Common Testing and Treatments for Newly Diagnosed Patients with Autism

NICOLE RINCON PA-C

ROSSIGNOL MEDICAL CENTER

24541 PACIFIC PARK DRIVE #210

ALISO VIEJO, CA 92656

PHONE: 321-259-7111

FAX: 949-407-7652

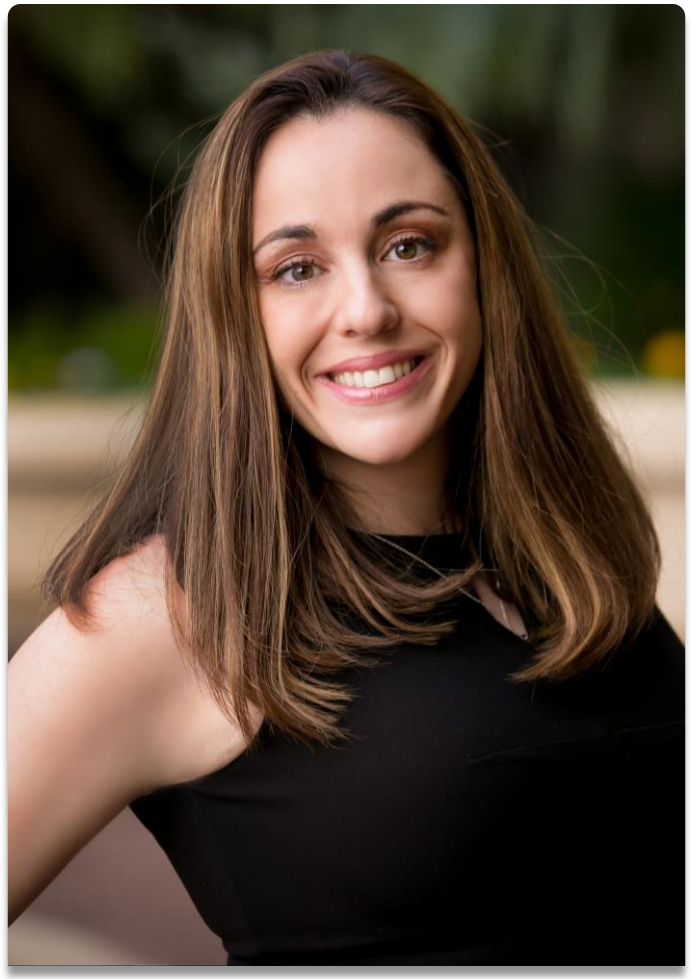
WWW.ROSSIGNOLMEDICALCENTER.COM

Disclaimer

While Nicole Rincon has attempted to make the information in this presentation as accurate as possible, the information is provided without any expressed or implied warranty. The purpose of this lecture is to provide information about different conditions or treatments that may affect individuals with autism and other conditions. Please be advised that Nicole Rincon is not giving medical advice and that circumstances may dictate different treatments. All of the reviewed treatments in this lecture are considered off-label and not FDA-approved. Before beginning any treatment, please consult with your or your child's physician. The use of every treatment in autism is "off-label" except for Risperidone and Aripiprazole for the treatment of irritability.

Nicole Rincon, MS, PA-C

- UCSD Biology major with emphasis in Microbiology and Genetics
- Background in nutritional counseling and wellness supplementation
- Currently practicing at Rossignol Medical Center



- Married in 2008
- Triplets born in 2012 at 34 weeks
- Happy and healthy kids

- At 15 months Ryan regressed
- At 25 months Alex regressed and lost all speech
- At 26 months Vivien began having seizures

After over 5 years of Biomedical intervention:

1. Ryan's behavior and receptive skills have improved
2. Alex mainstreamed and age appropriate for academics
3. Vivien is seizure free

First Visit- What to Expect

COMPREHENSIVE HISTORY

- Gestational
- Birth and early life history
- Developmental history and milestones
- History of regression?
- Medical disorders
- Family history

First Visit- What to Expect

Medical record review

- Previous lab testing and other tests
  - Blood / urine / hair and others
  - Imaging
  - EEG
- Previous treatments and reactions
  - Good/Bad/No change
- Anything missing, not tested or not treated?

First Visit- What to Expect

- Targeted physical examination
- Review / explanation of potential problems and plan for testing:
  - Mitochondrial dysfunction
  - Inflammation & Allergies
  - Oxidative stress & methylation
  - Toxicity
  - Seizures

Second Visit- What to Expect

- **Evaluation of previous treatments**
  - What went right or right
- **Review of testing**
- **Decision on new treatments**
  - If there have been good improvements, then treatment can be less aggressive
  - If older, not improving, or high severity, then may need to be more aggressive

Biomarkers

- Basic Biomarkers
- Endocrine
- Immune dysregulation
- Gastrointestinal (GI) dysfunction
- Toxicity
- Mitochondrial dysfunction

Basic Biomarkers

- Complete blood count (CBC): anemia, abnormal white count (low suggests viral infections), platelet count (high suggests inflammation), eosinophil count (high seen with allergies and parasites)
- Comprehensive metabolic (CMP): electrolytes, liver, kidney tests, low CO_2 suggests mitochondrial dysfunction or acidosis

Basic Biomarkers

- Magnesium: deficiency is associated with hyperactivity
- RBC Zinc: deficiency associated with inattention
- Other minerals: low chromium associated with pica, low lithium associated with irritability
- Iron (ferritin): deficiency associated with insomnia, restless legs syndrome, lower IQ, attention problems

Basic Biomarkers

- Cholesterol: deficiency associated with irritability, aggression and hyperactivity Tierney, 2008 Int Rev Psychiatry 20(2):165-70
- Testosterone: increase associated with aggression
- TSH: test for hypothyroidism which is associated with developmental delay and inattention

Endocrine Biomarkers

- Cortisol (8 am): low levels associated with adrenal insufficiency
- Anti-thyroid antibodies: seen in Hashimoto's thyroiditis
- Thyroid hormones (free T3 and free T4)
- Vitamin D (25-OH): low levels associated with increased oxidative stress and a compromised mucosal barrier (increased risk of IBD)

Kong et al., 2008 Am J Physiol Gastrointest Liver Physiol 294(1):G208-16

Biomarkers of Immune Dysregulation

- IgG with subclasses, IgM, IgA: markers of immunodeficiency, low levels also correlate with core autistic behaviors
- IgE: associated with allergies
- Antinuclear antibodies (ANA): reflects autoimmunity
- C-reactive protein and sed rate: inflammation
- Folate Receptor Antibodies (blocking and binding)- Associated with Cerebral Folate Deficiency

Autoimmunity & Cerebral Folate Deficiency

- Can be caused by folate receptor (FR) autoantibodies
- 2 Types: FR binding antibody and FR blocking antibody
- 70/93 (75%) of children with autism positive for at least one FR antibody (Frye et al, 2012)
- Without treatment, the concentration of autoantibodies increases over time

Biomarkers of Immune Dysregulation

- ASO / AntiDNAse B: confirm previous exposure to GABHS (group A beta-hemolytic streptococcus) in children without obvious strep exposure history
- Antigliadin antibodies: elevated in some people with celiac disease
- Food allergy panels (IgG and IgE)

Food Sensitivities

IgE: immediate

Often result in skin problems, hives, swelling, breathing problems, etc. This can be tested using a skin test or blood test

IgG: delayed or intolerance

Can result in more varied or vague symptoms like discomfort, stomach problems, sleep problems, joint pain, ear infections, or hyperactivity and behavioral problems

Diagnosing Food Sensitivities

IgE allergy testing (RAST, skin prick tests, blood)

IgG testing (skin prick test, blood)

- May indicate intestinal permeability

Elimination diet trials

- In my experience, this is the most reliable method.

Food Allergy in Infantile Autism

Study on cow's milk free diet

- Marked improvement in the behavioral symptoms of patients after a period of 8 weeks on an elimination diet.
- Our results lead us to hypothesize a relationship between food allergy and infantile autism as has already been suggested for other disturbances of the central nervous system.

Lucarelli, 1995 Panminerva Med 37(3):137-41

Biomarkers of GI Dysfunction

Stool Analysis (CDSA or CSA):

- Stool calprotectin: Marker of inflammatory bowel disease
- Stool eosinophil-X: marker of food allergy related bowel inflammation (inflammation can lead to increased permeability)
- Bile acids, enzymes (elastase), pH and fatty acids (butyrate)
- Stool culture and microscopic examination

GI Dysfunction

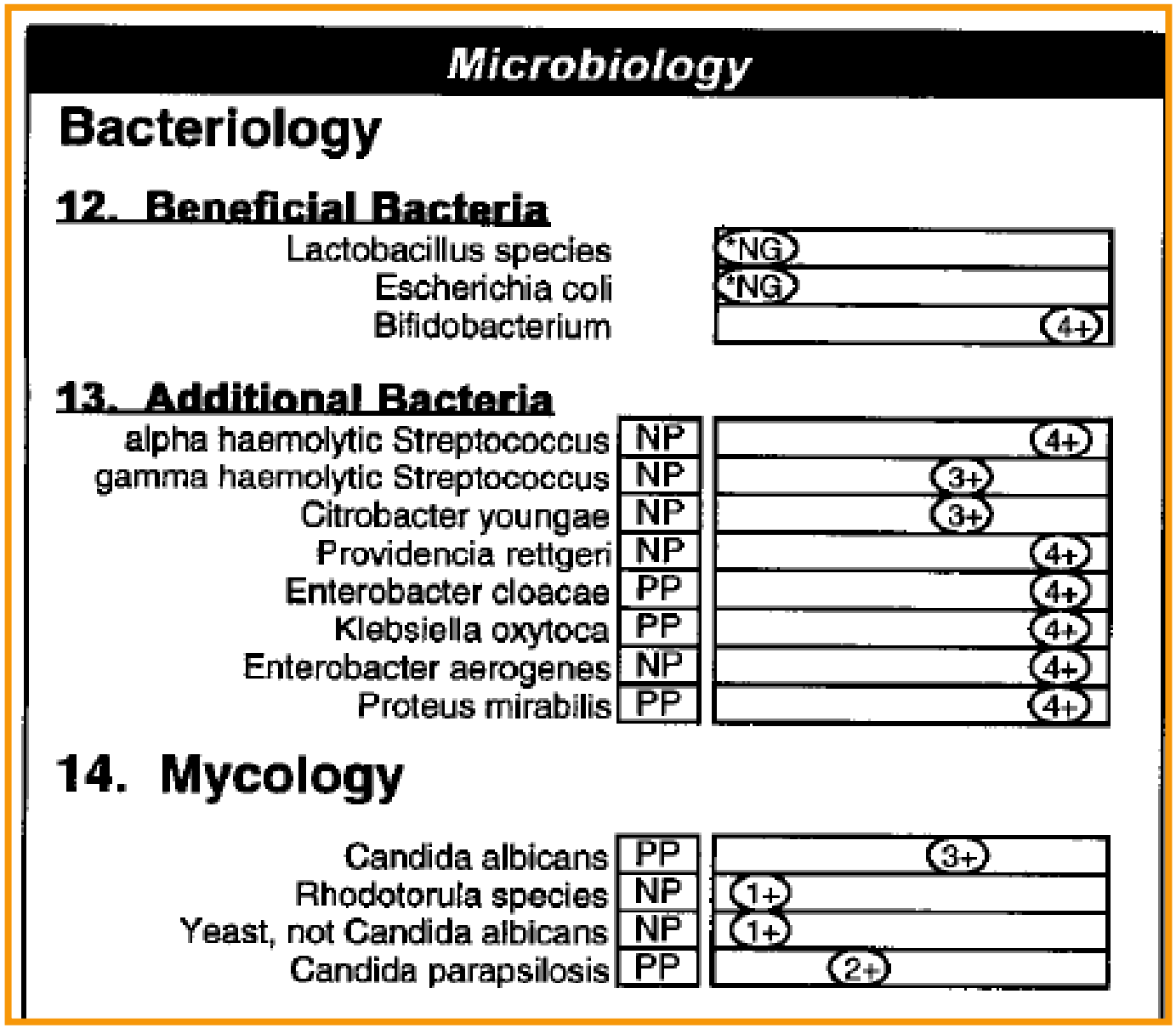
Altered intestinal permeability was found in 9 of the 21 (43%) autistic patients, but in none of the 40 controls.

- D'Eufemia et al., 1996 Acta Paediatr 85(9):1076-9

A high percentage of abnormal IPT values were found among patients with autism (36.7%) and their relatives (21.2%) compared with normal subjects (4.8%).

- Patients with autism on a reported gluten-casein-free diet had significantly lower IPT values compared with those who were on an unrestricted diet and controls
  - De Magistris et al., 2010 J Pediatr Gastroenterol Nutr

Stool Culture



Microbiology

Bacteriology

12. Beneficial Bacteria

Lactobacillus species		*NG
Escherichia coli		*NG
Bifidobacterium		4+

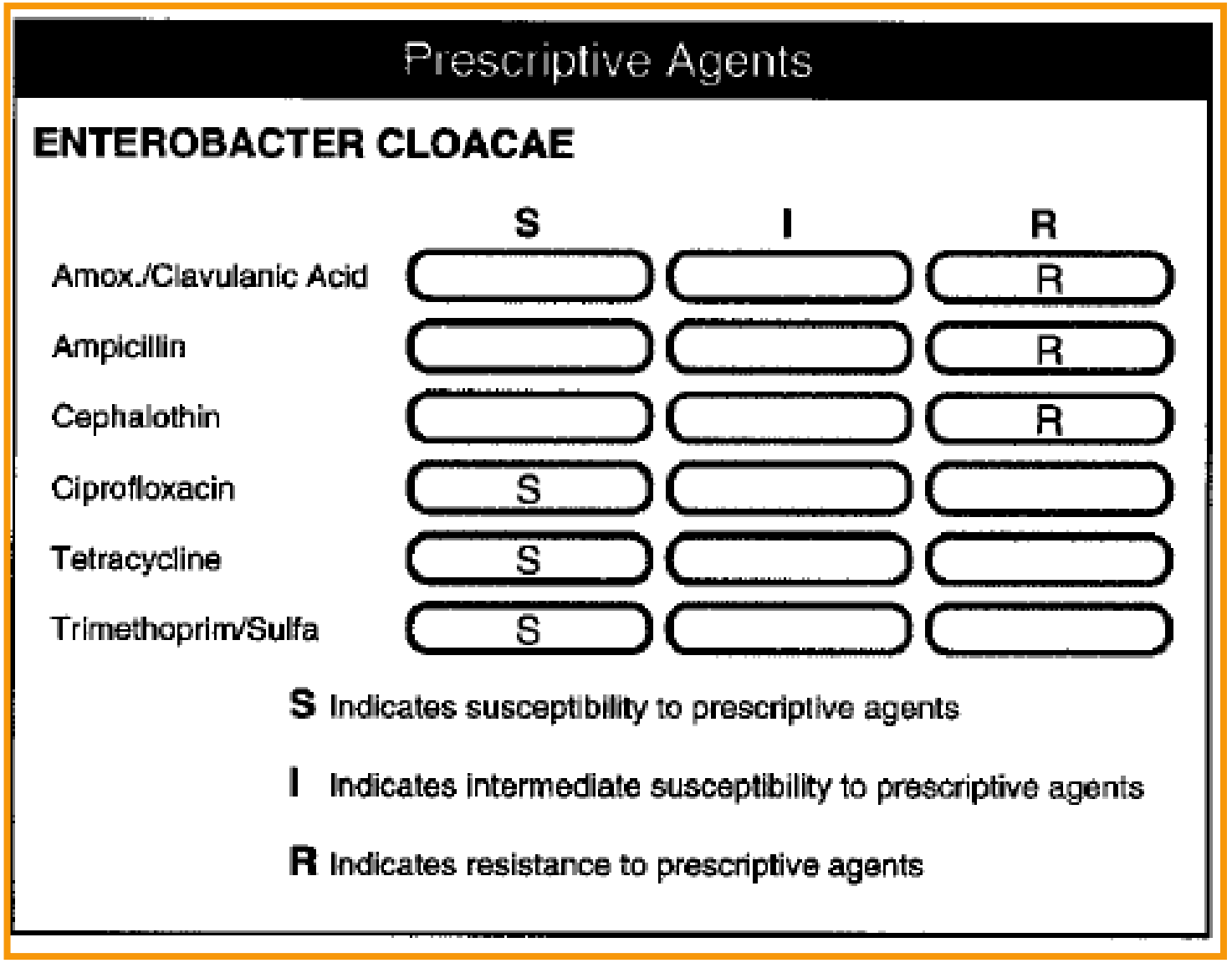
13. Additional Bacteria

alpha haemolytic Streptococcus	NP	4+
gamma haemolytic Streptococcus	NP	3+
Citrobacter youngae	NP	3+
Providencia rettgeri	NP	4+
Enterobacter cloacae	PP	4+
Klebsiella oxytoca	PP	4+
Enterobacter aerogenes	NP	4+
Proteus mirabilis	PP	4+

14. Mycology

Candida albicans	PP	3+
Rhodotorula species	NP	1+
Yeast, not Candida albicans	NP	1+
Candida parapsilosis	PP	2+

Stool Culture



Prescriptive Agents

ENTEROBACTER CLOACAE

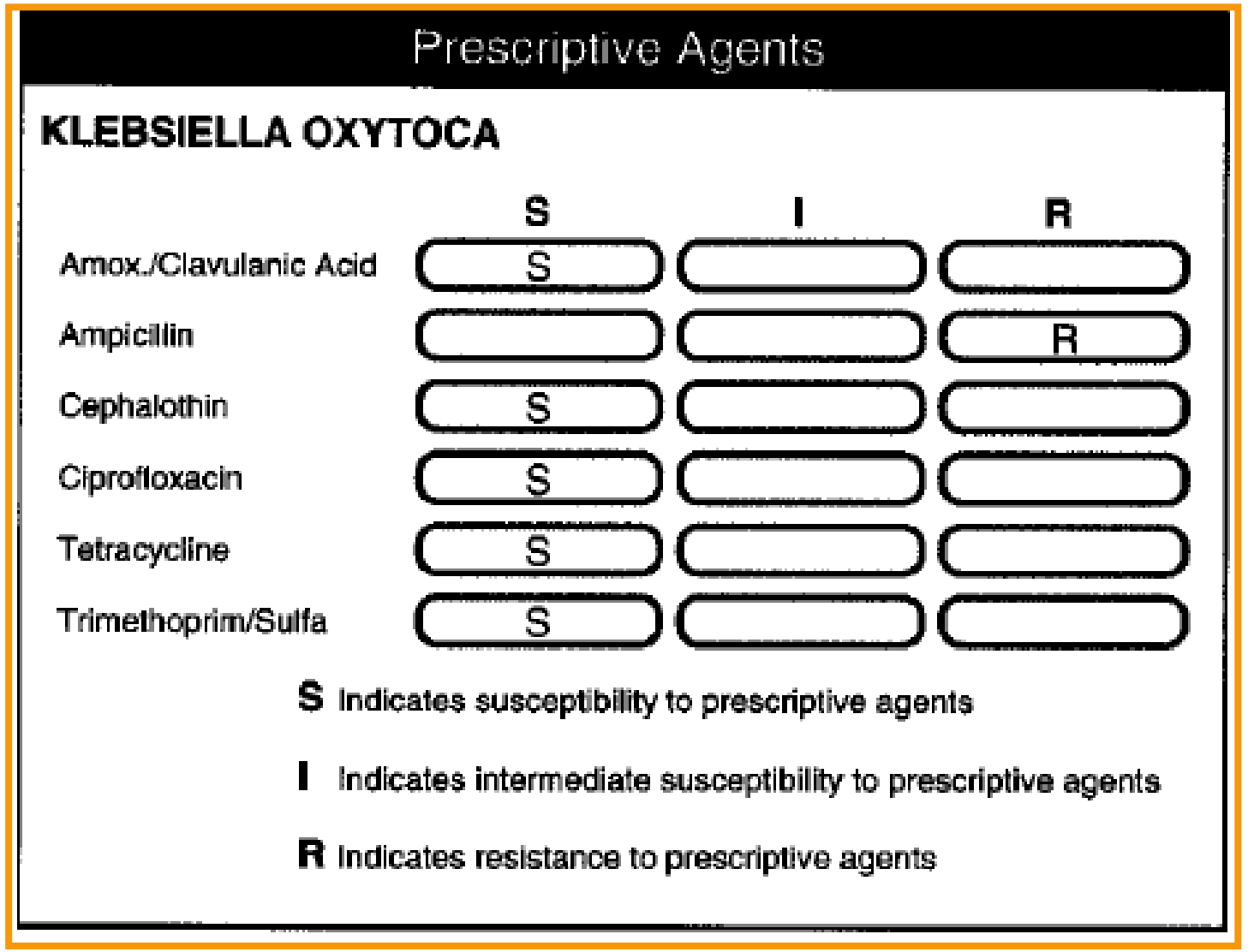
	S	I	R
Amox./Clavulanic Acid			R
Ampicillin			R
Cephalothin			R
Ciprofloxacin	S		
Tetracycline	S		
Trimethoprim/Sulfa	S		

S Indicates susceptibility to prescriptive agents

I Indicates intermediate susceptibility to prescriptive agents

R Indicates resistance to prescriptive agents

Stool Culture



Prescriptive Agents

KLEBSIELLA OXYTOCA

	S	I	R
Amox./Clavulanic Acid	S		
Ampicillin			R
Cephalothin	S		
Ciprofloxacin	S		
Tetracycline	S		
Trimethoprim/Sulfa	S		

S Indicates susceptibility to prescriptive agents

I Indicates intermediate susceptibility to prescriptive agents

R Indicates resistance to prescriptive agents

Azole Antifungals

CANDIDA ALBICANS

	S	I	R
Fluconazole	<=0.125		
Itraconazole	=0.125		
Ketoconazole	<=0.025		

S Indicates susceptibility to prescriptive agents

I Indicates intermediate susceptibility to prescriptive agents

R Indicates resistance to prescriptive agents

Azole Antifungals

CANDIDA PARAPSILOSIS

	S	I	R
Fluconazole	=1.0		
Itraconazole	<=0.06		
Ketoconazole	<=0.025		

S Indicates susceptibility to prescriptive agents

I Indicates intermediate susceptibility to prescriptive agents

R Indicates resistance to prescriptive agents

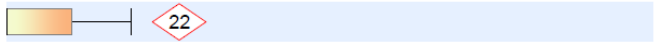
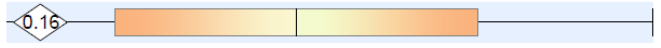
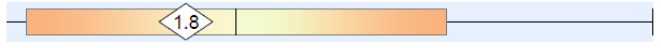
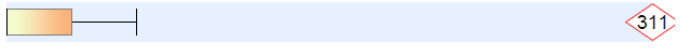
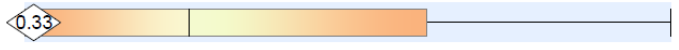
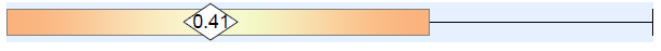
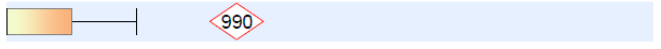
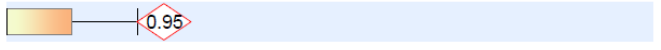
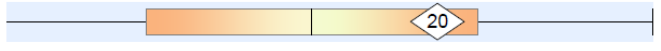
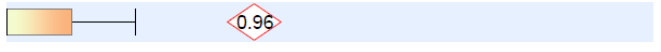
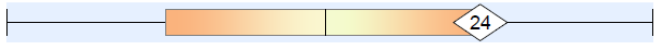
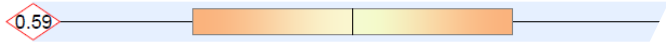
GI Dysfunction

Organic Acid Test (OAT):

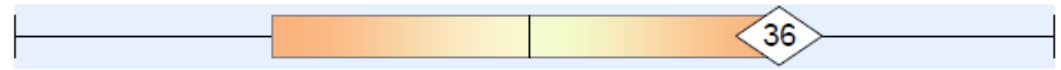
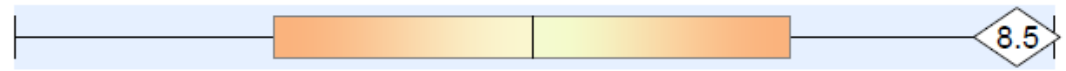
- Can identify dysbiosis
- Can indicate functional vitamin B12 and folate deficiency
- Can help identify mitochondrial dysfunction and oxidative stress

ıt Age:	3	*Time of Collection:*	07:30 AM
ient Sex:	M	*Print Date:*	01/15/2016

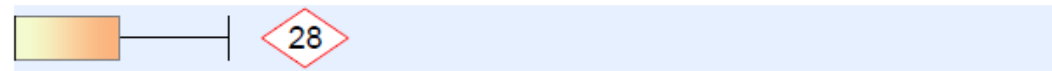
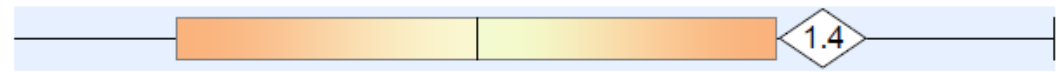
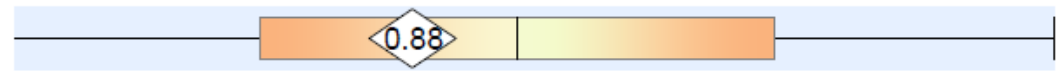
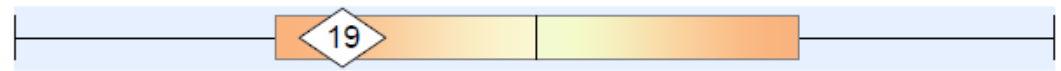
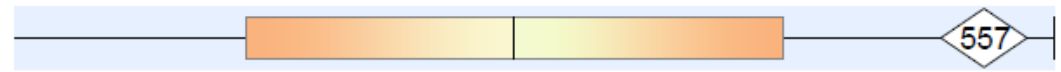
Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
Intestinal Microbial Overgrowth				
Yeast and Fungal Markers				
1 Citramalic	≤ 5.0		2.0	
2 5-Hydroxymethyl-2-furoic	≤ 28	H	49	
3 3-Oxoglutaric	≤ 0.46		0.31	
4 Furan-2,5-dicarboxylic	≤ 18	H	22	
5 Furancarbonylglycine	≤ 3.1		0.16	
6 Tartaric	≤ 6.5		1.8	
7 Arabinose	≤ 50	H	311	
8 Carboxycitric	≤ 25		0.33	
9 Tricarballylic	≤ 1.3		0.41	
Bacterial Markers				
10 Hippuric	≤ 680	H	990	
11 2-Hydroxyphenylacetic	≤ 0.86	H	0.95	
12 4-Hydroxybenzoic	≤ 3.0		2.8	
13 4-Hydroxyhippuric	≤ 30		20	
14 DHPPA (Beneficial Bacteria)	≤ 0.59	H	0.96	
Clostridia Bacterial Markers				
15 4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	2.0 - 32		24	
16 HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*	≤ 220		45	
17 4-Cresol *(C. difficile)*	≤ 84	H	171	
18 3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	0.60 - 14	L	0.59	

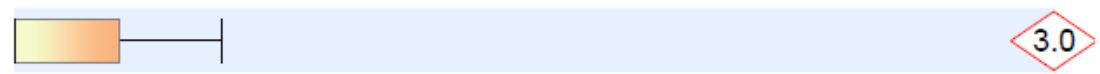
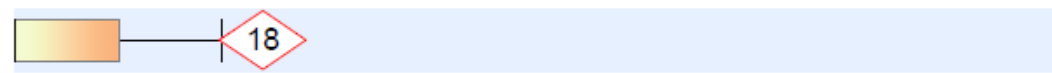
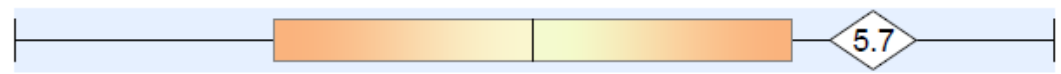
Glycolytic Cycle Metabolites

22	Lactic	2.6	-	48		36	
23	Pyruvic	0.32	-	8.8		8.5	

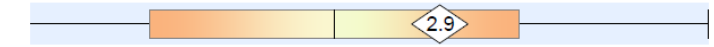
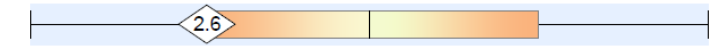
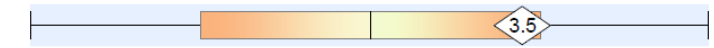
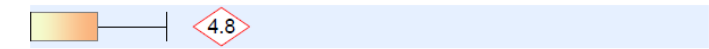
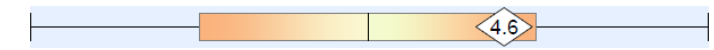
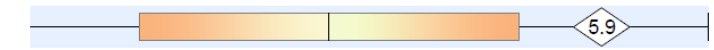
Mitochondrial Markers - Krebs Cycle Metabolites

24	Succinic		≤	23	H	28	
25	Fumaric		≤	1.8		1.4	
26	Malic		≤	2.3		0.88	
27	2-Oxoglutaric		≤	96		53	
28	Aconitic	9.8	-	39		19	
29	Citric		≤	597		557	

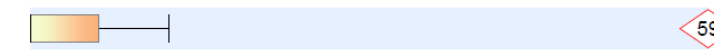
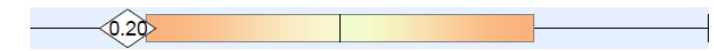
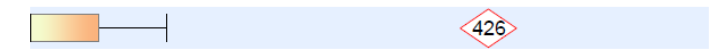
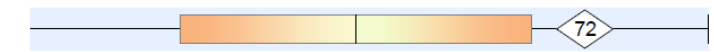
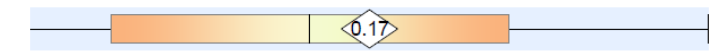
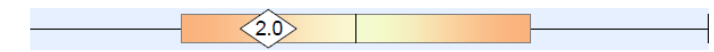
Mitochondrial Markers - Amino Acid Metabolites

30	3-Methylglutaric	0.01	-	0.97	H	3.0	
31	3-Hydroxyglutaric		≤	16	H	18	
32	3-Methylglutaconic		≤	6.9		5.7	

Ketone and Fatty Acid Oxidation

42	3-Hydroxybutyric		≤	4.8		2.9	
43	Acetoacetic		≤	10		2.6	
44	4-Hydroxybutyric		≤	4.7		0	
45	Ethylmalonic	0.06	-	4.8		3.5	
46	Methylsuccinic		≤	4.0	H	4.8	
47	Adipic	0.19	-	6.5		4.6	
48	Suberic		≤	7.0		5.9	
49	Sebacic		≤	0.61		0.04	

Nutritional Markers

Vitamin B12							
50	Methylmalonic ✱		≤	5.2		3.5	
Vitamin B6							
51	Pyridoxic (B6)		≤	53		12	
Vitamin B5							
52	Pantothenic (B5)		≤	14	H	59	
Vitamin B2 (Riboflavin)							
53	Glutaric ✱		≤	1.4		0.20	
Vitamin C							
54	Ascorbic	10	-	200	H	426	
Vitamin Q10 (CoQ10)							
55	3-Hydroxy-3-methylglutaric ✱		≤	88		72	
Glutathione Precursor and Chelating Agent							
56	N-Acetylcysteine (NAC)		≤	0.34		0.17	
Biotin (Vitamin H)							
57	Methylcitric ✱		≤	5.7		2.0	

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

Indicators of Detoxification

Glutathione

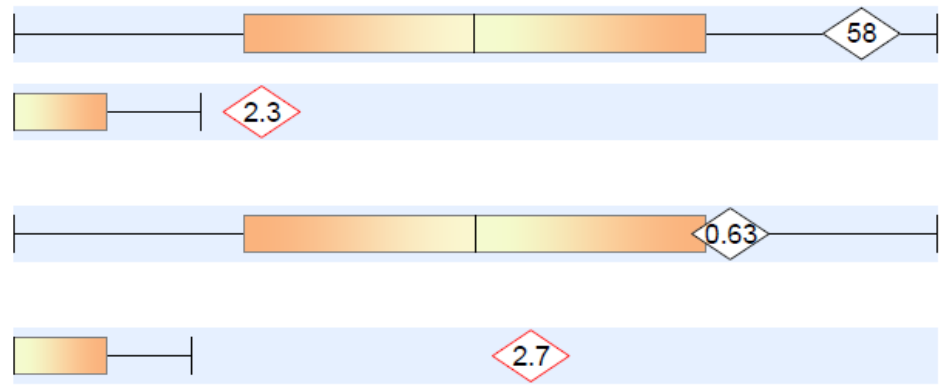
58	Pyroglutamic ✱	13	-	62		58
59	2-Hydroxybutyric ✱	0.19	-	2.0	H	2.3

Ammonia Excess

60	Orotic	0.04	-	0.80		0.63

Aspartame, salicylates, or GI bacteria

61	2-Hydroxyhippuric		≤	1.2	H	2.7



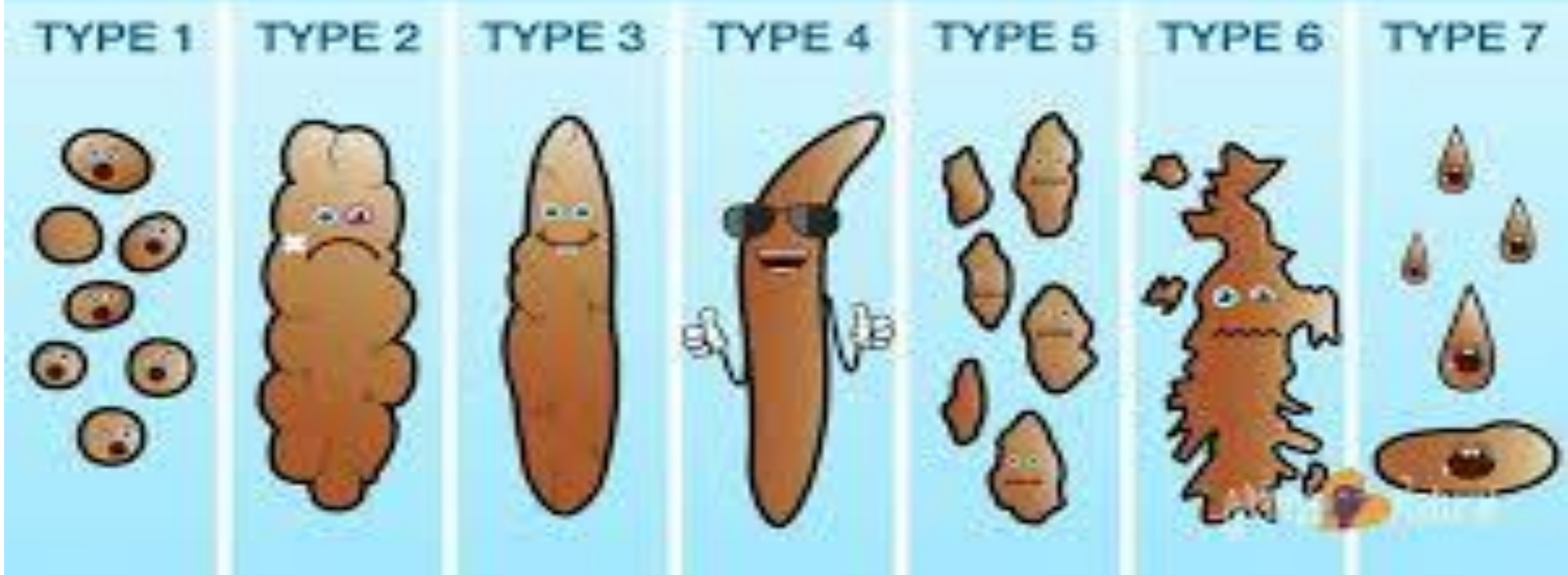
✱ ***A high value for this marker may indicate a Glutathione deficiency.***

GI Dysfunction

- Moderate or severe constipation was more frequent in the autistic group than in the control subjects (36% vs 10%).
- Multivariate regression analysis showed **consumption of milk** to be the strongest predictor of constipation in the autistic group.
- Constipation is a frequent finding in children with gastrointestinal symptoms and autism, particularly in the rectosigmoid colon, often with acquired megarectum.
  - Afzal et al., 2003 Pediatrics 112(4):939-42


R
RS
SUPINE

BRISTOL STOOL CHART



Biomarkers of Toxicity & Heavy metals

- Blood lead/mercury: increased levels associated with recent exposure
- Packed RBC test: can reflect exposure to toxic metals such as mercury, arsenic, lead, others
- Hair metals associated with recent exposure over the past 2-3 months
- Unprovoked urinary toxic metals: represents a measure of ongoing exposure to metals
- Provoked urinary toxic metals: increased output of metals after a chelator correlated to body burden of toxic metals

POTENTIALLY TOXIC METALS

METALS	RESULT µg/g CREAT	REFERENCE RANGE	WITHIN REFERENCE RANGE	ELEVATED	VERY ELEVATED
Aluminum	14	< 60			
Antimony	0.7	< 1.5			
Arsenic	31	< 130			
Beryllium	< dl	< 0.6			
Bismuth	< dl	< 20			
Cadmium	0.7	< 2			
Lead	73	< 5			
Mercury	9.9	< 5			
Nickel	3.7	< 15			
Platinum	< dl	< 1			
Thallium	0.3	< 1.1			
Thorium	< dl	< 0.5			
Tin	5.9	< 15			
Tungsten	0.3	< 1.5			
Uranium	< dl	< 0.2			

CREATININE

	RESULT mg/dL	REFERENCE RANGE	2SD LOW	1SD LOW	MEAN	1SD HIGH	2SD HIGH
Creatinine	74	25- 180					

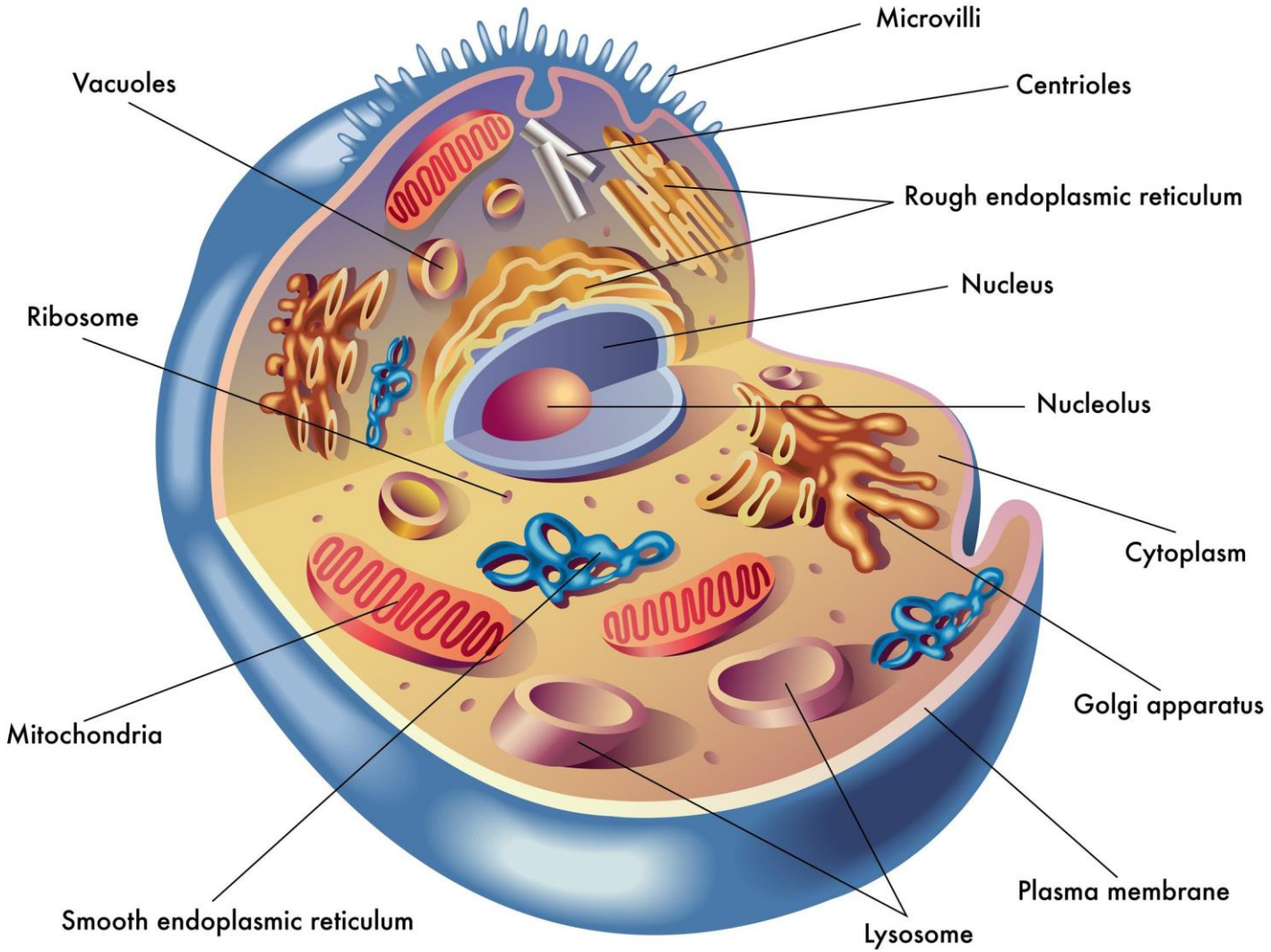
SPECIMEN DATA

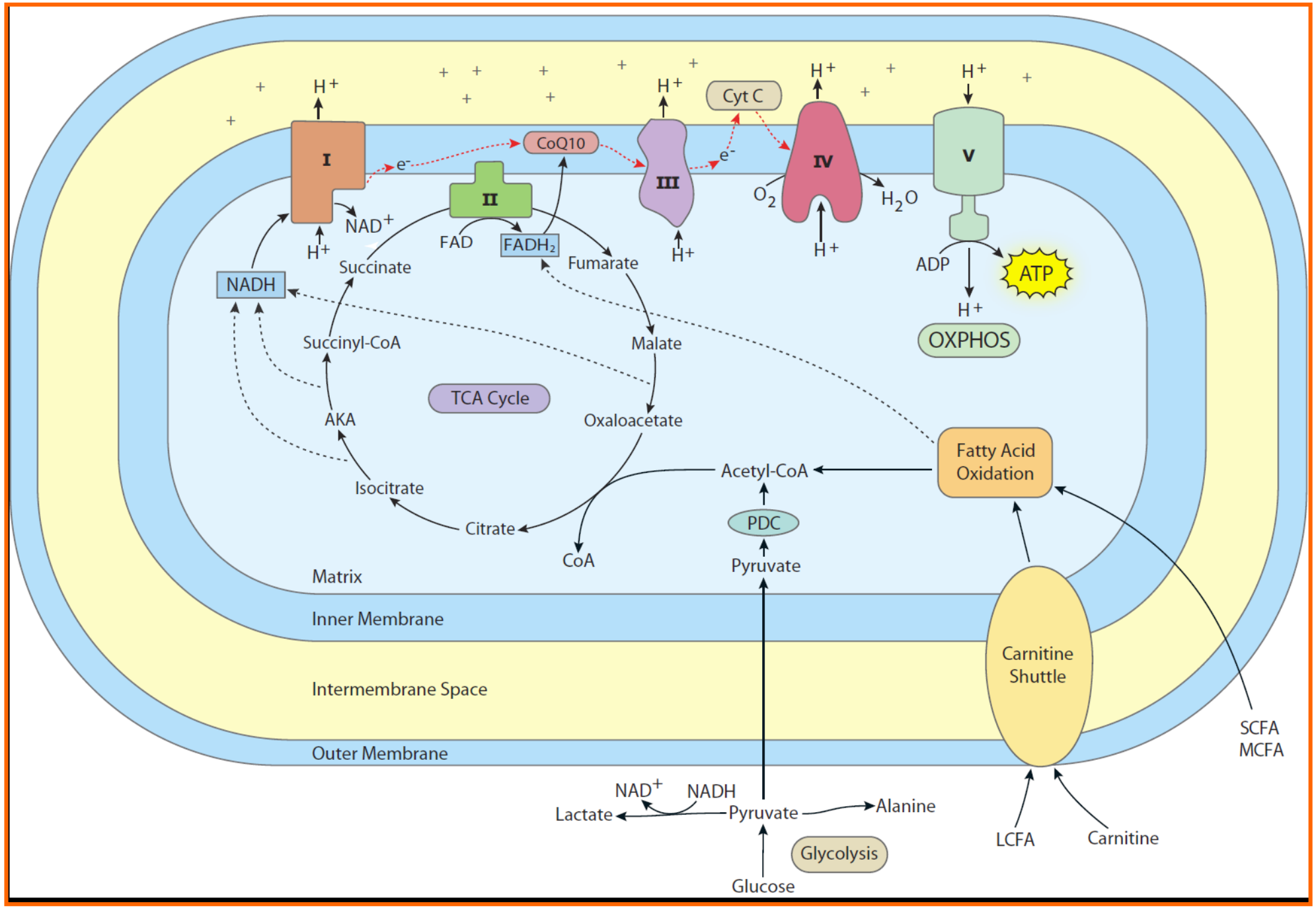
Comments: Results checked
Date Collected:
Date Received: 4/10/2009
Date Completed: 4/14/2009

Method: ICP-MS
<dl: less than detection limit
Provoking Agent: SUPP DMSA

Collection Period: timed: 6 hours
Volume:
Provocation: POST PROVOCATIVE

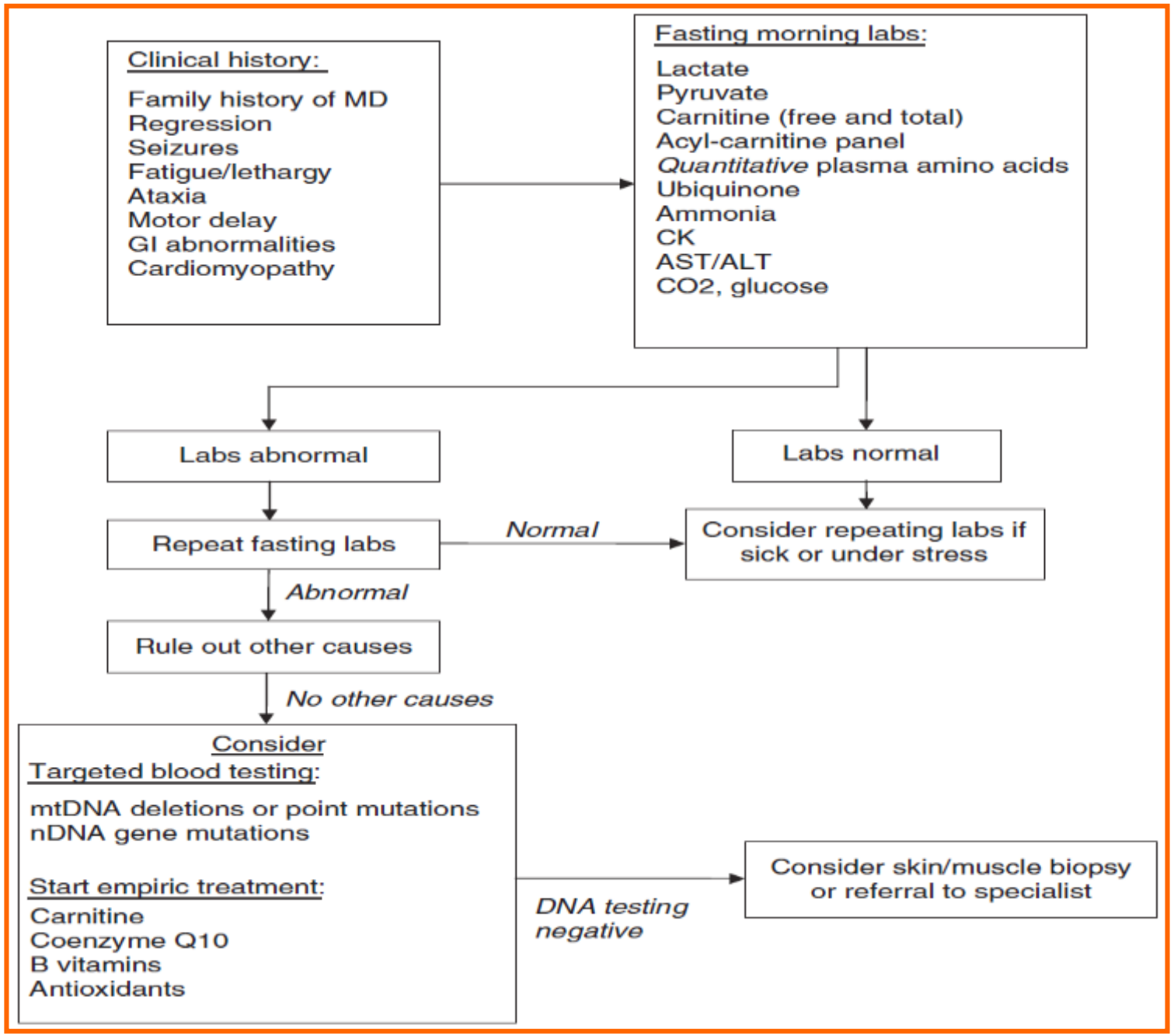
Biomarkers of Mitochondrial Dysfunction




H+
I
e-
CoQ10
II
FAD
FADH2
NAD+
H+
Succinate
Fumarate
NADH
III
Cyt C
IV
O2
H2O
V
ADP
ATP
OXPHOS
Succinyl-CoA
Malate
TCA Cycle
AKA
Oxaloacetate
Isocitrate
Citrate
CoA
Acetyl-CoA
Fatty Acid Oxidation
PDC
Pyruvate
Matrix
Inner Membrane
Intermembrane Space
Outer Membrane
Carnitine Shuttle
SCFA
MCFA
LCFA
Carnitine
NAD+
NADH
Lactate
Alanine
Glycolysis
Glucose

Mitochondrial Dysfunction

- Elevated ammonia
- Elevated lactic acid
- Elevated creatine kinase
- Quantitative plasma amino acids: Alanine to lysine > 2.5, high glycine, proline, sacrosine, tyrosine
- Low carnitine levels
- Elevated acylcarnitines
- Low CoEnzyme Q10
- Elevated pyruvate
- AST/ALT > 2.0
- Organic acid test, metabolic (urine)
- Low CO_2, increased anion gap



Rossignol and Frye, 2011 Mol Psychiatry, doi:10.1038/mp.2010.136

Seizures

Don’t forget about obtaining a 24 hour EEG!

Initial Blood Tests Summary

- CBC
- CMP
- Ferritin
- Cholesterol
- Magnesium
- RBC zinc
- Testosterone
- TSH
- Vitamin D
- AM cortisol

- Lead
- Mercury
- Homocysteine

- ASO
- AntiDNAse B
- ANA
- Antigliadin antibodies
- Food allergy panel
- CRP
- ESR

- Ammonia
- Lactic acid
- Creatine kinase
- Quantitative plasma amino acids
- Carnitine levels
- Acylcarnitine profile

Other Initial Testing

- OAT
- CDSA
- Hair metals testing
- 24 hour EEG

See a medical provider to determine the best tests for your child. No need to wait.

Other Considerations

- Assess environment for allergens and mold
- Assess for environmental toxins
- Investigate genetics or other SNPs

FAQ for Initial Visit

How Do I get my child to take these supplements
http://www.tacanow.org/family-resources/ideas-to-help-your-child-take- supplements/

How long will it take for these treatments to take effect?

How long will my child have to take these supplements?

What is the best thing I can do overall to help my child succeed?

NEVER GIVE UP!! (see your doctor every 3 months)

Nicole Rincon MS, PA-C

Rossignol Medical Center

California Office (Aliso Viejo, CA):
Phone: 321.259.7111

www.rossignolmedicalcenter.com

nicolerinconpa@gmail.com

TACA Conference
October 2019