randomized Trial of Soap and Water Hand Wash Versus Alcohol Hand Rub for Removal of *Clostridium difficile* Spores from Hands of Patients

Sirisha Kundrapu, MD et al Infection Control and Hospital Epidemiology Vol. 35, No. 2 (February 2014), pp. 204-206



### 7 yr old boy with autism baseline



## 7 yr old boy with autism after Body Biotics probiotics

В	acterial Metabolites					
10	2-Hydroxyphenylacetic		≤	1.1	0.45	0.45
11	4-Hydroxyphenylacetic		<b>\( \)</b>	30	20	20
12	4-Hydroxybenzoic	0.09		2.0	0.81	0.8
13	4-Hydroxyhippuric		<u>&lt;</u>	27	9.1	9.1
14	HPHPA		≤	227	51	51
15	4-Cresol (C. difficile)		<b>≤</b>	76	5.2	5.2
16	DHPPA (Beneficial Bacteria)		<	0.73	0.44	0.44

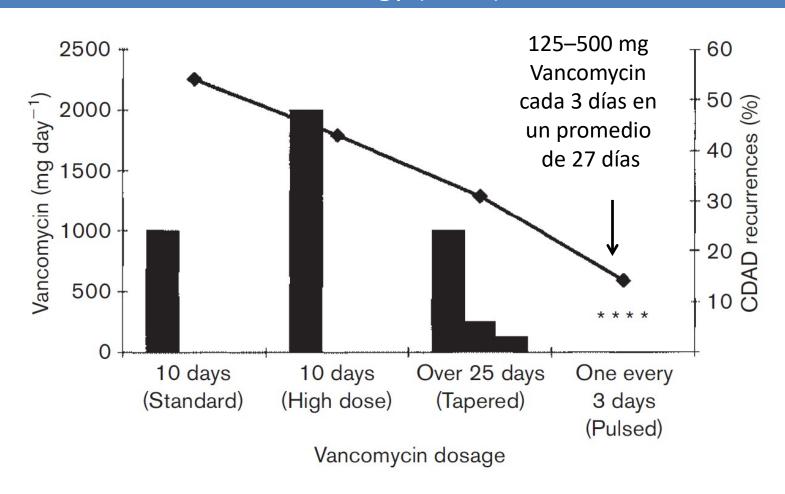
### 7 yr old boy with autism baseline

Y	east/Fungal Metabolites					
1	Citramalic	≤	5.3		2.3	2.3
2	5-Hydroxymethyl-2-furoic	≤	30		2.1	2.1
3	3-Oxoglutaric	<	0.52		0.26	0.26
4	Furan-2,5-dicarboxylic	≤	22		2.0	2.0
5	Furancarbonylglycine	<	3.6		0.21	0.2
6	Tartaric	<	3.9	Н	4.5	4.5
7	Arabinose	≤	56	Н	547	10X upper limit normal 547
8	Carboxycitric	≤	34		7.1	7.1
9	Tricarballylic	<	0.86		0.84	0.84

#### 7 year old autism after Body Biotics probiotics

	М	icrobial	Organic Acids Test	SHOW TOOIS PAILE
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Pati	ient Reference Population - Female	s Under Age 13
Yeast/Fungal Metabolite	es			
1 Citramalic	≤ 5.	3 2.4	2.4	
2 5-Hydroxymethyl-2-furoic	≤ 30	) 11	(11)	
3 3-Oxoglutaric	≤ 0.	52 0.4	45	0.45
4 Furan-2,5-dicarboxylic	≤ 22	2 11	11	
5 Furancarbonylglycine	≤ 3.	6 2.2	2.2	
6 Tartaric	≤ 3.	9 <b>H</b> 5.6	5.6	
7 Arabinose	≤ 56	6 <b>H</b> 69		her than uppe
8 Carboxycitric	≤ 34	1 1.8	limit of no	ormal 
9 Tricarballylic	≤ 0.	86 <b>H</b> 0.9	94 0.94	

# Los tratamientos alternativos para la enfermedad por *Clostridium difficile*: ¿qué funciona realmente? Lynne V. McFarland Journal of Medical Microbiology (2005), 54, 101–111





Artificial Sugars or Flavors,

Salt, Harmful Preservatives,

Januira Refrinaration!

and DOES NOT

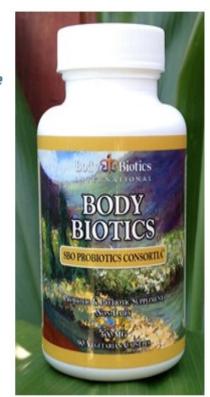
### BODY BIOTICS™ "Bio-Identical" SBO Probiotics Consortia™

A uniquely different Prebiotic & Probiotic, custom cultured to rebalance friendly gut flora, strengthen the immune system, provide messenger chemicals & restore optimal health. \*

For eons, humans naturally ingested friendly *soil born organisms* (SBOs) from chemical free organic foods they consumed each day. Little was known about these beneficial, life-supporting microbes before the mid to late 1900s, and in truth, not until the last ten years. Today, Probiotic researchers around the world work endlessly in their labs offering up more and more evidence to support the critical importance of these friendly bacteria that have all but *"gone missing"* from our daily diets. It has now become obvious to many, in the medical and alternative world, that replacing these missing organisms is paramount to digestive health and our long-term wellbeing.

BODY BIOTICS INTERNATIONAL, with a 37 year old Prebiotics & Probiotics formula, has long known the vital role that SBOs play in gut health for both humans and pets. From the moment we secured exclusive worldwide marketing rights to this formula (April/1995), we have remained steadfast in our commitment to provide the safest, most effective natural Probiotic to our customers.

With contradictory information and general confusion in today's Probiotics marketplace, we have reviewed the dynamics of our formulation, culturing process and ingredients; all, to offer our customers a better way of understanding the exceptional qualities of **RODY** 



BODY BIOTICS™ Bio-Identical SBO Probiotics Consortia™ with Prebiotics

### **Body Biotics Probiotics**

- http://bodybiotics.com
- Using standard Lactobacillus species
- Also contains SBO-Soil Based Organisms-Bacillus subtilis and licheniformis species that produce spores that kill other microorganisms
- Company claims species are on FDA "Generally recognized as safe" (GRAS) list
- May be unsafe for people with immune deficiency

## Applied Microbiology



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## The safety of *Bacillus subtilis* and *Bacillus indicus* as food probiotics

H.A. Hong, J.-M. Huang, R. Khaneja, L.V. Hiep, M.C. Urdaci, S.M. Cutting

First published: 29 February 2008 Full publication history

DOI: 10.1111/j.1365-2672.2008.03773.X View/save citation

Cited by: 43 articles Refresh Citing literature





View issue TOC Volume 105, Issue 2 August 2008 Pages 510–520

Simon M. Cutting, School of Biological Sciences, Royal Holloway, University of London, Egham, Surrey, TW20 0EX, UK. E-mail: s.cutting@rhul.ac.uk

**Significance and Impact of the Study:** The results support the use of *B. subtilis* and *B. indicus* strains as food supplements.

Diq Dis Sci. 2008 Apr;53(4):954-63. Epub 2007 Oct 13.

#### The safety of two Bacillus probiotic strains for human use.

Sorokulova IB1, Pinchuk IV, Denayrolles M, Osipova IG, Huang JM, Cutting SM, Urdaci MC.

Author information

#### Abstract

Open/close author information list

Probiotics based on Bacillus strains have been increasingly proposed for prophylactic and therapeutic use against several gastro-intestinal diseases. We studied safety for two Bacillus strains included in a popular East European probiotic. Bacillus subtilis strain that was sensitive to all antibiotics listed by the European Food Safety Authority. Bacillus licheniformis strain was resistant to chloramphenical and clindamycin. Both were non-hemolytic and did not produce Hbl or Nhe enterotoxins. No bceT and cytK toxin genes were found. Study of acute toxicity in BALB/c mice demonstrated no treatment-related deaths. The oral LD(50) for both strains was more than 2 x 10(11) CFU. Chronic toxicity studies were performed on mice, rabbits, and pigs and showed no signs of toxicity or histological changes in either organs or tissues. We demonstrated that while certain risks may exist for the B. licheniformis strain considering antibiotic resistance, B. subtilis strain may be considered as non-pathogenic and safe for human consumption.

Conclusion: B. subtilis strain may be considered as non-pathogenic and safe for human consumption.

#### Caution

J Med Microbiol. 2012 Dec;61(Pt 12):1766-9. doi: 10.1099/jmm.0.042275-0. Epub 2012 Aug 23.

Combined Bacillus licheniformis and Bacillus subtilis infection in a patient with oesophageal perforation.

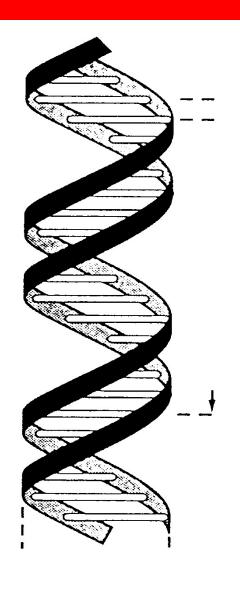
Jeon YL1, Yang JJ, Kim MJ, Lim G, Cho SY, Park TS, Suh JT, Park YH, Lee MS, Kim SC, Lee HJ.

Author information

#### Abstract

Species of the genus Bacillus are a common laboratory contaminant, therefore, isolation of these organisms from blood cultures does not always indicate infection. In fact, except for Bacillus anthracis and Bacillus cereus, most species of the genus Bacillus are not considered human pathogens, especially in immunocompetent individuals. Here, we report an unusual presentation of bacteraemia and mediastinitis due to co-infection with Bacillus subtilis and Bacillus licheniformis, which were identified by 16S RNA gene sequencing, in a patient with an oesophageal perforation.

## DNA-deoxyribonucleic acid



- Encoded repository of heredity
- Watson and Crick-1954
- DNA on chromosomes in higher organisms, corn, mice, humans
- DNA –naked in bacteria, viruses, mitochondria
- Same code in all living things on earth

#### **GPL-SNP 1000**

- Test that includes more than 1000 genetic variations (single nucleotide polymorphisms-SNPs) that are important in autism and other mental illnesses
- Test can be done on blood or saliva
- Results include interpretations-50 pages average
- Consultations with experts are additional charges
- If abnormalities are genetic, supplements or other treatments may need to be lifelong

# Case study of 3 yr old with autismovalate genes

GRHPR	glyoxylate reductase	rs309458	++	No disease associated with this snp
HAO1	glycolate oxidase	rs941426	+-	Primary hyperoxaluria
HAO1	glycolate oxidase	rs2423334	+-	Primary hyperoxaluria

- + unfavorable SNP
- favorable SNP

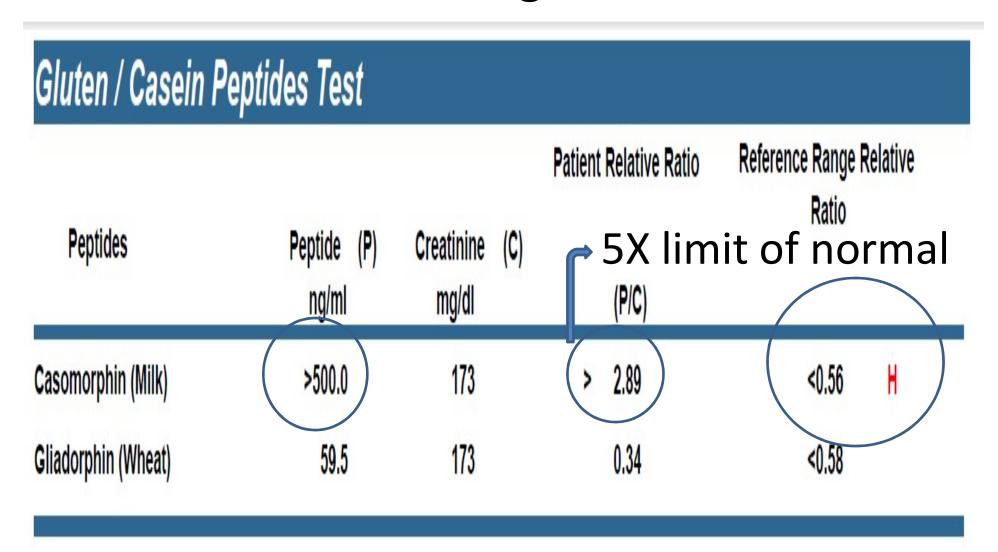
## Case study of 3 yr old with autismoxalate genes



## Case study of autism-genes that breakdown opiate peptides

DPP4	dipeptidyl peptidase IV	rs4664443	++	Increased risk of obesity
DPP4	dipeptidyl peptidase IV	rs1558957	++	Increased risk of cardiovascular disease
DPP4	dipeptidyl peptidase IV	rs10490422	++	Increased risk of cardiovascular disease
DPP4	dipeptidyl peptidase IV	rs13015258	++	Altered lipid profile

## Case study of 3 yr old with autism-DPP IV genes



#### Case study of autism-oxytocin related genes

OXT	oxytocin/neurophysin I prepropeptid	rs2770378		+-	Increased risk of autism
OXT	oxytocin/neurophysin I prepropeptid	rs2740208		++	Increased risk of autism
OXTR	oxytocin receptor	rs237885		+-	Increased risk of autism and schizophrenia
OXTR	oxytocin receptor	rs2268493		+-	Increased risk of autism and schizophrenia
OXTR	oxytocin receptor	rs53576	l	++	Increased risk of autism and schizophrenia
OXTR	oxytocin receptor	rs2268496		+-	No disease associated with this snp
OXTR	oxytocin receptor	rs237898		+-	Increased risk of autism and schizophrenia

#### Case study of autism-neurotransmitter function

COMT	catechol-o-methyltransfe	erase	rs	4633		+-	Schizophrenia	
COMT	catechol-o-methyltransfe	erase	rs4680		ألد	+-	Schizophrenia	
MAOA	monoamine oxidase	A	rs	6323		++	Brunner syndrome	
AHCY	S-Adenosyl homacysteine hydrolase	rs819	171		+-	Alteration in biologic methylations		
AHCY	S-Adenosyl homacysteine hydrolase	rs819	133	ııl	+-	A	Iteration in biologic methylations	
AHCY	S-Adenosyl homacysteine hydrolase	rs819	147 ■■□		+-	Alt	teration in biological methylations	
AHCY	S-Adenosyl homacysteine hydrolase	rs819	146		+-		Increased risk of aneurysm	

#### Case study autism-methylation

Gene	Description	RS Number	Pathogenicity	Phenotype	Disease Associated
MTHFR	Methylenetetrahydrofolat e reductase	rs1801131	ııl	++	Disrupted folate metabolism
MTRR	5-methyltetrahydrofolate- homocysteine methyltransferase reductase	rs1801394		+-	"neural tube defects, folate-sensitive, susceptibility to down syndrome"
MTRR	5-methyltetrahydrofolate- homocysteine methyltransferase reductase	rs2287780		+-	No disease associated with this snp
MTRR	5-methyltetrahydrofolate- homocysteine methyltransferase reductase	rs1802059		+-	No disease associated with this snp

#### Case study autism-methylation

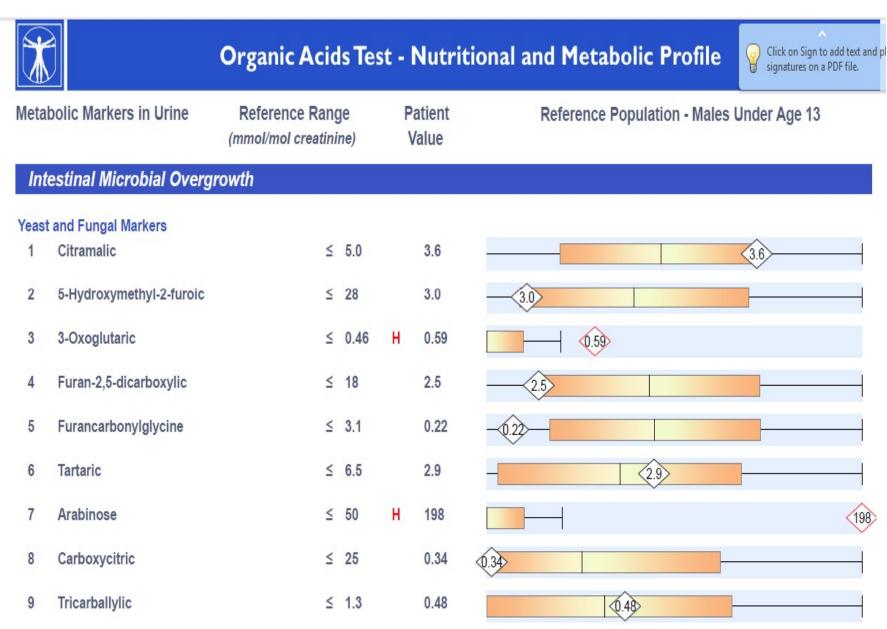
			<u> </u>	
ВНМТ	betaine-homocystein methlatransferase	rs651852	++	Increased risk of neural tube defects and adhd
ВНМТ	betaine-homocystein methlatransferase	rs506500	++	No disease associated with this snp
ВНМТ	betaine-homocystein methlatransferase	rs567754	++	Increased risk of spina bifida
ВНМТ	betaine-homocystein methlatransferase	rs694290	++	No disease associated with this snp
ВНМТ	betaine-homocystein methlatransferase	rs558133	++	Increased risk of neural tube defects
ВНМТ	betaine-homocystein methlatransferase	rs585800	++	Increased risk of adhd

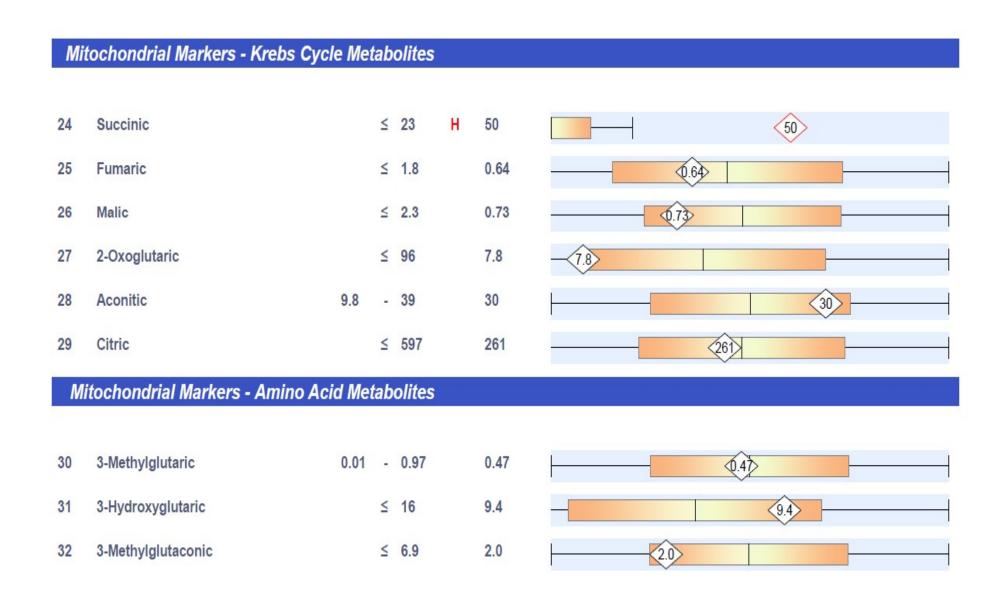
#### Case study autism-homocysteine detoxification

CBS	cystathionine beta- synthase	rs2124459	++	No disease associated with this snp
CBS	cystathionine beta- synthase	rs9325622	++	No disease associated with this snp
CBS	cystathionine beta- synthase	rs1801181	++	Increased risk of neural tube defects
CBS	cystathionine beta- synthase	rs2851391	++	Homocysteine levels are altered
CBS	cystathionine beta- synthase	rs234714	++	Change in plasma homocysteine levels
CBS	cystathionine beta- synthase	rs2850144	++	No disease associated with this snp

bolic Markers in Urine		_				Reference Population - Males Under Age 13			
Indicators of Detoxification									
thione									
Pyroglutamic *	13		62		37	37			
2-Hydroxybutyric *	0.19		2.0		1.3	1.3			
Ammonia Excess									
Orotic	0.04		0.80		0.38	<b>1</b> 38			
Aspartame, salicylates, or GI bacteria									
2-Hydroxyhippuric		<b>\leq</b>	1.2	Н	5.3	5.3			
	dicators of Detoxification  athione Pyroglutamic *  2-Hydroxybutyric *  onia Excess Orotic  rtame, salicylates, or GI bacte	dicators of Detoxification  athione Pyroglutamic * 13  2-Hydroxybutyric * 0.19  aonia Excess Orotic 0.04  artame, salicylates, or GI bacteria	(mmol/mol creatini dicators of Detoxification  athione Pyroglutamic * 13 -  2-Hydroxybutyric * 0.19 -  nonia Excess Orotic 0.04 -  artame, salicylates, or GI bacteria	(mmol/mol creatinine)  dicators of Detoxification  athione Pyroglutamic * 13 - 62  2-Hydroxybutyric * 0.19 - 2.0  conia Excess Orotic 0.04 - 0.80  artame, salicylates, or GI bacteria	(mmol/mol creatinine)  dicators of Detoxification  athione Pyroglutamic * 13 - 62  2-Hydroxybutyric * 0.19 - 2.0  conia Excess Orotic 0.04 - 0.80  artame, salicylates, or GI bacteria	(mmol/mol creatinine) Value  dicators of Detoxification  athione  Pyroglutamic * 13 - 62 37  2-Hydroxybutyric * 0.19 - 2.0 1.3  conia Excess Orotic 0.04 - 0.80 0.38  artame, salicylates, or GI bacteria			

<sup>\*</sup> A high value for this marker may indicate a Glutathione deficiency.





Ne	urotransmitter Metabolites							
Pheny	Phenylalanine and Tyrosine Metabolites							
33 (dopa	Homovanillic (HVA)	0.49		13		4.8	4.8	
34 (nore)	Vanillylmandelic (VMA) pinephrine, epinephrine)	0.72		6.4		4.0	4.0	
35	HVA / VMA Ratio	0.23	•	2.8		1.2	1.2	
Trypt	ophan Metabolites							
36 (serot	5-Hydroxyindoleacetic (5-HIAA) onin)		<	11		0.71	-0.7)	
37	Quinolinic	0.48		8.8		3.4	3.4	
38	Kynurenic		≤	4.2		0.18	0.18	
39	Quinolinic / 5-HIAA Ratio		≤	2.5	Н	4.8	4.8	

