

# Conference 4 – Markers of Oxidative Stress

Metamatrix Clinical Laboratory  
Teleconference Series

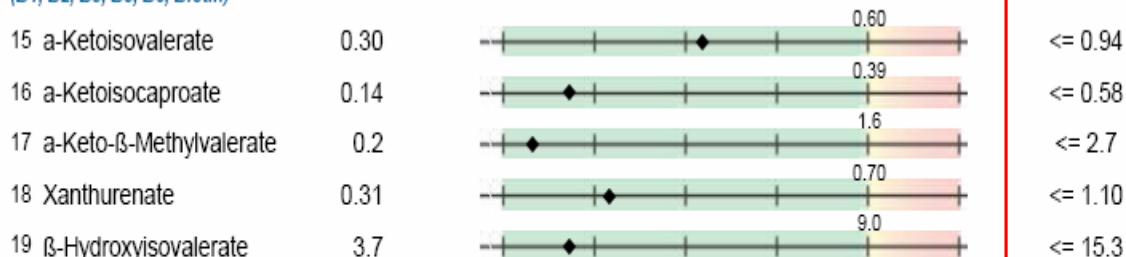
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### B-Complex Vitamin Markers

(B1, B2, B3, B5, B6, Biotin)



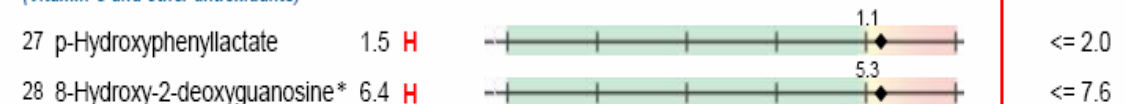
### Methylation Cofactor Markers

(B12, Folate)



### Oxidative Damage and Antioxidant Markers

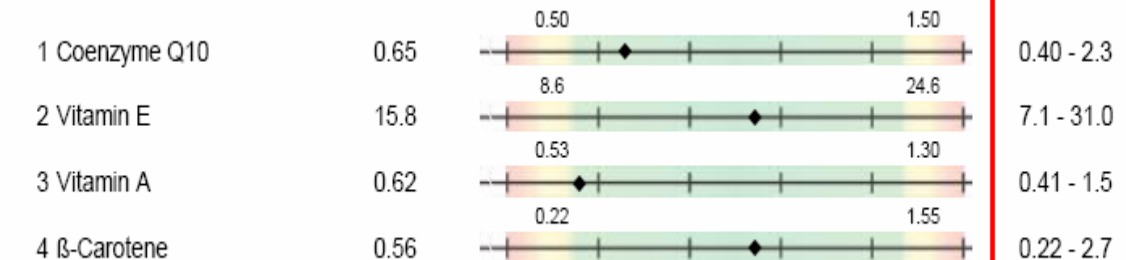
(Vitamin C and other antioxidants)



### TOXICANTS AND DETOXIFICATION

#### Detoxification Indicators

(Arg, NAC, Met, Mg and antioxidants)



### Joe: liver cancer

#### PRE-Treatment ION TEST

Medical History: This person is a 72 year old male, "robust" for age. Eats a healthy diet, no supplementation. Diagnosed with liver cancer.

Lab Results: High inflammatory marker quinolinate, high oxidative stress analytes p-hydroxyphenyllactate (HPLA) and 8-hydroxy 2' deoxyguanosine (8-OHdG), and high xylene exposure marker 2-methylhippurate.

Antioxidant vitamin status is within normal limits for CoQ10, vitamin E, vitamin A and beta-carotene. B complex markers are normal except for FIGLU, a marker for folic acid insufficiency.

Background Biochemistry: para-hydroxyphenyllactate is a marker for tumor growth, and for hepatic encephalopathy in patients with cirrhosis. Tumor cells contain esterases which hydrolyze native methyl-p-hydroxyphenyllactate to the free acid, HPLA. Deficient Me-HPLA means loss of regulatory control. 8-OH-2dG is a product of DNA oxidative damage, formed in a protomutagenic DNA lesion reaction with oxygen radicals, commonly found in chronic liver disease.

Clinician-Determined Treatment: 5,000 mg vitamin C w/ bioflavonoids, 200 mg CoQ10, 400 mg lipoic acid, 1200 mg n-acetyl cysteine, and more, including 3000 mg of a concentrated veg/fruit antioxidant formula and 120 grams of protein in a prepared powder

**B-Complex Vitamin Markers**

(B1, B2, B3, B5, B6, Biotin)

15	a-Ketoisovalerate	3.90	H	0.60
16	a-Ketoisocaproate	1.22	H	0.39
17	a-Keto-β-Methylvalerate	2.9	H	1.6
18	Xanthurenate	0.37		0.70
19	β-Hydroxyisovalerate	6.9		9.0

**Methylation Cofactor Markers**

(B12, Folate)

20	Methylmalonate	2.1		2.3
21	Formiminoglutamate	2.68	H	1.45

25	Kynurenate	1.8	H	1.5
26	Quinolinate	14.5	H	10.2

**Oxidative Damage and Antioxidant Markers**

(Vitamin C and other antioxidants)

27	p-Hydroxyphenyllactate	2.7	H	1.1
28	8-Hydroxy-2-deoxyguanosine*	16.9	H	5.3

**TOXICANTS AND DETOXIFICATION**

**Detoxification Indicators**

(Arg, NAC, Met, Mg and antioxidants)

29	2-Methylhippurate	0.101	H	0.050
30	Orotate	0.2		1.0
31	Glucarate	12.5	H	7.0

1	Coenzyme Q10	2.60	H	0.50 - 1.50
2	Vitamin E	24.7	H	8.6 - 24.6
3	Vitamin A	0.33	L	0.53 - 1.30
4	β-Carotene	0.98		0.22 - 1.55

<= 0.94  
 <= 0.58  
 <= 2.7  
 <= 1.10  
 <= 15.3  
 <= 3.4  
 <= 2.87  
 <= 2.5  
 <= 16.5  
 <= 2.0  
 <= 7.6  
 <= 0.100  
 <= 1.6  
 <= 11.9

**Joe: liver cancer  
 POST chemotherapy/supplementation  
 ION TEST**  
 Two months later.

Lab Results: High inflammatory marker quinolinate remains, higher oxidative stress analytes p-hydroxyphenyllactate (HPLA) and 8-hydroxy 2' deoxyguanosine (8-OHdG), and higher xylene exposure marker 2-methylhippurate, high glucarate (general Phase I and II detox marker), newly elevated B complex markers.

Antioxidant vitamin status (serum) is reflecting supplementation, with exception of vitamin A, which was not added and appears lower than two months ago.

In spite of the high levels of CoQ10 and vitamin E there is significant overloading of oxidative stress protection systems, apparently due to the chemotherapy.

Oxidative Damage and Antioxidant Markers  
(Vitamin C and other antioxidants)

27	p-Hydroxyphenyllactate	0.8		1.1	<= 2.0
28	8-Hydroxy-2-deoxyguanosine	7.1 <b>H</b>		6.4	<= 8.6

**Cardiovascular Health Profile**

Methodology: Automated Chemistry, Immunometric Assay, Competitive Immunology, HPLC, ICP-MS

	Results		Reference Limits
<u>Lipoprotein Factors</u>			
Total Cholesterol	161		<= 200 mg/dL
HDL Cholesterol	69		30 - 85 mg/dL
LDL Cholesterol (Direct)	99		<= 130 mg/dL
Triglycerides	54		35 - 160 mg/dL
Lipoprotein (a)	5		<= 37 mg/dL

Lipoprotein Ratios

LDL/HDL	1.0	<= 3.3
Total/HDL	2.0	<= 4.5

Male		Female		Risk (*)
LDL/HDL	Total/HDL	LDL/HDL	Total/HDL	
1.0	3.4	1.5	3.3	0.5xAverage
3.6	5.0	3.2	4.4	1.0xAverage
6.3	9.6	5.0	7.1	2.0xAverage
8.0	23.4	6.1	11.0	3.0xAverage

\*Adapted from the Framingham Heart Study

Chronic Inflammatory Markers

Ferritin	35		28 - 397	ng/mL
Fibrinogen	265		175 - 400	mg/dL
c-Reactive Protein (HS)	0.4		<= 3.0	mg/L

**Lance: wellness check  
2005**

Medical History: This person is a healthy, 80 year old male, has been a vegan for 40 years. He was tested as a wellness check., having no health concerns.

Lab Results: Elevated 8-OHdG, normal HPLA. Excellent cardio profile. In a healthy patient the finding of high 8-OHdG gives warning of a specific type of metabolic susceptibility, Episodes of widely varying life stressors can precipitate clinically significant oxidant damage with loss of organ reserve.

Oxidative Damage and Antioxidant Markers  
(Vitamin C and other antioxidants)

27	p-Hydroxyphenyllactate	0.3		1.1	<= 2.0
28	8-Hydroxy-2-deoxyguanosine *43.6	H		5.3	<= 7.6

**Cardiovascular Health Profile**

Methodology: Automated Chemistry, Immunometric Assay, Competitive Immunology, HPLC, ICP-MS

	Results		Reference Limits	
<u>Lipoprotein Factors</u>				
Total Cholesterol	109		<= 200	mg/dL
HDL Cholesterol	42		30 - 85	mg/dL
LDL Cholesterol (Direct)	71		<= 130	mg/dL
Triglycerides	36		35 - 160	mg/dL
Lipoprotein (a)	4		<= 37	mg/dL

Lipoprotein Ratios

LDL/HDL	1.7	<= 3.3
Total/HDL	2.6	<= 4.5

Male		Female		Risk (*)
LDL/HDL	Total/HDL	LDL/HDL	Total/HDL	
1.0	3.4	1.5	3.3	0.5xAverage
3.6	5.0	3.2	4.4	1.0xAverage
6.3	9.6	5.0	7.1	2.0xAverage
8.0	23.4	6.1	11.0	3.0xAverage

\*Adapted from the Framingham Heart Study

Chronic Inflammatory Markers

Ferritin	31		28 - 397	ng/mL	
Fibrinogen	493	H		175 - 400	mg/dL
c-Reactive Protein (HS)	0.3		<= 3.0	mg/L	

**Lance: Unexplained bruising/extreme oxidative stress**  
**2006**

Medical History: This was a second wellness check , but Lance had noticed he now bruises easily.

Lab Results: Markedly elevated 8-OHdG, still normal HPLA. Elevated fibrinogen, significantly lower total cholesterol than in 2005

Here we have evidence that a precipitating (triggering) event has in fact produced massive oxidative challenge that very likely is a cause of the onset of easy bruising.

1 Coenzyme Q10	0.39 L		0.40 - 2.3
2 Vitamin E	11.7		7.1 - 31.0
3 Vitamin A	0.19 L		0.41 - 1.5
4 β-Carotene	< 0.2 L		0.22 - 2.7

**B-Complex Vitamin Markers**  
(B1, B2, B3, B5, B6, Biotin)

15 α-Ketoisovalerate	< 0.1		<= 0.94
16 α-Ketoisocaproate	0.51 H		<= 0.58
17 α-Keto-β-Methylvalerate	0.3		<= 2.7
18 Xanthurenate	0.73 H		<= 1.10
19 β-Hydroxyisovalerate	19.4 H		<= 15.3

**Methylation Cofactor Markers**  
(B12, Folate)

20 Methylmalonate	1.5		<= 3.4
21 Formiminoglutamate	4.15 H		<= 2.87

25 Kynurenate	1.9 H		<= 2.5
26 Quinolinate	35.6 H		<= 16.5

**Oxidative Damage and Antioxidant Markers**  
(Vitamin C and other antioxidants)

27 p-Hydroxyphenyllactate	1.0		<= 2.0
28 8-Hydroxy-2-deoxyguanosine*20.7 H			<= 7.6

**TOXICANTS AND DETOXIFICATION**

**Detoxification Indicators**  
(Arg, NAC, Met, Mg and antioxidants)

29 2-Methylhippurate	0.090 H		<= 0.100
30 Orotate	1.1 H		<= 1.6
31 Glucarate	2.1		<= 11.9

**Melissa – drug-induced oxidative stress**

Medical history: This 16 y/o female presents with severe muscle pain and flu-like symptoms. She has been using minocycline for many months for acne.

Lab results: The urinary organic acid data shows greatly elevated 8-OHdG and quinolinate with positive biochemical markers for vitamin B6 (xanthurenate), biotin (B-hydroxyisovalerate) and, especially, folic acid (formiminoglutamate) insufficiency.

Serum levels of vitamin A, beta-carotene and coenzyme Q10 are low, showing specific points of antioxidant weakness. (Other tests reveal elevated liver enzymes and high ANA.)

The oxidative stress is complicated by low essential fatty acid status, so it is especially important to provide balanced antioxidant support before aggressive supplementation with fish oils or other polyunsaturated fatty sources.



Clinician-determined intervention: B complex, ascorbate, fat-soluble vitamins, zinc (even though low normal status), magnesium

## Oxidative Damage and Antioxidant Markers

(Vitamin C and other antioxidants)

27	p-Hydroxyphenyllactate	3.5	H		<= 2.0
28	8-Hydroxy-2-deoxyguanosine *	7.7	H		<= 7.6

\* Units for 8-Hydroxy-2-deoxyguanosine are ng/mg creatinine

30	Orotate	2.4	H		<= 1.6
31	Glucarate	12.2	H		<= 11.9

### Lydia: oxidative stress

Medical history: This 72 y/o female has COPD, emphysema, severe fatigue, CHF and is a former smoker. She takes Mucinex, Actinel, Spireva, Coreg and Xanax

Lab results: Organix testing show elevated HPLA, 8-OHdG, orotate and glucarate.

Background biochemistry: HPLA and 8-OHdG as above. Orotate indicates increased ammonia levels in liver, and requires magnesium for its metabolism.

Clinical intervention: High dose vitamin C with quercetin, bioflavonoids, magnesium.

According to this data, it appears that the combination of multiple drug detoxification loading and restricted pulmonary gas exchange has produced both increased cell division rates and oxidative stress that has exceeded the capacity of the antioxidant systems.