B12 and Folate-Deficient Anemia - Part Two

All right, let's look at some cases. The first patient is a 29-year-old female. Her chief complaints were chronic pain and flare-ups, back problems for 15-plus years, knee issues for 10-plus years, neck issues for five-plus years, two wrist surgeries, knee surgery, and then she had done extensive chiropractic and physical therapy that had not helped. She had significant digestive issues, and she had been on a vegan diet for the past 15 years.

Of course, we're wondering—when you see all of these bone-related joint problems and then someone who has been on a vegan diet for 15 years, the first thing that you're thinking about, I hope, is nutrient deficiency. Both vegans and vegetarians have been shown to have a higher risk of osteoporosis and osteopenia due to deficiency of a number of nutrients that are important for bone health.

Marker	Value	Functional Range	Lab Range
Glucose	84	75 - 90	65 - 99
Hemoglobin A1c	4.8	4.8 – 5.4	4.8 - 5.6
Uric Acid	5.5	3.2 - 5.5	2.5 - 7.1
BUN	10	13 – 18	6 - 20
Creatinine	0.63	0.85 – 1.1	0.57 - 1
BUN/Creatinine Ratio	16	9 – 23	8 - 20
Sodium	139	134 – 140	134 - 144
Potassium	3.7	4.0 – 4.5	3.5 - 5.2
Chloride	102	100 – 106	97 - 108
C02	26	25 – 30	18 - 29
Calcium	9.3	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.5	3.5 – 4.0	2.5 - 4.5
Magnesium	1.7	2.0 – 2.6	1.6 - 2.3
Protein, total	6.4	6.9 – 7.4	6.0 - 8.5
Albumin	4.4	4.0 – 5.0	3.5 - 5.5
Globulin	2.0	2.4 – 2.8	1.5 - 4.5
A/G ratio	2.2	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.7	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	60	42 – 107	39 - 117
LDH	159	140 - 180	119 - 226
AST	19	10 - 30	0 - 40
ALT	21	10 - 22	0 - 32
GGT	17	0 - 28	0 - 60
TIBC	267	250 – 350	250 - 450
UIBC	58	150 - 375	131 - 425
Iron	209	85 – 135	27 - 159
Iron saturation	78	15 – 45	15 - 55
Ferritin	86	15 - 120	15 - 150
Vitamin B-12	1083	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	29.1	35 - 60	30.0 - 100.0
Cholesterol, total	161	150 - 250	100 - 199
Triglycerides	104	50 – 100	0 - 149
HDL	48	55 – 85	> 39
LDL	92	0 - 175	0 - 99
T. Chol / HDL Ratio	3.4	< 3	0 - 4.4
Triglycerides / HDL Ratio	2.17	< 2	< 3.8
CRP-hs	0.23	< 1.0	0.00 - 3.00
Homocysteine	5.5	< 7.0	0.0 - 15.0

Marker	Value	Functional Range	Lab Range
TSH	2.850	0.5 – 2.5	0.45 - 4.50
T4, total	6.1	6.0 – 12	4.5 - 12
T3 Uptake	28	28 - 35	24 - 39
T3, Total	87	100 – 180	71 - 180
Copper	99		72 - 166
Zinc	79		56 - 134
Zinc / Copper Ratio	0.80	> 0.85	
Serum Methylmalonic Acid (MMA)	179	0 - 325	0 - 378
WBC	3.7	5.0 – 8.0	3.4 - 10.8
RBC	4.28	4.4 – 4.9	3.77 - 5.28
Hemoglobin	14.5	13.5 - 14.5	11.1 - 15.9
Hematocrit	43.1	37 - 44	34 - 46.6
MCV	101	85 – 92	79 - 97
MCH	33.9	27.7 – 32.0	26.6 - 33.0
MCHC	33.6	32 – 35	31.5 - 35.7
RDW	12.3	11.5 – 15.0	12.3 - 15.4
Platelets	158	150 – 415	150 - 379
Neutrophils	50	40 – 60	
Lymphocytes	36	25 – 40	
Monocytes	9	4.0 – 7.0	
Eosinophils	5	0.0 – 3.0	
Basophils	0	0.0 – 3.0	

We talked about this patient back in the B12 deficiency unit. She had pernicious anemia. You can see here. Her red blood cells are functionally low. Hemoglobin and hematocrit are normal, but her MCV and MCH are lab-high. Her B12 is lab-high too because she was taking a multivitamin with cyanocobalamin, which is an inferior synthetic form of B12, which she clearly wasn't absorbing very well or well enough. Then, she also had iron overload because she was taking iron supplements to compensate for the low intake of iron on a vegan diet, and that led to very high iron levels. She was also magnesium deficient, as you can see. It is very likely she was deficient in K2 because of her bone issues, and K2 is important for bone health. No evidence of calcium deficiency according to serum calcium here, but it is almost low in the functional range at 9.3. I would probably run an ionized calcium on her to get a little bit more info, since it is a little more accurate of a marker. She has relatively low vitamin D, which affects calcium metabolism and bone health as well. Lots going on here to consider.

The next patient is a 41-year-old female. Poor digestion, irregular bowel symptoms, and some abdominal pain for about two years. Became very anemic earlier in the year before I had seen her, which was corrected with an iron supplement, according to her, and also developed alopecia areata, hair loss. This patient had been vegetarian for her entire life and vegan for the last two years.

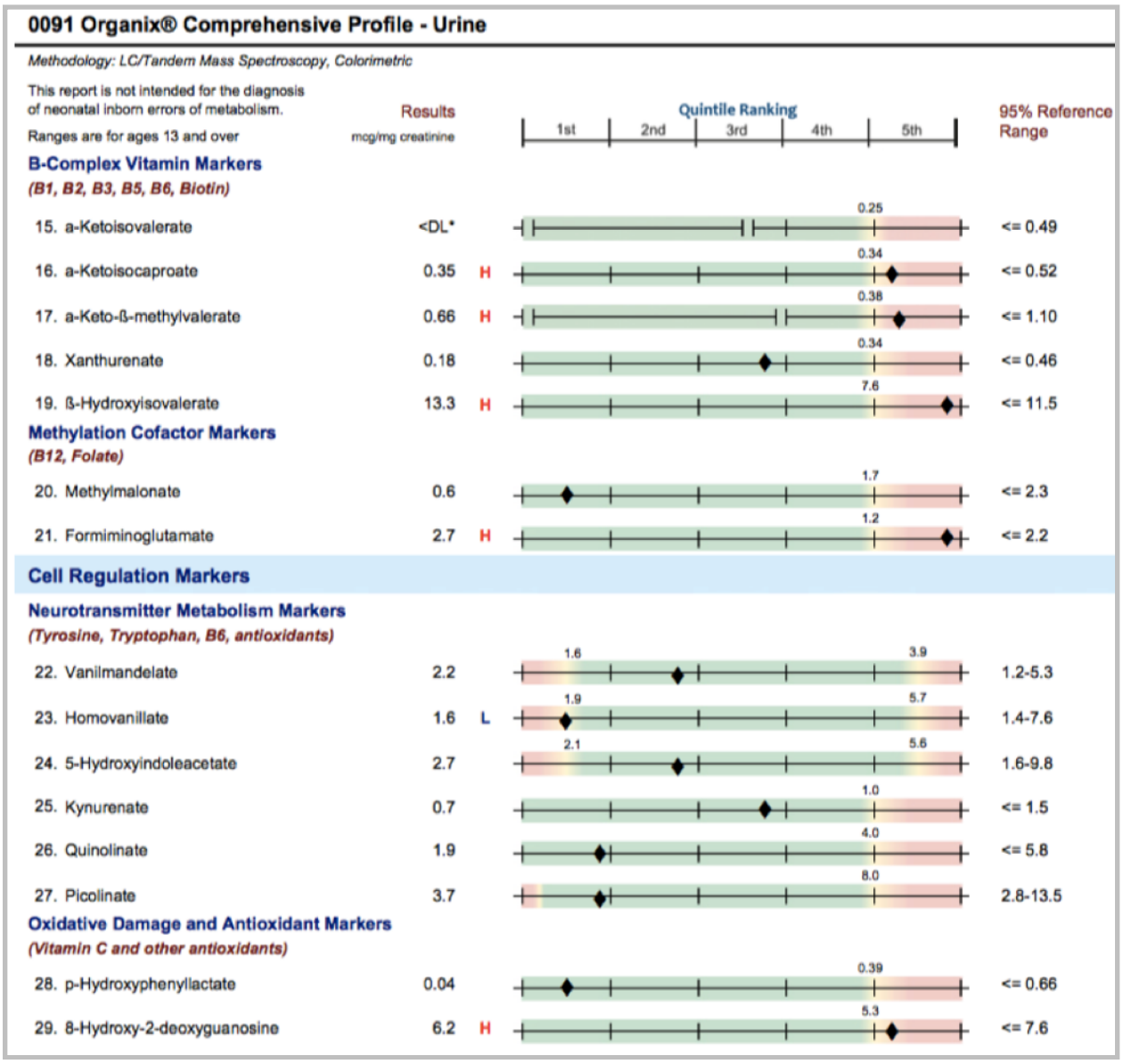
Marker	Value	Functional Range	Lab Range
Glucose	87	75 - 90	65 - 99
Hemoglobin A1c	5.8	4.8 – 5.4	4.8 - 5.6
Uric Acid	4.4	3.2 - 5.5	2.5 - 7.1
BUN	12	13 – 18	6 - 24
Creatinine	0.92	0.85 – 1.1	0.57 - 1
BUN/Creatinine Ratio	13	9 – 23	9 - 23
Sodium	141	134 – 140	134 - 144
Potassium	4.5	4.0 – 4.5	3.5 - 5.2
Chloride	102	100 – 106	97 - 108
C02	23	25 – 30	18 - 29
Calcium	9.5	9.2 – 10.1	8.7 - 10.2
Phosphorus	4.2	3.5 – 4.0	2.5 - 4.5
Magnesium	2.3	2.0 – 2.6	1.6 - 2.3
Protein, total	6.9	6.9 – 7.4	6.0 - 8.5
Albumin	4.3	4.0 – 5.0	3.5 - 5.5
Globulin	2.6	2.4 – 2.8	1.5 - 4.5
A/G ratio	1.7	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.6	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	57	42 – 107	39 - 117
LDH	142	140 - 180	119 - 226
AST	15	10 - 30	0 - 40
ALT	11	10 - 22	0 - 32
GGT	15	0 - 28	0 - 60
TIBC	351	250 – 350	250 - 450
UIBC	194	150 - 375	131 - 425
Iron	157	85 – 135	27 - 159
Iron saturation	45	15 – 45	15 - 55
Ferritin	28	15 - 120	15 - 150
Vitamin B-12	222	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	9.7	35 - 60	30.0 - 100.0
Cholesterol, total	157	150 - 250	100 - 199
Triglycerides	59	50 – 100	0 - 149
HDL	54	55 – 85	> 39
LDL	91	0 - 175	0 - 99
T. Chol / HDL Ratio	2.9	< 3	0 - 4.4
Triglycerides / HDL Ratio	1.09	< 2	< 3.8
CRP-hs	0.09	< 1.0	0.00 - 3.00
Homocysteine	18.2	< 7.0	0.0 - 15.0

Marker	Value	Functional Range	Lab Range
TSH	1.790	0.5 – 2.5	0.45 - 4.50
T4, total	6.8	6.0 – 12	4.5 - 12
T3 Uptake	26	28 - 35	24 - 39
T3, Total	104	100 – 180	71 - 180
Copper	92		72 - 166
Zinc	65		56 - 134
Zinc / Copper Ratio	0.71	> 0.85	
Serum Methylmalonic Acid (MMA)	645	0 - 325	0 - 378
WBC	3.6	5.0 – 8.0	3.4 - 10.8
RBC	4.44	4.4 – 4.9	3.77 - 5.28
Hemoglobin	12.5	13.5 - 14.5	11.1 - 15.9
Hematocrit	38.5	37 - 44	34 - 46.6
MCV	87	85 – 92	79 - 97
MCH	28.2	27.7 – 32.0	26.6 - 33.0
MCHC	32.5	32 – 35	31.5 - 35.7
RDW	14.2	11.5 – 15.0	12.3 - 15.4
Platelets	261	150 – 415	150 - 379
Neutrophils	49	40 – 60	
Lymphocytes	34	25 – 40	
Monocytes	9	4.0 – 7.0	
Eosinophils	7	0.0 – 3.0	
Basophils	1	0.0 – 3.0	

If you look at her B12, it is almost out of the lab range at 222. The lab range is 211 on the bottom. Serum methylmalonic acid is high at 645. That's quite high. The lab range only goes up to 378, and the functional range is 345, so that is very high. Homocysteine is very high at 18.2, out of the lab range. Red blood cells are normal, but hemoglobin is functionally low at 12.5. This is a pretty clear case of B12-deficient functional anemia, possibly folate deficiency too. You can't tell with these labs because we didn't have a serum folate on her, so you would need to run FIGLU and possibly serum and red blood cell folate or more advanced methylation testing in order to determine that. You can see her vitamin D level, by the way, which is 9.7, one of the lowest that I've seen. This is a patient who is clearly being adversely affected by her dietary choices. Again, I don't try to convince patients that they should follow a Paleo diet necessarily, but I do educate them about the effects of their dietary choices and talk to them about what I think a more appropriate choice might be given the lab results and given the fact that they have come to me for advice on optimizing their health.

Gene & Variation	rsID	Alleles	Result
COMT V158M	rs4680	AG	+/-
COMT H62H	rs4633	CT	+/-
COMT P199P	rs769224	GG	-/-
VDR Bsm	rs1544410	CT	+/-
VDR Taq	rs731236	AG	+/-
MAO A R297R	rs6323	GT	+/-
ACAT1-02	rs3741049	GG	-/-
MTHFR C677T	rs1801133	AA	+/+
MTHFR 03 P39P	rs2066470	GG	-/-
MTHFR A1298C	rs1801131	TT	-/-
MTR A2756G	rs1805087	AA	-/-
MTRR A66G	rs1801394	AG	+/-
MTRR H595Y	rs10380	CC	-/-
MTRR K350A	rs162036	AA	-/-
MTRR R415T	rs2287780	CT	+/-
MTRR A664A	rs1802059	GG	-/-
BHMT-02	rs567754	TT	+/+
BHMT-04	rs617219	AC	+/-
BHMT-08	rs651852	CT	+/-
AHCY-01	rs819147	TT	-/-
AHCY-02	rs819134	AA	-/-
AHCY-19	rs819171	TT	-/-
CBS C699T	rs234706	GG	-/-
CBS A360A	rs1801181	AG	+/-
CBS N212N	rs2298758	GG	-/-
SHMT1 C1420T	rs1979277	GG	-/-

This patient was homozygous for MTHFR C677T and heterozygous for many other polymorphisms that can affect methylation. If you see someone who has markers for megaloblastic anemia and MTHFR mutations, you probably should test their folate as well as their B12.



0091 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

This report is not intended for the diagnosis of neonatal inborn errors of metabolism.
Ranges are for ages 13 and over

	Results (mcg/mg creatinine)		Quintile Ranking (1st–5th)	95% Reference Range
B-Complex Vitamin Markers *(B1, B2, B3, B5, B6, Biotin)*				
15. a-Ketoisovalerate	<DL*		0.25	<= 0.49
16. a-Ketoisocaproate	0.35	H	0.34	<= 0.52
17. a-Keto-ß-methylvalerate	0.66	H	0.38	<= 1.10
18. Xanthurenate	0.18		0.34	<= 0.46
19. ß-Hydroxyisovalerate	13.3	H	7.6	<= 11.5
Methylation Cofactor Markers *(B12, Folate)*				
20. Methylmalonate	0.6		1.7	<= 2.3
21. Formiminoglutamate	2.7	H	1.2	<= 2.2
Cell Regulation Markers				
Neurotransmitter Metabolism Markers *(Tyrosine, Tryptophan, B6, antioxidants)*				
22. Vanilmandelate	2.2		1.6 – 3.9	1.2-5.3
23. Homovanillate	1.6	L	1.9 – 5.7	1.4-7.6
24. 5-Hydroxyindoleacetate	2.7		2.1 – 5.6	1.6-9.8
25. Kynurenate	0.7		1.0	<= 1.5
26. Quinolinate	1.9		4.0	<= 5.8
27. Picolinate	3.7		8.0	2.8-13.5
Oxidative Damage and Antioxidant Markers *(Vitamin C and other antioxidants)*				
28. p-Hydroxyphenyllactate	0.04		0.39	<= 0.66
29. 8-Hydroxy-2-deoxyguanosine	6.2	H	5.3	<= 7.6

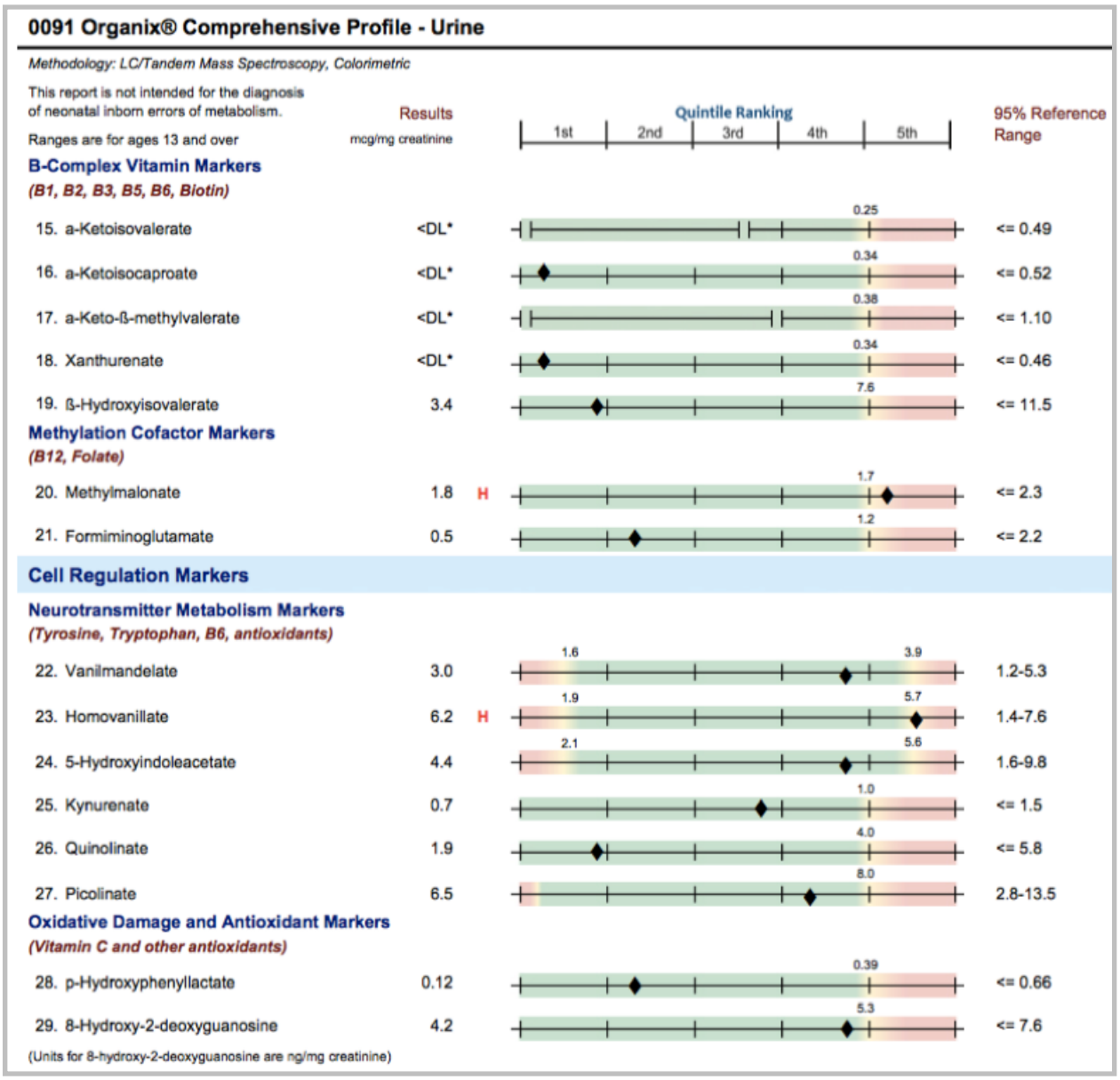
We did test her folate. That is part of our basic case review workup, and her FIGLU, as you can see here, is high. The upper end of the range is 2.2, and she is at 2.7. For some reason, her urinary methylmalonic acid was low, whereas her serum was high. That is unusual, but it highlights the need to run both of those markers in some cases.

The next patient is a 53-year-old female with chief complaint of GI issues, hypothyroidism, hypotension, hair loss, irritability, and decreased libido.

Marker	Value	Functional Range	Lab Range
Glucose	84	75 – 90	65 - 99
Hemoglobin A1c	5.3	4.4 – 5.4	4.8 - 5.6
Uric Acid	4.8	3.2 - 5.5	2.5 - 7.1
BUN	11	13 – 18	6 - 24
Creatinine	0.76	0.85 – 1.1	0.57 - 1
Sodium	143	135 – 140	134 - 144
Potassium	4.3	4.0 – 4.5	3.5 - 5.2
Chloride	103	100 – 106	97 - 108
C02	26	25 – 30	18 - 29
Calcium	8.9	9.2 – 10.1	8.7 - 10.2
Phosphorus	4.1	3.5 – 4.0	2.5 - 4.5
Magnesium	2.2	2.0 – 2.6	1.6 - 2.6
Protein, total	7.0	6.9 – 7.4	6.0 - 8.5
Albumin	4.2	4.0 – 5.0	3.5 - 5.5
Globulin	2.8	2.4 – 2.8	1.5 - 4.5
A/G ratio	1.5	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.4	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	68	42 – 107	39 - 117
LDH	150	140 - 180	119 - 226
AST	16	10 - 30	0 - 40
ALT	17	10 - 22	0 - 32
GGT	10	0 - 28	0 - 60
TIBC	282	250 – 350	250 - 450
UIBC	205	150 - 375	150 - 375
Iron	77	85 – 135	35 - 155
Iron saturation	27	15 – 40	15 - 55
Ferritin	85	MW: 30 - 150	15 - 150
Cholesterol, total	183	150 – 250	100 - 199
Triglycerides	35	50 – 100	0 - 149
HDL	59	55 – 85	> 39
LDL	117	0 – 175	0 - 99
T. Chol / HDL Ratio	3.1	< 3	0 4.4
Triglycerides / HDL Ratio	0.59	< 2	< 3.8
TSH	1.830	0.5 – 2.5	0.45 - 4.50
T4, total	5.9	6.0 – 12	4.5 - 12
T3 Uptake	30	28 - 35	24 - 39
T3, Total	89	100 – 180	71 - 180
Vitamin D, 25-hydroxy	13.2	35 - 60	30 - 100

Marker	Value	Functional Range	Lab Range
WBC	5.8	5.0 – 8.0	3.4 - 10.8
RBC	4.18	4.4 – 4.9	3.77 - 5.28
Hemoglobin	12.8	13.5 - 14.5	11.1 - 15.9
Hematocrit	40.2	37 - 44	34 - 46.6
MCV	96	85 – 92	79 - 97
MCH	30.6	27.7 – 32.0	26.6 - 33.0
MCHC	31.8	32 – 35	31.5 - 35.7
RDW	13.1	11.5 – 15.0	12.3 - 15.4
Platelets	254	150 – 415	150 - 379
Neutrophils	52	40 – 60	
Lymphocytes	36	25 – 40	
Monocytes	7	4.0 – 7.0	
Eosinophils	4	0.0 – 3.0	
Basophils	1	0.0 – 3.0	
Additional Tests:			
T3, Free	2.7	2.5 - 4.0	2 - 4.4
T4, Free	1.04	1 - 1.5	0.82 - 1.77
Thyroid – TPO Ab	6		0 - 34
Thyroid – TGA	<1.0		0 - 0.9
CRP-hs	1.1	< 1.0	0.00 - 3.00
Homocysteine	6.9	< 9.0	0.0 - 15.0
Vitamin B-12	645	450 – 2000	211 - 946

Her red blood cells and hemoglobin were functionally low. MCV and MCHC were functionally high. Homocysteine and B12 were normal in the serum.



0091 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

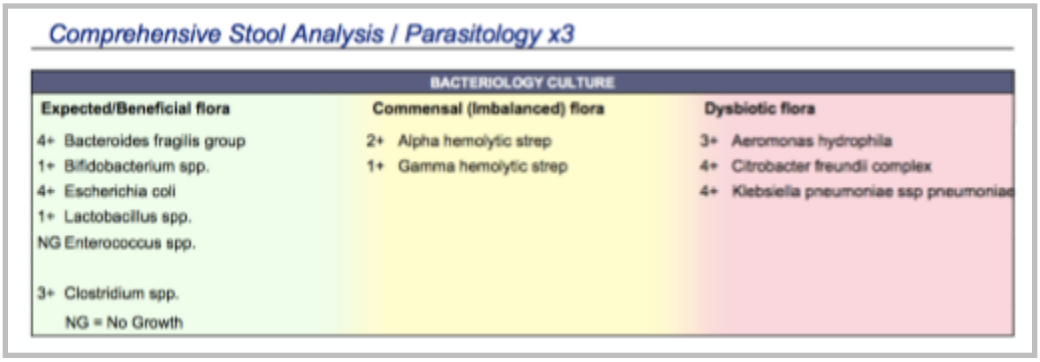
This report is not intended for the diagnosis of neonatal inborn errors of metabolism.

Ranges are for ages 13 and over

	Results (mcg/mg creatinine)		Quintile Ranking (1st–5th)	95% Reference Range
B-Complex Vitamin Markers *(B1, B2, B3, B5, B6, Biotin)*				
15. a-Ketoisovalerate	<DL*		0.25	<= 0.49
16. a-Ketoisocaproate	<DL*		0.34	<= 0.52
17. a-Keto-ß-methylvalerate	<DL*		0.38	<= 1.10
18. Xanthurenate	<DL*		0.34	<= 0.46
19. ß-Hydroxyisovalerate	3.4		7.6	<= 11.5
Methylation Cofactor Markers *(B12, Folate)*				
20. Methylmalonate	1.8	H	1.7	<= 2.3
21. Formiminoglutamate	0.5		1.2	<= 2.2
Cell Regulation Markers				
Neurotransmitter Metabolism Markers *(Tyrosine, Tryptophan, B6, antioxidants)*				
22. Vanilmandelate	3.0		1.6 – 3.9	1.2-5.3
23. Homovanillate	6.2	H	1.9 – 5.7	1.4-7.6
24. 5-Hydroxyindoleacetate	4.4		2.1 – 5.6	1.6-9.8
25. Kynurenate	0.7		1.0	<= 1.5
26. Quinolinate	1.9		4.0	<= 5.8
27. Picolinate	6.5		8.0	2.8-13.5
Oxidative Damage and Antioxidant Markers *(Vitamin C and other antioxidants)*				
28. p-Hydroxyphenyllactate	0.12		0.39	<= 0.66
29. 8-Hydroxy-2-deoxyguanosine	4.2		5.3	<= 7.6

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

Check out her urinary methylmalonic acid. It's high at 1.8. It is in the lab range that Genova offers, but remember back in the B12 unit, I suggested 1.5 as the cut point.



Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE		
Expected/Beneficial flora	**Commensal (Imbalanced) flora**	**Dysbiotic flora**
4+ Bacteroides fragilis group	2+ Alpha hemolytic strep	3+ Aeromonas hydrophila
1+ Bifidobacterium spp.	1+ Gamma hemolytic strep	4+ Citrobacter freundii complex
4+ Escherichia coli		4+ Klebsiella pneumoniae ssp pneumoniae
1+ Lactobacillus spp.		
NG Enterococcus spp.		
3+ Clostridium spp.		
NG = No Growth		

She also has significant dysbiosis on the Doctor's Data stool test, both insufficiency and pathogenic dysbiosis. In this situation, it's really surprising that homocysteine isn't elevated given her high methylmalonic acid, and again, it's a reminder of the importance of using several markers in the assessment.

Gene & Variation	rsID	Alleles	Result
COMT V158M	rs4680	AA	+/+
COMT H62H	rs4633	TT	+/+
COMT P199P	rs769224	GG	-/-
VDR Bsm	rs1544410	TT	+/+
VDR Taq	rs731236	GG	-/-
MAO-A R297R	rs6323	GG	-/-
ACAT1-02	rs3741049	GG	-/-
MTHFR C677T	rs1801133	AA	+/+
MTHFR 03 P39P	rs2066470	GG	-/-
MTHFR A1298C	rs1801131	TT	-/-
MTR A2756G	rs1805087	AA	-/-
MTRR A66G	rs1801394	AG	+/-
MTRR H595Y	rs10380	__	no call
MTRR K350A	rs162036	AG	+/-
MTRR R415T	rs2287780	__	no call
MTRR A664A	rs1802059	GG	-/-
BHMT-02	rs567754	CC	-/-
BHMT-04	rs617219	__	no call
BHMT-08	rs651852	CC	-/-
AHCY-01	rs819147	TT	-/-
AHCY-02	rs819134	__	no call
AHCY-19	rs819171	TT	-/-
CBS C699T	rs234706	GG	-/-
CBS A360A	rs1801181	AG	+/-
CBS N212N	rs2298758	__	no call
SHMT1 C1420T	rs1979277	__	no call

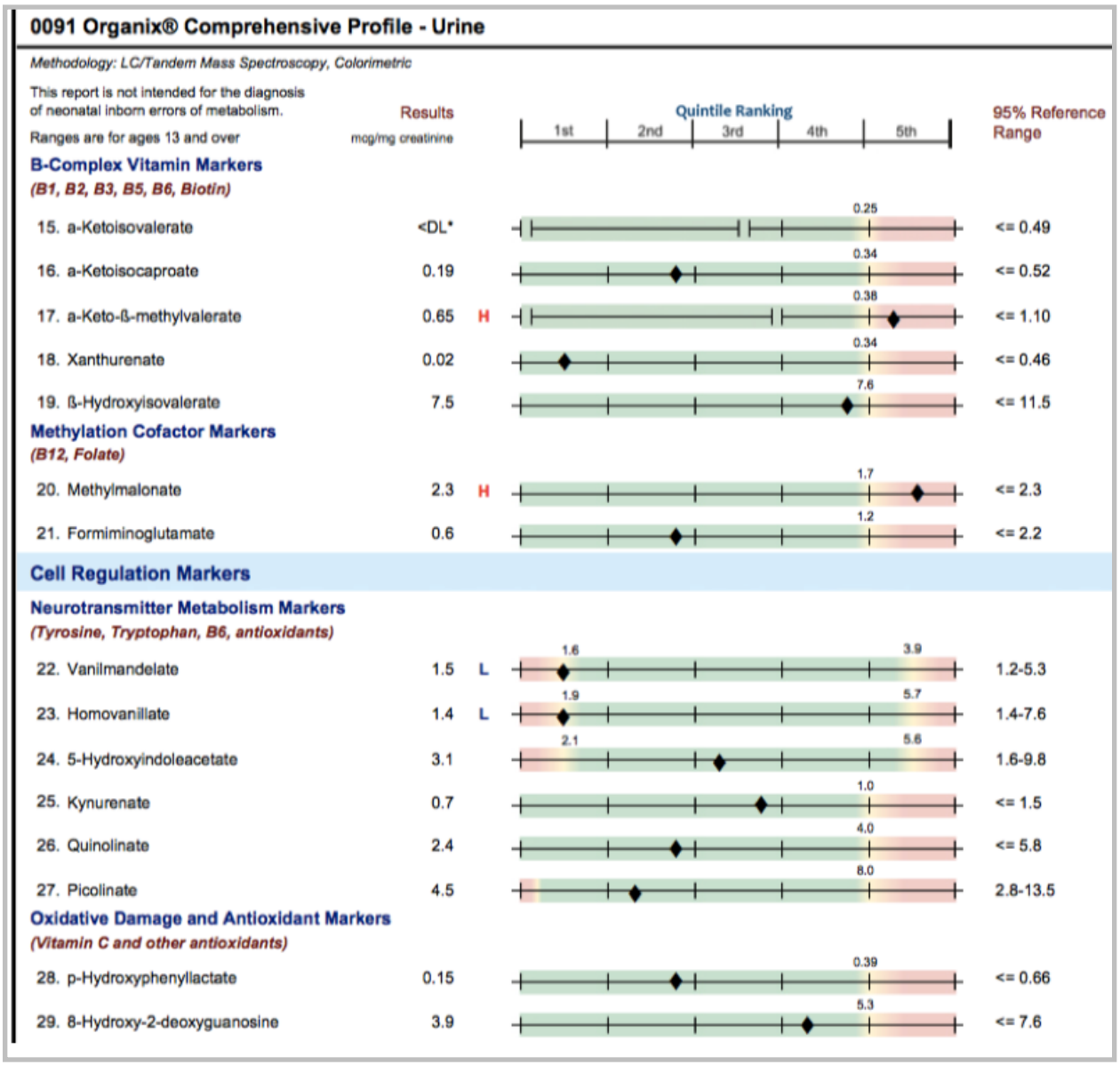
Her gene panel showed that she was also homozygous for MTHFR as well as two variants of COMT and VDR BSM. In this case, MTHFR is not clearly causing folate deficiency because her homocysteine and FIGLU are normal. This is a reminder, and I'm going to be—you've probably already heard me say this maybe in other venues, but I'm going to say it here multiple times—which is that genes don't tell the whole story. We talked about homozygosity for C677T reducing enzyme activity by 70 to 75 percent. That sounds like a lot, and it is, but in some cases, that remaining 25 to 30 percent enzyme activity is going to be sufficient when the patient is following a nutrient-dense diet, and they don't have a lot of significant environmental challenges affecting their methylation or other SNPs that are affecting their methylation. This is why I have such a problem with the idea of just running a gene panel and making supplement recommendations on the basis of only genetic results. I think that is irresponsible and not supported by the scientific literature.

The next patient is a 43-year-old female with chief complaint of chronic postnasal drip, lichen sclerosus, difficulty conceiving, slow healing from injuries, and wanting to improve overall health.

Marker	Value	Functional Range	Lab Range
Glucose	84	75 – 90	65 - 99
Hemoglobin A1c	5.5	4.4 – 5.4	4.8 - 5.6
Uric Acid	4.5	3.2 - 5.5	2.5 - 7.1
BUN	13	13 – 18	6 - 24
Creatinine	0.90	0.85 – 1.1	0.57 - 1
Sodium	139	135 – 140	134 - 144
Potassium	4.4	4.0 – 4.5	3.5 - 5.2
Chloride	99	100 – 106	97 - 108
C02	23	25 – 30	18 - 29
Calcium	9.1	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.8	3.5 – 4.0	2.5 - 4.5
Magnesium	1.8	2.0 – 2.6	1.6 - 2.6
Protein, total	6.7	6.9 – 7.4	6.0 - 8.5
Albumin	4.5	4.0 – 5.0	3.5 - 5.5
Globulin	2.2	2.4 – 2.8	1.5 - 4.5
A/G ratio	2.0	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.5	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	41	42 – 107	39 - 117
LDH	134	140 - 180	119 - 226
AST	20	10 - 30	0 - 40
ALT	22	10 - 22	0 - 32
GGT	10	0 - 28	0 - 60
TIBC	267	250 – 350	250 - 450
UIBC	163	150 - 375	150 - 375
Iron	104	85 – 135	35 - 155
Iron saturation	39	15 – 45	15 - 55
Ferritin	70	15 - 120	15 - 150
Cholesterol, total	197	150 – 250	100 - 199
Triglycerides	55	50 – 100	0 - 149
HDL	56	55 – 85	> 39
LDL	130	0 – 175	0 - 99
T. Chol / HDL Ratio	3.5	< 3	0 - 4.4
Triglycerides / HDL Ratio	0.98	< 2	< 3.8
TSH	2.150	0.5 – 2.5	0.45 - 4.50
T4, total	7.6	6.0 – 12	4.5 - 12.0
T3 Uptake	31	28 - 35	24 - 39
T3, Total	80	100 – 180	71 - 180
Vitamin D, 25-hydroxy	44.5	35 - 60	30.0 - 100.0

Marker	Value	Functional Range	Lab Range
WBC	5.0	5.0 – 8.0	3.4 - 10.8
RBC	4.53	4.4 – 4.9	3.77 - 5.28
Hemoglobin	13.3	13.5 - 14.5	11.1 - 15.9
Hematocrit	41.5	37 - 44	34.0 - 46.6
MCV	92	85 – 92	79 - 97
MCH	29.4	27.7 – 32.0	26.6 - 33.0
MCHC	32	32 – 35	31.5 - 35.7
RDW	13.3	11.5 – 15.0	12.3 - 15.4
Platelets	219	150 – 415	150 - 379
Neutrophils	66	40 – 60	
Lymphocytes	23	25 – 40	
Monocytes	8	4.0 – 7.0	
Eosinophils	3	0.0 – 3.0	
Basophils	0	0.0 – 3.0	
Additional Tests:			
CRP-hs	1.3	< 1.0	0.00 - 3.00
Homocysteine	6.9	< 9.0	0.0 - 15.0
Vitamin B-12	342	450 – 2000	211 - 946
Copper	107		72 - 166
Zinc	103		56 - 134
Zinc / Copper Ratio	0.96	> 0.85	
Serum Methylmalonic Acid (MMA)	166	0 - 325	0 - 378

B12 is borderline low. Hemoglobin is very slightly below the functional range, but otherwise, as you can see, aside from a few markers that are just outside of the functional range, there aren't really very many patterns that are of concern here.



0091 Organix® Comprehensive Profile - Urine

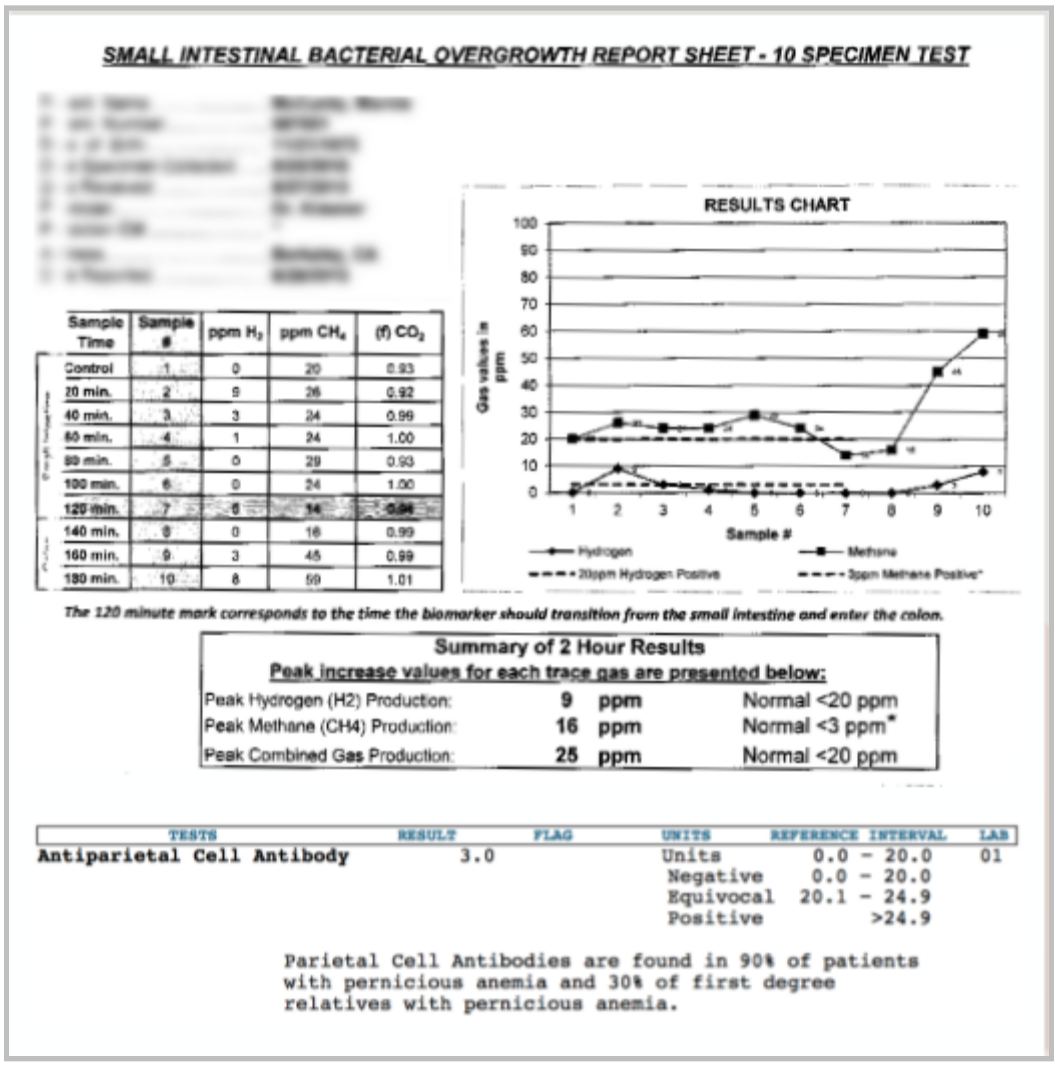
Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

This report is not intended for the diagnosis of neonatal inborn errors of metabolism.

Ranges are for ages 13 and over

	Results		Quintile Ranking (1st 2nd 3rd 4th 5th)	95% Reference Range
	mcg/mg creatinine			
B-Complex Vitamin Markers *(B1, B2, B3, B5, B6, Biotin)*				
15. a-Ketoisovalerate	<DL*		0.25	<= 0.49
16. a-Ketoisocaproate	0.19		0.34	<= 0.52
17. a-Keto-ß-methylvalerate	0.65	H	0.38	<= 1.10
18. Xanthurenate	0.02		0.34	<= 0.46
19. ß-Hydroxyisovalerate	7.5		7.6	<= 11.5
Methylation Cofactor Markers *(B12, Folate)*				
20. Methylmalonate	2.3	H	1.7	<= 2.3
21. Formiminoglutamate	0.6		1.2	<= 2.2
Cell Regulation Markers				
Neurotransmitter Metabolism Markers *(Tyrosine, Tryptophan, B6, antioxidants)*				
22. Vanilmandelate	1.5	L	1.6 – 3.9	1.2-5.3
23. Homovanillate	1.4	L	1.9 – 5.7	1.4-7.6
24. 5-Hydroxyindoleacetate	3.1		2.1 – 5.6	1.6-9.8
25. Kynurenate	0.7		1.0	<= 1.5
26. Quinolinate	2.4		4.0	<= 5.8
27. Picolinate	4.5		8.0	2.8-13.5
Oxidative Damage and Antioxidant Markers *(Vitamin C and other antioxidants)*				
28. p-Hydroxyphenyllactate	0.15		0.39	<= 0.66
29. 8-Hydroxy-2-deoxyguanosine	3.9		5.3	<= 7.6

Her Organix test showed pretty high MMA at 2.3, so it's almost out of the lab range, definitely B12 deficiency.



SMALL INTESTINAL BACTERIAL OVERGROWTH REPORT SHEET - 10 SPECIMEN TEST

[redacted]

Sample Time	Sample #	ppm H_2	ppm CH_4	(f) CO_2
Control	1	0	20	0.93
20 min.	2	9	26	0.92
40 min.	3	3	24	0.99
60 min.	4	1	24	1.00
80 min.	5	0	29	0.93
100 min.	6	0	24	1.00
120 min.	7	6	14	0.94
140 min.	8	0	16	0.99
160 min.	9	3	45	0.99
180 min.	10	8	59	1.01

RESULTS CHART

Gas values in ppm

Sample #

Hydrogen — Methane — 20ppm Hydrogen Positive — 3ppm Methane Positive*

The 120 minute mark corresponds to the time the biomarker should transition from the small intestine and enter the colon.

Summary of 2 Hour Results

Peak increase values for each trace gas are presented below:

Peak Hydrogen (H2) Production:	9 ppm	Normal <20 ppm
Peak Methane (CH4) Production:	16 ppm	Normal <3 ppm*
Peak Combined Gas Production:	25 ppm	Normal <20 ppm

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Antiparietal Cell Antibody	3.0		Units	0.0 - 20.0	01
			Negative	0.0 - 20.0	
			Equivocal	20.1 - 24.9	
			Positive	>24.9	

Parietal Cell Antibodies are found in 90% of patients with pernicious anemia and 30% of first degree relatives with pernicious anemia.

Then, her SIBO results were positive for methane-predominant SIBO. Because her MMA is so high and serum B12 was borderline low, we ran intrinsic factor and antiparietal cell antibodies. Only antiparietal cell antibodies are pictured here, but they were both negative. This is not full-blown macrocytic anemia, but if B12 deficiency continued, it may become that over time, and our job as functional medicine practitioners is to catch things as early on in the process as possible because they are easier to treat that way.

The next patient is a 25-year-old female with chief complaint of digestive problems, brain fog, and food intolerances.

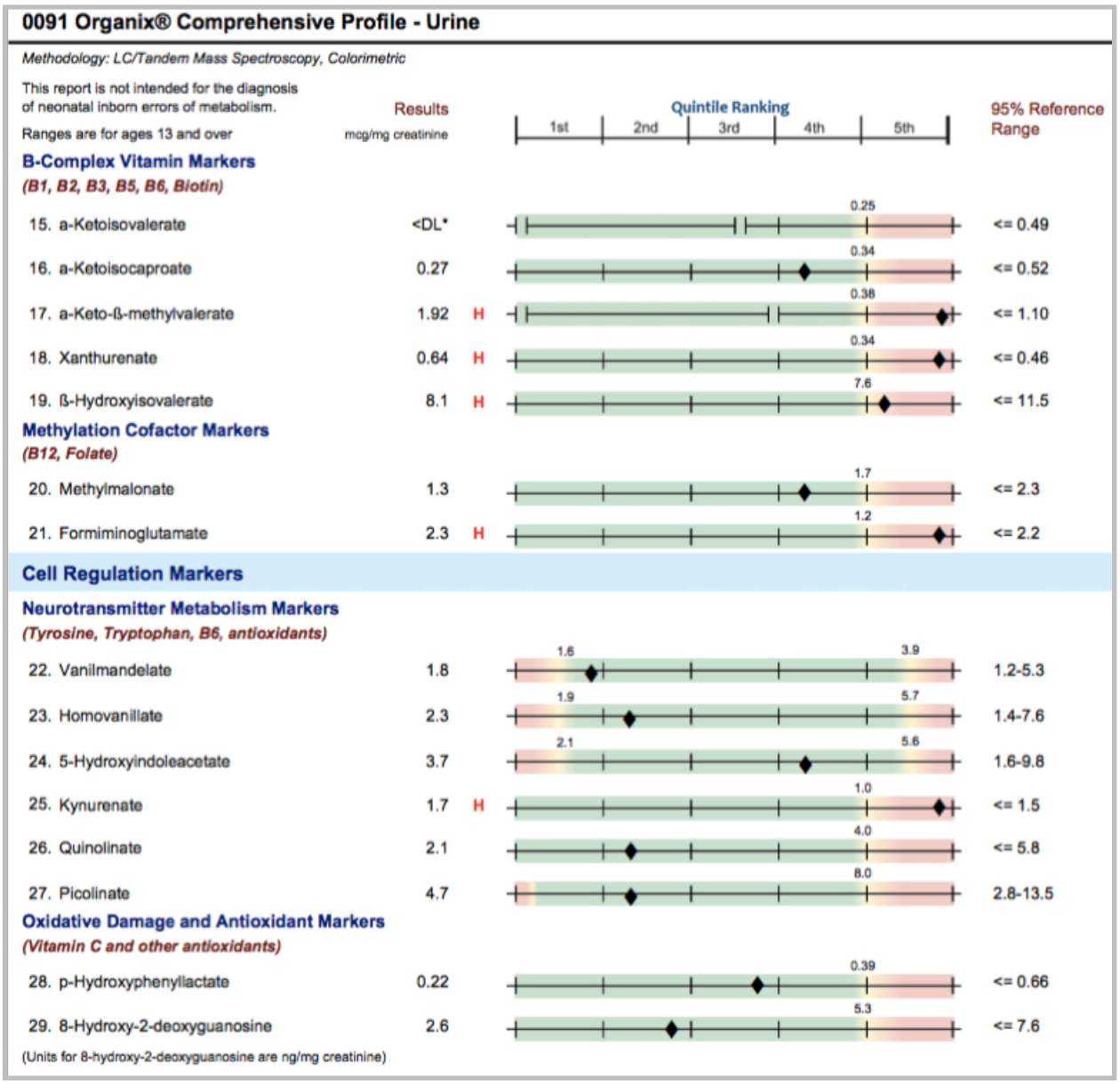
Marker	Value	Functional Range	Lab Range
Glucose	92	75 – 90	65 - 99
Hemoglobin A1c	5.1	4.4 – 5.4	4.8 - 5.6
Uric Acid	4.9	3.2 - 5.5	2.5 - 7.1
BUN	11	13 – 18	6 - 20
Creatinine	0.92	0.85 – 1.1	0.57 - 1
Sodium	138	135 – 140	134 - 144
Potassium	4.4	4.0 – 4.5	3.5 - 5.2
Chloride	102	100 – 106	97 - 108
C02	22	25 – 30	18 - 29
Calcium	9.7	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.8	3.5 – 4.0	2.5 - 4.5
Magnesium	2.2	2.0 – 2.6	1.6 - 2.6
Protein, total	6.9	6.9 – 7.4	6.0 - 8.5
Albumin	4.5	4.0 – 5.0	3.5 - 5.5
Globulin	2.4	2.4 – 2.8	1.5 - 4.5
A/G ratio	1.9	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.7	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	46	42 – 107	39 - 117
LDH	109	140 - 180	119 - 226
AST	15	10 - 30	0 - 40
ALT	9	10 - 22	0 - 32
GGT	14	0 - 28	0 - 60
TIBC	330	250 – 350	250 - 450
UIBC	141	150 - 375	150 - 375
Iron	189	85 – 135	35 - 155
Iron saturation	57	15 – 45	15 - 55
Ferritin	91	15 - 120	15 - 150
Cholesterol, total	212	150 – 250	100 - 189
Triglycerides	76	50 – 100	0 - 149
HDL	87	55 – 85	> 39
LDL	110	0 – 175	0 - 119
T. Chol / HDL Ratio	2.4	< 3	0 - 4.4
Triglycerides / HDL Ratio	0.87	< 2	< 3.8
TSH	2.330	0.5 – 2.5	0.45 - 4.50
T4, total	9.2	6.0 – 12	4.5 - 12.0
T3 Uptake	31	28 - 35	24 - 39
T3, Total	102	100 – 180	71 - 180
Vitamin D, 25-hydroxy	34.2	35 - 60	30.0 - 100.0

Marker	Value	Functional Range	Lab Range
WBC	5.2	5.0 – 8.0	3.4 - 10.8
RBC	4.43	4.4 – 4.9	3.77 - 5.28
Hemoglobin	13.8	13.5 - 14.5	11.1 - 15.9
Hematocrit	41.7	37 - 44	34.0 - 46.6
MCV	94	85 – 92	79 - 97
MCH	31.2	27.7 – 32.0	26.6 - 33.0
MCHC	33.1	32 – 35	31.5 - 35.7
RDW	12.3	11.5 – 15.0	12.3 - 15.4
Platelets	215	150 – 415	150 - 379
Neutrophils	50	40 – 60	
Lymphocytes	41	25 – 40	
Monocytes	7	4.0 – 7.0	
Eosinophils	1	0.0 – 3.0	
Basophils	1	0.0 – 3.0	
Additional Tests:			
CRP-hs	1	< 1.0	0.00 - 3.00
Homocysteine	10.8	< 9.0	0.0 - 15.0
Vitamin B-12	244	450 – 2000	211 - 946
Copper	133		72 - 166
Zinc	114		56 - 134
Zinc / Copper Ratio	0.86	> 0.85	
Serum Methylmalonic Acid (MMA)	72	0 - 325	0 - 378

Serum B12 is almost below the lab range at 244. Homocysteine is functionally high at 10.8, and red blood cell indices are normal except MCV, which is functionally high at 94. Also note that she has iron overload as well, with iron saturation at 57 percent. Serum iron is lab-high at 189, and UIBC is lab-low at 141.

Gene & Variation	rsID	Alleles	Result
COMT V158M	rs4680	AG	+/-
COMT H62H	rs4633	CT	+/-
COMT P199P	rs769224	GG	-/-
VDR Bsm	rs1544410	CT	+/-
VDR Taq	rs731236	AG	+/-
MAO A R297R	rs6323	GT	+/-
ACAT1-02	rs3741049	GG	-/-
MTHFR C677T	rs1801133	AA	+/+
MTHFR 03 P39P	rs2066470	GG	-/-
MTHFR A1298C	rs1801131	TT	-/-
MTR A2756G	rs1805087	AA	-/-
MTRR A66G	rs1801394	AG	+/-
MTRR H595Y	rs10380	CC	-/-
MTRR K350A	rs162036	AA	-/-
MTRR R415T	rs2287780	CT	+/-
MTRR A664A	rs1802059	GG	-/-
BHMT-02	rs567754	TT	+/+
BHMT-04	rs617219	AC	+/-
BHMT-08	rs651852	CT	+/-
AHCY-01	rs819147	TT	-/-
AHCY-02	rs819134	AA	-/-
AHCY-19	rs819171	TT	-/-
CBS C699T	rs234706	GG	-/-
CBS A360A	rs1801181	AG	+/-
CBS N212N	rs2298758	GG	-/-
SHMT1 C1420T	rs1979277	GG	-/-

At this point, I was suspicious of B12 deficiency given her low serum B12 and high homocysteine, but we still didn't know about folate. We didn't have serum or red blood cell folate for her. We did have her genetic panel, which showed that she was homozygous for MTHFR C677T and heterozygous for a number of other SNPs.



0091 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

This report is not intended for the diagnosis of neonatal inborn errors of metabolism.
Ranges are for ages 13 and over

	Results (mcg/mg creatinine)		Quintile Ranking (1st 2nd 3rd 4th 5th)	95% Reference Range
B-Complex Vitamin Markers *(B1, B2, B3, B5, B6, Biotin)*				
15. a-Ketoisovalerate	<DL*		0.25	<= 0.49
16. a-Ketoisocaproate	0.27		0.34	<= 0.52
17. a-Keto-ß-methylvalerate	1.92	H	0.38	<= 1.10
18. Xanthurenate	0.64	H	0.34	<= 0.46
19. ß-Hydroxyisovalerate	8.1	H	7.6	<= 11.5
Methylation Cofactor Markers *(B12, Folate)*				
20. Methylmalonate	1.3		1.7	<= 2.3
21. Formiminoglutamate	2.3	H	1.2	<= 2.2
Cell Regulation Markers				
Neurotransmitter Metabolism Markers *(Tyrosine, Tryptophan, B6, antioxidants)*				
22. Vanilmandelate	1.8		1.6 – 3.9	1.2-5.3
23. Homovanillate	2.3		1.9 – 5.7	1.4-7.6
24. 5-Hydroxyindoleacetate	3.7		2.1 – 5.6	1.6-9.8
25. Kynurenate	1.7	H	1.0	<= 1.5
26. Quinolinate	2.1		4.0	<= 5.8
27. Picolinate	4.7		8.0	2.8-13.5
Oxidative Damage and Antioxidant Markers *(Vitamin C and other antioxidants)*				
28. p-Hydroxyphenyllactate	0.22		0.39	<= 0.66
29. 8-Hydroxy-2-deoxyguanosine	2.6		5.3	<= 7.6

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

I suspected she may be folate deficient as well as B12 deficient. Again, this is where the urine organic acids can come in handy. Her FIGLU was 2.3, which is high. The upper end of the range is 2.2. Her methylmalonic acid was 1.3. That is below the suggested cut point but at the upper end of the range.

INFLAMMATION

	Within	Outside	Reference Range
Lactoferrin	3.6		< 7.3 µg/mL
Calprotectin*	23		<= 50 µg/g
Lysozyme*		2190	<= 600 ng/mL
White Blood Cells	None		None - Rare
Mucus	Neg		Neg

Lactoferrin and **Calprotectin** are reliable markers for differentiating organic inflammation (IBD) from function symptoms (IBS) and for management of IBD. Monitoring levels of fecal lactoferrin and calprotectin can play an essential role in determining the effectiveness of therapy, are good predictors of IBD remission, and can indicate a low risk of relapse. **Lysozyme*** is an enzyme secreted at the site of inflammation in the GI tract and elevated levels have been identified in IBD patients. **White Blood Cells** (WBC) and **Mucus** in the stool can occur with bacterial and parasitic infections, with mucosal irritation, and inflammatory bowel diseases such as Crohn's disease or ulcerative colitis.

IMMUNOLOGY

	Within	Outside	Reference Range
Secretory IgA*		888	51 - 204 mg/dL

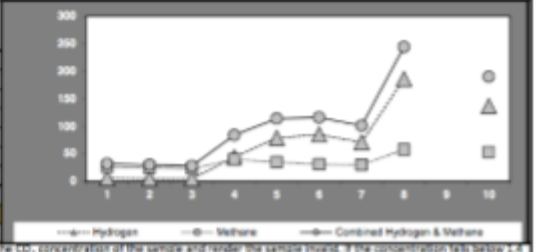
Secretory IgA* (sIgA) is secreted by mucosal tissue and represents the first line of defense of the GI mucosa and is central to the normal function of the GI tract as an immune barrier. Elevated levels of sIgA have been associated with an upregulated immune response.

This patient had significant gut inflammation. Her lysozyme was 2,190. The upper end of that range is 600, if you recall from the gut unit, and her secretory IgA was 888, which is very high, as 204 is the upper end of that range.

Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

	Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 %*
1	Baseline	6	26	32	OK
2	20 min	5	25	30	OK
3	40 min	5	23	28	OK
4	60 min	44	40	84	OK
5	80 min	79	35	114	OK
6	100 min	85	31	116	OK
7	120 min	71	30	101	OK
8	140 min	186	58	244	OK
9	160 min				QNS
10	180 min	137	53	190	OK



*Dilutions of the sample may occur during the sampling procedure which may decrease the CO_2 concentration of the sample and render the sample invalid. If the concentration falls below 2.4 %, the entry for CO_2 will be marked as Quantity Not Sufficient (QNS) and the entries for H_2 and CH_4 will be highlighted. If the sample is otherwise unusable the entry for CO_2 will be marked as Not Available (N/A) and the entries for H_2 and CH_4 will be highlighted. See notes section for details if cells are highlighted and blank or highlighted and contain N/A or QNS.

Analysis

Combined baseline total =	32	H	≤20ppm
Greatest H_2 increase over the lowest preceding value within first 120 minutes =	80	H	≤20ppm
Greatest CH_4 increase over the lowest preceding value within first 120 minutes =	17	H	≤12ppm
Greatest combined H_2 & CH_4 increase over the lowest preceding value within first 120 minutes =	88	H	≤15ppm

Interpretation

SIBO Suspected - Elevated Hydrogen	Increases of hydrogen greater than 20ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	POSITIVE
SIBO Suspected - Elevated Methane	Increases of methane greater than 12ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	POSITIVE
SIBO Suspected - Elevated Combined Hydrogen & Methane Gasses	Increases in combined hydrogen and methane gas values greater than 15ppm over the lowest preceding value are indicative of bacterial overgrowth.	POSITIVE

She was positive for both hydrogen and methane-predominant SIBO. In my experience, it's always a combination of genetics and environmental factors, so this patient was homozygous for MTHFR

C677T, but she had GI malabsorption as well, and that probably is what sent her over the edge and was likely contributing to the poor absorption of B12 as well.

As with iron-deficiency anemia, the treatment of B12- or folate-deficient anemia starts with addressing underlying causes. In many cases, as I mentioned, this will be nutritional, but you have to dig deeper if their intake of nutrients appears to be sufficient. For example, is there some GI malabsorption that is causing deficiency of that nutrient? Refer to the iron-deficiency anemia presentation for some of the underlying causes of anemia in general, and then we cover contributing factors in this presentation, which would be GI and malabsorption issues primarily.

You can refer back to the B12 deficiency presentation for the treatment of B12 deficiency. Here, we're just going to focus on how to address folate deficiency, since that is the only part of this we haven't talked about yet.