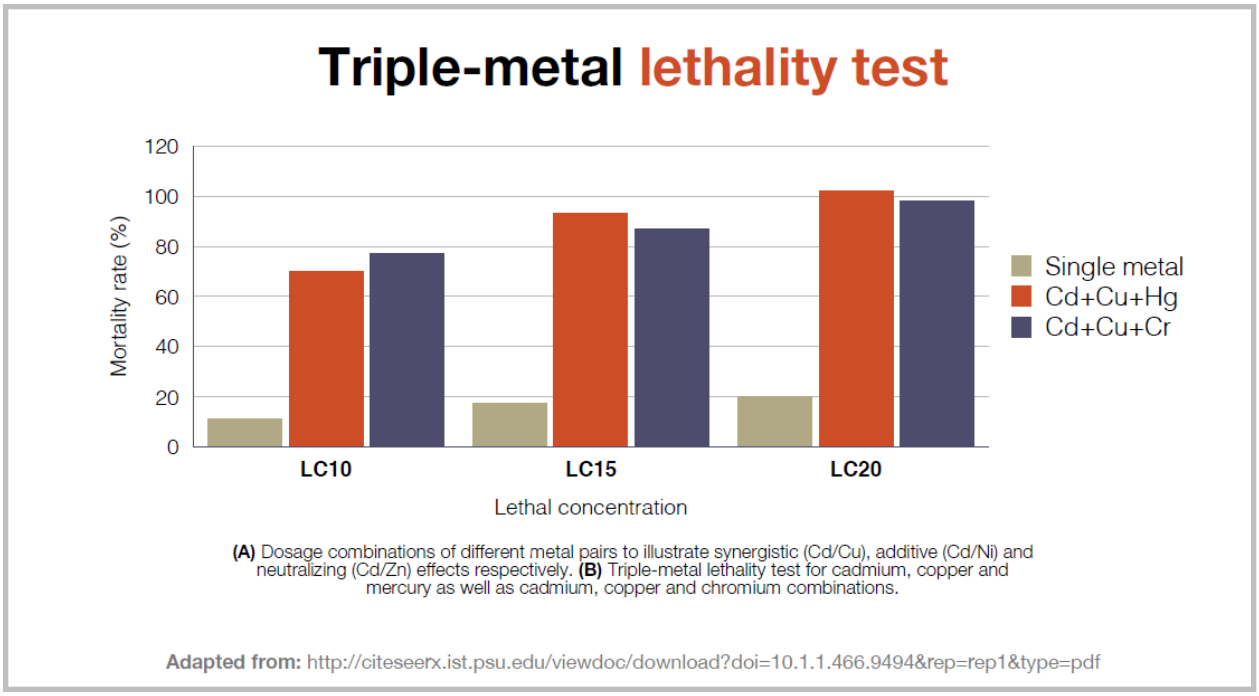
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Zinc-Copper Imbalance - Part Two

For years it was assumed that high copper is a risk factor for heart attack, but yet, this is yet another cause of mistaking correlation with causation. Inflammation has been shown to increase blood copper levels, as we've discussed, and inflammation increases the risk of heart attack, so it's very likely that inflammation is causing both the increase in heart attack and the increase in serum copper rather than excess copper intake causing an increased risk of heart disease.

Some dietary guidelines suggest that the safe upper limit for copper is 10 mg per day. However, more recent research has shown that the safe upper limit may be five times higher than that, 50 mg per day for adults. Only a few studies have looked at the relationship between more accurate markers of copper status and cardiovascular disease in humans. For example, leukocyte copper status, which is a marker of copper in the tissue, is lower in people with cardiovascular disease, and people who die of heart attacks generally have less copper in their hearts than people who die of other causes. Now, this could also be an effect rather than a cause of heart attack, but given the research that we've reviewed regarding copper's connection with inflammation and copper's role as an acute-phase reactant, it's at least plausible that these relationships are causal rather than just an association.

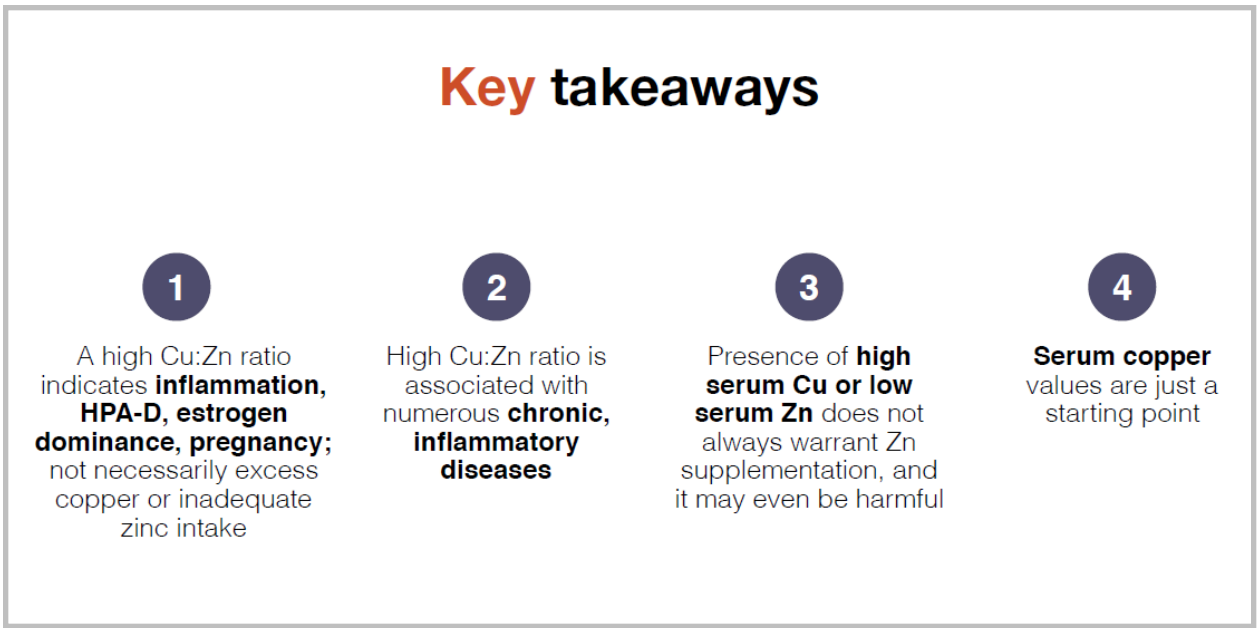


(A) Dosage combinations of different metal pairs to illustrate synergistic (Cd/Cu), additive (Cd/Ni) and neutralizing (Cd/Zn) effects respectively. **(B)** Triple-metal lethality test for cadmium, copper and mercury as well as cadmium, copper and chromium combinations.

Adapted from: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.466.9494&rep=rep1&type=pdf

This isn't to say that true zinc deficiency or copper excess doesn't occur and that they don't have consequences. It's well established that the toxic effects of certain metals can either be synergistic or additive, depending on the metals. For example, one study showed that over 20 years of occupational exposure to copper, copper lead, and copper iron was associated with a higher risk of

Parkinson's, but the odds ratio was significantly higher for the combos than it was for copper alone. Another study showed that pro-oxidant copper ions affect glutathione in several ways, which in turn potentiates the effects of mercury toxicity. Finally, copper has a strongly synergistic toxic effect with other metals, especially cadmium. I've put a table, or a chart, rather, from one of these studies on this slide to give you a visual example of this.



What do we make of all this data? There are several important takeaways. First, an elevated copper-to-zinc ratio is often an indicator of inflammation, HPA axis dysfunction, estrogen dominance, or pregnancy. Number two, high copper-to-zinc ratios are associated with numerous chronic inflammatory diseases, including coronary heart disease, autism spectrum disorder, Alzheimer's disease, rheumatoid arthritis, shortened sleep duration, and several other conditions, but most research suggests that the elevated serum copper and low serum zinc observed in these conditions is an effect rather than a cause.

Number three, the presence of high serum copper or low serum zinc doesn't always warrant zinc supplementation, and, in fact, zinc supplementation for a long time may cause copper deficiency. Some studies suggest that mercury and cadmium toxicity may make copper accumulation and zinc deficiency more likely. Number four, serum copper values are just a starting point and should never be used in isolation to make a diagnosis. If serum copper is elevated or decreased, we need to use other markers such as ceruloplasmin, 24-hour urine copper, ALT, AST, and, less commonly, liver biopsy to further clarify the diagnostic picture.

Functional Zn:Cu range: 0.85–1.2

One last thing before we dive into lab results. This is a little confusing because, so far, we've been talking about the copper-to-zinc ratio with copper as the enumerator, but I express the ratio as zinc-to-copper on my blood chemistry panel with zinc as the enumerator. The zinc-to-copper ratio in healthy humans is between 0.85 and maybe 1.2 depending on the study you look at, so we're talking about roughly equal amounts of zinc to copper. Studies have shown that a ratio of 0.5 or lower is associated with significant morbidity and mortality.

I've set the range at 0.85 to 1.2 for optimal levels. The lower end of that range is based on some of the studies that I just mentioned. The upper end of the range is based more on concerns about copper deficiency when zinc is significantly higher than copper. Anything below the 0.85 threshold may suggest an inflammatory process, HPA axis dysfunction, estrogen dominance, or pregnancy, and anything above the 1.2 threshold may suggest that the patient is taking zinc supplements. If they are not taking zinc supplements, there are some genetic causes that can lead to zinc elevation, and the patient may be suffering from copper deficiency.

Marker	Lab Range	Functional Range
Zinc	56–134	64–126
Copper	72–166	81–157

Here are the lab and functional ranges for copper and zinc. Again, I don't think that looking at these in isolation is nearly as useful as looking at the ratio between copper and zinc, but it is helpful to have an idea when you look at them individually what the values should be. Now, in this case, the functional ranges are simply the lab range shrunken by 20 percent. There is not a lot of hard data for a functional range for zinc and copper, and, again, it's important to look at the ratio between the two for the full picture.

Marker	Value	Functional Range	Lab Range
Glucose	78	75 - 90	65 - 99
Hemoglobin A1c	5.6	4.4 – 5.4	4.8 - 5.6
Uric Acid	4.5	3.2 - 5.5	2.5 - 7.1
BUN	12	13 – 18	6 - 20
Creatinine	0.74	0.7 – 1.0	0.57 - 1.00
BUN/Creatinine Ratio	16	9 – 23	8 - 20
Sodium	138	135 – 140	134 - 144
Potassium	3.8	4.0 – 4.5	3.5 - 5.2
Chloride	98	100 – 106	97 - 108
C02	21	25 – 30	18 - 29
Calcium	9.1	9.2 – 10.1	8.7 - 10.2
Phosphorus	4.5	3.0 – 4.0	2.5 - 4.5
Magnesium	1.9	2.0 – 2.6	1.6 - 2.6
Protein, total	7.6	6.9 – 7.4	6.0 - 8.5
Albumin	4.3	4.0 – 5.0	3.5 - 5.5
Globulin	3.3	2.4 – 2.8	1.5 - 4.5
A/G ratio	1.3	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.3	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	141	42 – 107	39 - 117
LDH	196	140 - 180	119 - 226
AST	16	10 - 23	0 - 40
ALT	27	10 - 20	0 - 32
GGT	98	5 - 21	0 - 60
TIBC	436	275 – 425	250 - 450
UIBC	416	175 - 350	150 - 375
Iron	20	40 – 135	35 - 155
Iron saturation	5	17 – 45	15 - 55
Ferritin	6	30 - 100	15 - 150
Vitamin B-12	389	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	32.9	35 - 60	30.0 - 100.0
Cholesterol, total	145	150 - 250	100 - 199
Triglycerides	127	50 – 100	0 - 149
HDL	47	55 – 85	> 39
LDL	73	0 - 175	0 - 99
T. Chol / HDL Ratio	3.1	< 3	0 - 4.4
Triglycerides / HDL Ratio	2.70	< 2	< 3.8

Marker	Value	Functional Range	Lab Range
CRP-hs	5.93	< 1.0	0.00 - 3.00
Homocysteine	11.2	< 7.0	0.0 - 15.0
TSH	2.660	0.5 – 2.5	0.45 - 4.500
T4, total	7.0	6.0 – 12	4.5 - 12.0
T3 Uptake	27	28 - 35	24 - 39
T3, Total	126	100 – 180	71 - 180
Copper	134		72 - 166
Zinc	79		56 - 134
Zinc / Copper Ratio	0.59	> 0.85	
Serum Methylmalonic Acid (MMA)	107	< 300	0 - 378
WBC	8.1	5.0 – 8.0	3.4 - 10.8
RBC	5.11	4.4 – 4.9	3.77 - 5.28
Hemoglobin	11.2	13.5 - 14.5	11.1 - 15.9
Hematocrit	37.2	37 - 44	34 - 46.6
MCV	73	85 – 92	79 - 97
MCH	21.9	27.7 – 32.0	26.6 - 33.0
MCHC	30.1	32 – 35	31.5 - 35.7
RDW	17.6	11.5 – 15.0	12.3 - 15.4
Platelets	376	150 – 415	150 - 379
Neutrophils	46	40 – 60	
Lymphocytes	38	25 – 40	
Monocytes	9	4.0 – 7.0	
Eosinophils	6	0.0 – 3.0	
Basophils	1	0.0 – 3.0	

All right, let's talk about some cases now. The first patient is a 22-year-old female who had a complete colectomy eight years ago and now has a J-pouch. We talked about her in the iron-deficiency section. Her zinc-to-copper ratio was 0.59, which is well below the 0.85 threshold, but note that both zinc and copper are well within the lab range for her. This is why it is so important to look at the ratio and not just individual values. Her zinc is 79, and the range is 56 to 134, and her copper is 134 in a range of 72 to 166, yet her zinc-to-copper ratio is 0.59, well below the threshold. Also note that she has significant iron-deficiency anemia. It's likely she is also copper deficient, and given her absorption problems, deficiencies of iron, B12, vitamin D, and magnesium, it seems likely that GI malabsorption of copper is happening here. It's also likely that the elevation of copper that we're seeing relative to zinc is related to inflammation as well. She has ulcerative colitis and was in an active flare when this test was taken, so if you look at her CRP, it's almost 6. Her homocysteine is 11.2, and her alkaline phosphatase is 141. Giving this patient zinc is likely not the best course of action, unless copper is also given, and we'll talk more about that in the treatment section later. In fact, giving this patient more dietary copper may actually help her to recover from iron-deficiency anemia.

Marker	Value	Functional Range	Lab Range
Glucose	97	75 - 90	65 - 99
Hemoglobin A1c	5.1	4.4 – 5.4	4.8 - 5.6
Uric Acid	4.0	3.2 - 5.5	2.5 - 7.1
BUN	6	13 – 18	6 - 20
Creatinine	0.63	0.7 – 1.0	0.57 - 1.00
BUN/Creatinine Ratio	10	9 – 23	8 - 20
Sodium	137	135 – 140	134 - 144
Potassium	4.3	4.0 – 4.5	3.5 - 5.2
Chloride	103	100 – 106	97 - 108
C02	22	25 – 30	18 - 29
Calcium	9.8	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.4	3.0 – 4.0	2.5 - 4.5
Magnesium	1.9	2.0 – 2.6	1.6 - 2.6
Protein, total	7.1	6.9 – 7.4	6.0 - 8.5
Albumin	4.0	4.0 – 5.0	3.5 - 5.5
Globulin	3.1	2.4 – 2.8	1.5 - 4.5
A/G ratio	1.3	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	<0.2	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	53	42 – 107	39 - 117
LDH	150	140 - 180	119 - 226
AST	21	10 - 23	0 - 40
ALT	26	10 - 20	0 - 32
GGT	13	5 - 21	0 - 60
TIBC	431	275 – 425	250 - 450
UIBC	376	175 - 350	150 - 375
Iron	55	40 – 135	35 - 155
Iron saturation	13	17 – 45	15 - 55
Ferritin	25	30 - 100	15 - 150
Vitamin B-12	517	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	50.3	35 - 60	30.0 - 100.0
Cholesterol, total	185	150 - 250	100 - 199
Triglycerides	143	50 – 100	0 - 149
HDL	79	55 – 85	> 39
LDL	77	0 - 175	0 - 99
T. Chol / HDL Ratio	2.3	< 3	0 - 4.4
Triglycerides / HDL Ratio	1.81	< 2	< 3.8

Marker	Value	Functional Range	Lab Range
CRP-hs	4.77	< 1.0	0.00 - 3.00
Homocysteine	5.7	< 7.0	0.0 - 15.0
TSH	0.014	0.5 – 2.5	0.45 - 4.500
T4, total	12.6	6.0 – 12	4.5 - 12.0
T3 Uptake	20	28 - 35	24 - 39
T3, Total	241	100 – 180	71 - 180
T3, Free	4.5	2.5 - 4.0	2 - 4.4
T4, Free	1.28	1 - 1.5	0.82 - 1.77
Copper	192		72 - 166
Zinc	76		56 - 134
Zinc / Copper Ratio	0.40	> 0.85	
Serum Methylmalonic Acid (MMA)	95	< 300	0 - 378
WBC	5.7	5.0 – 8.0	3.4 - 10.8
RBC	4.89	4.4 – 4.9	3.77 - 5.28
Hemoglobin	14.0	13.5 - 14.5	11.1 - 15.9
Hematocrit	40.8	37 - 44	34 - 46.6
MCV	83	85 – 92	79 - 97
MCH	28.6	27.7 – 32.0	26.6 - 33.0
MCHC	34.3	32 – 35	31.5 - 35.7
RDW	14.9	11.5 – 15.0	12.3 - 15.4
Platelets	379	150 – 415	150 - 379
Neutrophils	41	40 – 60	
Lymphocytes	46	25 – 40	
Monocytes	11	4.0 – 7.0	
Eosinophils	1	0.0 – 3.0	
Basophils	1	0.0 – 3.0	

The next patient is a 20-year-old female with chief complaint of 4 x 1 cm thyroid nodule. She had been in discussion with surgeons and an endocrinologist at Stanford and had had imaging over the last six to nine months that showed stability in the nodule. Ultrasound and biopsy were pretty convincing for a benign lesion. She also had some complaints of occasional digestive issues. Her serum copper was elevated out of the lab range at 192. Zinc was low-normal at 76, in the range of 56 to 134, so this led to a zinc-to-copper ratio of 0.4, which is below even the 0.5 cutoff that suggests significant morbidity and mortality. You'll see with her TSH of 0 and her high T4 and T3, she was hyperthyroid, which is consistent with a thyroid nodule, although her thyroid antibodies were normal on this test. She was also iron deficient and had high fasting blood sugar, at least in the functional range at 97. She had high CRP at 4.77, which again is consistent with this inflammatory picture. Finally, she was on oral contraceptives. I hadn't done a hormone profile for her yet, but I suspect her estrogen would be high, and all of these things can increase copper and decrease the zinc-to-copper ratio, as you know.

TEST	RESULT			
Array 3 – Wheat/Gluten Proteome Reactivity & Autoimmunity	**IN RANGE (Normal)**	**EQUIVOCAL***	**OUT OF RANGE**	**REFERENCE (ELISA Index)**
Wheat IgG	0.89			0.3-1.5
Wheat IgA	0.64			0.1-1.2
Wheat Germ Agglutinin IgG	0.81			0.4-1.3
Wheat Germ Agglutinin IgA		1.05		0.2-1.1
Native & Deamidated Gliadin 33 IgG	0.74			0.2-1.2
Native & Deamidated Gliadin 33 IgA	0.60			0.1-1.1
Alpha Gliadin 17-mer IgG	0.69			0.1-1.5
Alpha Gliadin 17-mer IgA		1.06		0.1-1.1
Gamma Gliadin 15-mer IgG	0.67			0.5-1.5
Gamma Gliadin 15-mer IgA	0.29			0.1-1.0
Omega Gliadin 17-mer IgG	0.55			0.3-1.2
Omega Gliadin 17-mer IgA	0.47			0.1-1.2
Glutenin 21-mer IgG			1.57	0.1-1.5
Glutenin 21-mer IgA	0.55			0.1-1.3
Gluteomorphin + Prodynorphin IgG			1.82	0.3-1.2
Gluteomorphin + Prodynorphin IgA		0.92		0.1-1.2
Gliadin-Transglutaminase Complex IgG		1.18		0.3-1.4
Gliadin-Transglutaminase Complex IgA	0.48			0.2-1.5
Transglutaminase-2 IgG	0.90			0.3-1.6
Transglutaminase-2 IgA	1.05			0.1-1.6
Transglutaminase-3 IgG	0.77			0.2-1.6
Transglutaminase-3 IgA	0.77			0.1-1.5
Transglutaminase-6 IgG	0.57			0.2-1.5
Transglutaminase-6 IgA	0.54			0.1-1.5

Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	1+ Gamma hemolytic strep	
4+ Bifidobacterium spp.	2+ Klebsiella oxytoca	
4+ Escherichia coli	1+ Staphylococcus aureus	
2+ Lactobacillus spp.		
1+ Enterococcus spp.		
1+ Clostridium spp.		
NG = No Growth		

BACTERIA INFORMATION

Expected /Beneficial bacteria make up a significant portion of the total microflora in a healthy & balanced GI tract. These beneficial bacteria have many health-protecting effects in the GI tract including manufacturing vitamins, fermenting fibers, digesting proteins and carbohydrates, and propagating anti-tumor and anti-inflammatory factors.
Clostridia are prevalent flora in a healthy intestine. Clostridium spp. should be considered in the context of balance with other expected/beneficial flora. Absence of clostridia or over abundance relative to other expected/beneficial flora indicates bacterial imbalance. If *C. difficile* associated disease is suspected, a Comprehensive Clostridium culture or toxigenic *C. difficile* DNA test is recommended.
Commensal (Imbalanced) bacteria are usually neither pathogenic nor beneficial to the host GI tract. Imbalances can occur when there are insufficient levels of beneficial bacteria and increased levels of commensal bacteria. Certain commensal bacteria are reported as dysbiotic at higher levels.
Dysbiotic bacteria consist of known pathogenic bacteria and those that have the potential to cause disease in the GI tract. They can be present due to a number of factors including: consumption of contaminated water or food, exposure to chemicals that are toxic to beneficial bacteria; the use of antibiotics, oral contraceptives or other medications; poor fiber intake and high stress levels.

YEAST CULTURE

Normal flora	Dysbiotic flora
1+ Candida glabrata	

MICROSCOPIC YEAST

Result:	Expected:
Many	None - Rare

The microscopic finding of yeast in the stool is helpful in identifying whether there is proliferation of yeast. Rare yeast may be normal; however, yeast observed in higher amounts (few, moderate, or many) is abnormal.

YEAST INFORMATION

Yeast normally can be found in small quantities in the skin, mouth, intestine and mucocutaneous junctions. Overgrowth of yeast can infect virtually every organ system, leading to an extensive array of clinical manifestations. Fungal diarrhea is associated with broad-spectrum antibiotics or alterations of the patient's immune status. Symptoms may include abdominal pain, cramping and irritation. When investigating the presence of yeast, disparity may exist between culturing and microscopic examination. Yeast are not uniformly dispersed throughout the stool. this may lead to undetectable or low levels of yeast identified by microscopy, despite a cultured amount of yeast. Conversely, microscopic examination may reveal a significant amount of yeast present, but no yeast cultured. Yeast does not always survive transit through the intestines rendering it unviable.

She was still eating gluten, so I did a Cyrex Array 3 and found reactivity to several epitopes of gliadin and also gliadin transglutaminase complex, gluteomorphin, prodynorphin, glutenin, and wheat germ and glutenin, so this is suggestive of autoimmunity. Stool tests showed significant fungal overgrowth, so she has several indicators of inflammation, and that is the most likely explanation for her high copper and low zinc rather than dietary intake.

Marker	Value	Functional Range	Lab Range
Glucose	93	75 - 90	60 - 150
BUN	16	13 – 18	7 - 27
Creatinine	0.67	0.85 – 1.1	0 - 1.11
BUN/Creatinine Ratio	24	8 – 19	9 - 23
Sodium	136	135 – 140	133 - 145
Potassium	4.0	4.0 – 4.5	3.5 - 5.3
Chloride	102	100 – 106	100 - 111
C02	27	25 – 30	24 - 33
Magnesium	1.9	2.0 – 2.6	2 - 2.6
Vitamin B-12	398	450 – 2000	> 199
Vitamin D, 25-hydroxy	36	35 - 60	20.0 - 79.0
Cholesterol, total	197	150 - 240	0 - 239
Triglycerides	99	50 – 100	0 - 499
HDL	59	55 – 85	> 49
LDL	118	0 - 175	0 - 159
T. Chol / HDL Ratio	3.3	< 3	0 - 4.4
Triglycerides / HDL Ratio	1.68	< 2	< 3.8
CRP-hs	<0.1	< 1.0	0.00 - 0.50
Homocysteine	9.7	< 7.0	0.0 - 12.0
TSH	1.250	0.5 – 2.5	0.10 - 5.50
Copper	86		70 - 175
Zinc	55		60 - 130
Zinc / Copper Ratio	0.64	> 0.85	
WBC	4.6	5.0 – 8.0	3.5 - 12.5
RBC	4.29	4.4 – 4.9	3.6 - 5.7
Hemoglobin	12.9	14 - 15	11.5 - 15
Hematocrit	39.7	40 - 48	34 - 46.0
MCV	92	85 – 92	80 - 100
Platelets	282	150 – 415	140 - 400
Neutrophils	69	40 – 60	
Lymphocytes	23	25 – 40	
Monocytes	6	4.0 – 7.0	
Eosinophils	2	0.0 – 3.0	
Basophils	0	0.0 – 3.0	

The next patient is a 36-year-old female with chief complaint of declining overall health through the past 20 years. It started with migraines when she was in high school. She had a significant history of joint inflammation and pain. Took a lot of NSAIDs, especially in college because she was active and needed to address the pain and inflammation and didn't know how else to do it. She had significant bloating and GI problems. In her case, zinc was below the lab range at 55, and the lab's range was 60 to 130. Her copper was also on the low end, but the zinc-to-copper ratio was still low at 0.64. It's important to realize, again, that this can happen even when copper is relatively low, so her copper was kind of at the bottom of the range, but her zinc was lower relative to copper, which resulted in a low copper-to-zinc ratio. It's a similar phenomenon to estrogen dominance even when progesterone and estrogen are both low. Her magnesium and B12 are on the low end, and this suggested that there could be a problem with nutrient absorption.

How to read the graphical representation of results

Sex Hormones

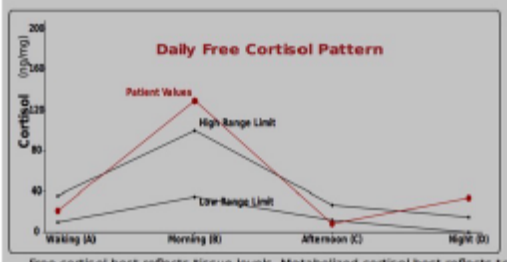
Total Estrogen
(Sum of 8 Estrogen Metabolites)

Progesterone
(Serum Equivalent, ng/mL)

Testosterone

See Pages 2 & 3 for a thorough breakdown of sex hormone metabolites

Adrenal Hormones



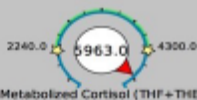
Total DHEA Production

Age	Range
20-40	800-2500
40-60	530-1550
>60	400-1350

Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)

24hr Free Cortisol
(A+B+C+D)

cortisol metabolism



Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production. See pages 4 and 5 for a more complete breakdown.

Patient Reported Hormone Therapies: ROA 1=oral, 2=sublingual, 3=transdermal cream, 4=transdermal gel, 5=vaginal/labial, 6=rectal mucosa, 7=patch, 8=pellet, 9=injection, 10=other

☑ Not taking any listed hormones

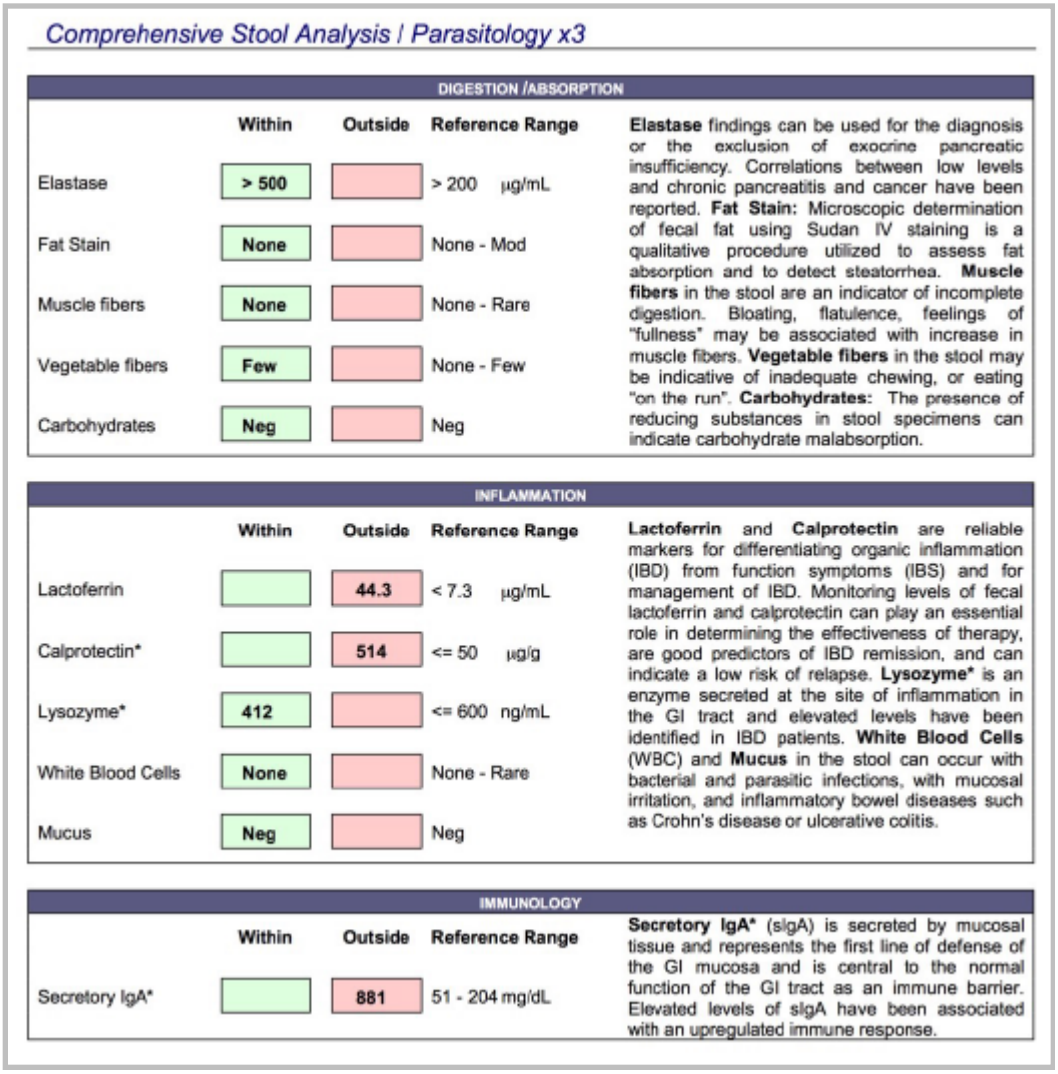
Do you take DIM/I-3-C regularly? ☐ Yes ☐ No	List Any other relevant drugs, supplements or others: Sumatriptan

All units are given in ng/mg creatinine

Patient reports irregular menstrual cycles

Last Menstrual Period - 2015-08-10

Progesterone Serum Equivalent is a calculated value based on urine pregnanediol. This value may not accurately reflect serum when progesterone is taken by mouth.



Comprehensive Stool Analysis / Parasitology x3

DIGESTION /ABSORPTION

	Within	Outside	Reference Range
Elastase	> 500		> 200 µg/mL
Fat Stain	None		None - Mod
Muscle fibers	None		None - Rare
Vegetable fibers	Few		None - Few
Carbohydrates	Neg		Neg

Elastase findings can be used for the diagnosis or the exclusion of exocrine pancreatic insufficiency. Correlations between low levels and chronic pancreatitis and cancer have been reported. **Fat Stain:** Microscopic determination of fecal fat using Sudan IV staining is a qualitative procedure utilized to assess fat absorption and to detect steatorrhea. **Muscle fibers** in the stool are an indicator of incomplete digestion. Bloating, flatulence, feelings of "fullness" may be associated with increase in muscle fibers. **Vegetable fibers** in the stool may be indicative of inadequate chewing, or eating "on the run". **Carbohydrates:** The presence of reducing substances in stool specimens can indicate carbohydrate malabsorption.

INFLAMMATION

	Within	Outside	Reference Range
Lactoferrin		44.3	< 7.3 µg/mL
Calprotectin*		514	<= 50 µg/g
Lysozyme*	412		<= 600 ng/mL
White Blood Cells	None		None - Rare
Mucus	Neg		Neg

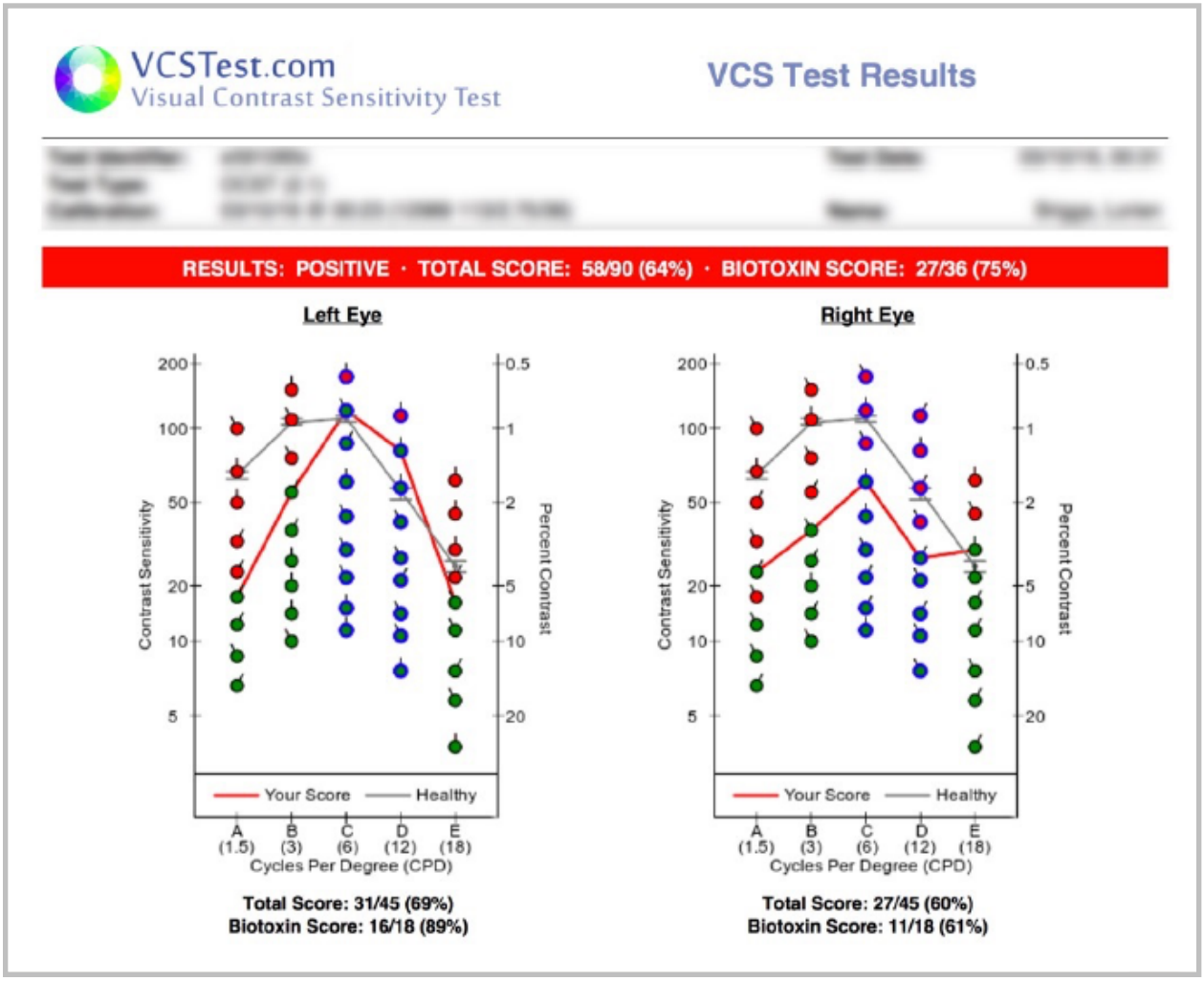
Lactoferrin and **Calprotectin** are reliable markers for differentiating organic inflammation (IBD) from function symptoms (IBS) and for management of IBD. Monitoring levels of fecal lactoferrin and calprotectin can play an essential role in determining the effectiveness of therapy, are good predictors 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*		881	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.

However, there were several other issues that could be causing depressed zinc and elevated copper relative to zinc, including HPA axis dysfunction with high free and metabolized cortisol and high DHEA and estrogen dominance, with high total estrogens here and low progesterone. She also had significant gut inflammation, which was suggestive of inflammatory bowel disease. We did follow-up serology for IBD, which was negative, but referred her out for an MRE or colonoscopy.



Her visual contrast sensitivity result strongly suggested the possibility of biotoxin illness or chronic inflammatory response syndrome. Follow-up biomarker testing is in progress now, but CIRS is, of course, defined by inflammation. It's an inflammatory condition by definition. So, once again, is the low zinc and low zinc-to-copper ratio that we're seeing in this patient due to inadequate dietary intake, malabsorption, inflammation, or some combination of all of the above? She has HPA axis dysfunction and estrogen dominance as well, both of which can cause a low zinc-to-copper ratio. She has significant gut inflammation, which could certainly contribute and also decrease the absorption of both zinc and copper, which could explain her low levels of both, and she may have CIRS. So, in this case, I think it's probably all of the above: HPA axis dysfunction, estrogen, inflammation causing elevation of copper relative to zinc, and maybe malabsorption of both zinc and copper, which is leading to low, relatively low levels of zinc and low-normal levels of copper.