KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Zinc-Copper Imbalance - Part Three

Marker	Value	Functional Range	Lab Range
Glucose	78	75 - 90	70 - 99
Hemoglobin A1c	5.4	4.4 – 5.4	4.8 - 5.6
BUN	10	13 – 18	8 - 22
Creatinine	0.82	0.85 – 1.1	0.44 - 1.27
BUN/Creatinine Ratio	12	8 – 19	8 - 19
Sodium	141	135 – 140	135 - 145
Potassium	4.3	4.0 – 4.5	3.3 - 5
Chloride	105	100 – 106	95 - 110
C02	26	25 – 30	24 - 32
Calcium	9.9	9.2 – 10.1	8.6 - 10.5
Magnesium	2.1	2.0 – 2.6	1.6 - 2.6
Protein, total	7.1	6.9 – 7.4	6.3 - 8.3
Albumin	3.8	4.0 – 5.0	3.4 - 4.8
Bilirubin, total	1.2	0.1 – 1.2	0.3 - 1.3
Alkaline Phosphatase	61	42 – 107	35 - 115
LDH	198	140 - 180	119 - 226
ALT	15	10 - 26	0 - 32
TIBC	461	275 – 425	280 - 400
Iron	92	40 – 135	42 - 135
Iron saturation	20	17 – 45	15 - 55
Ferritin	31	30 - 100	10 - 291
Vitamin B-12	337	450 - 2000	213 - 816
Vitamin D, 25-hydroxy	20.6	35 - 60	30.0 - 100.0
Cholesterol, total	164	150 - 240	100 - 199
Triglycerides	57	50 – 100	0 - 149
HDL	64	55 – 85	> 39
LDL	89	0 - 175	0 - 99
T. Chol / HDL Ratio	2.6	< 3	0 - 5.0
Triglycerides / HDL Ratio	0.89	< 2	< 3.8

Marker	Value	Functional Range	Lab Range
CRP-hs	<0.1	< 1.0	0.00 - 0.80
Homocysteine	9.1	< 7.0	3.8 - 11.0
TSH	1.880	0.5 – 2.5	0.35 - 3.30
T3, Free	3.3	2.5 - 4.0	1.7 - 3.7
T4, Free	0.73	1 - 1.5	0.56 - 1.64
Thyroid – TPO Ab	16		0 - 35
Thyroid – TGA	<20		0 - 40
Copper	190		80 - 155
Zinc	53		55 - 150
Zinc / Copper Ratio	0.28	> 0.85	
Serum Methylmalonic Acid (MMA)	0.21	< 300	0 - 378
WBC	6.6	5.0 – 8.0	4.5 - 11
RBC	4.65	4.4 – 4.9	3.7 - 5.5
Hemoglobin	14.3	14 - 15	12 - 16
Hematocrit	42.4	40 - 48	34 - 46.0
MCV	91.3	85 – 92	80 - 100
MCH	30.7	27.7 – 32.0	27.0 - 33.0
MCHC	33.6	32 – 35	32.0 - 36.0
RDW	13.1	11.5 – 15.0	0.0 - 14.7
Platelets	209	150 – 415	130 - 400
Neutrophils	56.2	40 – 60	
Lymphocytes	34.9	25 – 40	
Monocytes	6.6	4.0 – 7.0	
Eosinophils	1.7	0.0 – 3.0	
Basophils	0.6	0.0 – 3.0	

The next patient is a 23-year-old female with chief complaint of gut issues, constipation or cramping, recent anxiety, and overweight. She was taking oral contraceptive pills, so immediately, you should be thinking about estrogen, since estrogen can increase copper levels. Her serum copper was significantly elevated at 190, in the range of 80 to 155, and her serum zinc was below the lab range at 53, in a range of 55 to 150. This led to a zinc-to-copper ratio of 0.28, which is one of the lowest that I've ever seen. Her vitamin D, 25(OH)D, was also low at 20.6, and her serum B12 was borderline low at 337.

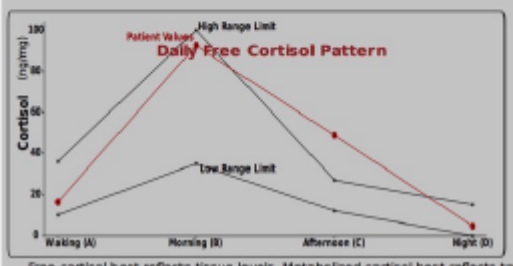
Hormone Testing Summary

How to read the graphical representation of results

Sex Hormones

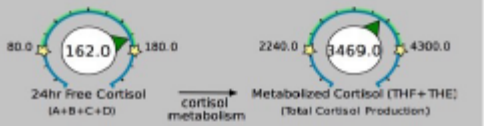
See Pages 2 & 3 for a thorough breakdown of sex hormone metabolites

Adrenal Hormones



Total DHEA Production

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



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

Hormone	Brand	ROA (1-10)	Dose (mg)	Date Last Used	Times per Day	Length of use

☒ Not taking any listed hormones

Do you take DIM/I-3-C regularly? ☐ Yes ☒ No

List Any other relevant drugs, supplements or others:

All units are given in ng/mg creatinine

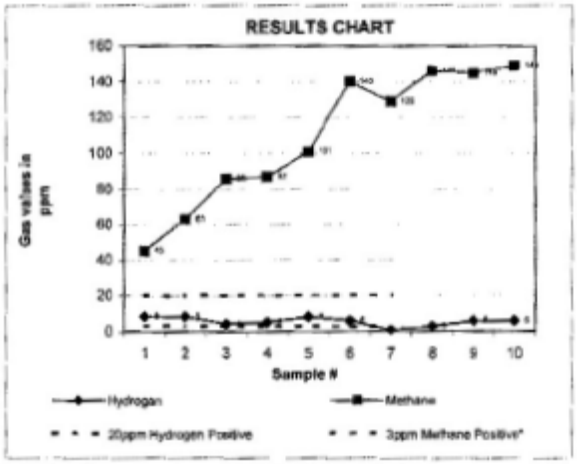
Patient reports regular menstrual cycles

Last Menstrual Period - 2015-09-09

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

SMALL INTESTINAL BACTERIAL OVERGROWTH REPORT SHEET - 10 SPECIMEN TEST

	Sample Time	Sample #	ppm H_2	ppm CH_4	(f) CO_2
Small Intestine	Control	1	8	45	1.28
	20 min.	2	8	63	1.23
	40 min.	3	4	86	1.23
	60 min.	4	5	87	1.23
	80 min.	5	8	101	1.17
	100 min.	6	6	140	1.17
	120 min.	7	1	129	1.24
Colon	140 min.	8	3	146	1.16
	160 min.	9	6	146	1.18
	180 min.	10	6	149	1.23



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:	**7 ppm**	Normal <20 ppm
Peak Methane (CH4) Production:	**94 ppm**	Normal <3 ppm*
Peak Combined Gas Production:	**101 ppm**	Normal <20 ppm

RESULT: BASED ON THE CRITERIA USED IN THIS STUDY, PRESENCE OF BACTERIAL OVERGROWTH IS SUPPORTED

NOTES:

Her hormone profile revealed a PCOS-like presentation: high total estrogens, low progesterone, and high testosterone. Her SIBO results were strongly positive for methane overproduction. She had a peak methane of 140 at 100 minutes, which is one of the highest I've ever seen. Again, in this patient, the most likely explanation for the decreased zinc-to-copper ratio is inflammation and also probably estrogen dominance.

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Copper, Urine					
Copper, Urine	6		ug/L	Not Estab.	01
			Detection Limit = 1		
Creatinine(Crt),U	0.37		g/L	0.30 - 3.00	01
			Detection Limit = 0.10		
Copper/Crt Ratio	16		ug/g creat	0 - 49	
Copper,Urine 24 Hr	17		ug/24 hr	3 - 35	
		High		>3.00	
Homocyst(e)ine, Plasma	10.2		umol/L	0.0 - 15.0	01
TSH	1.300		uIU/mL	0.450 - 4.500	01
Thyroxine (T4)	8.7		ug/dL	4.5 - 12.0	01
T3 Uptake	25		%	24 - 39	01
Free Thyroxine Index	2.2			1.2 - 4.9	
Triiodothyronine (T3)	109		ng/dL	71 - 180	01
Copper, Serum	94		ug/dL	72 - 166	02
			Detection Limit = 5		
Zinc, Plasma or Serum	95		ug/dL	56 - 134	02
			Detection Limit = 5		

In this case, I ran a urine copper test to get another read on toxicity because her zinc-to-copper ratio was so low, and as you can see here, her 24-hour urine copper was completely normal. After treating her gut and hormones, follow-up testing revealed a zinc-to-copper ratio of 1. Her serum copper was 94, and her serum zinc was 95, as you can see at the bottom of the slide, so addressing the underlying issues lead to a resolution of the low zinc-to-copper ratio.

Tests Ordered
Copper, Serum; Zinc, Plasma or Serum; Venipuncture

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Copper, Serum	87		ug/dL	72 - 166	01
			Detection Limit = 5		
Zinc, Plasma or Serum	**167**	**High**	ug/dL	56 - 134	01
Verified by repeat analysis					
			Detection Limit = 5		

Here is a patient with a high zinc-to-copper ratio, and you can see serum zinc is elevated at 167, in a range of 56 to 134, and serum copper is 87, which was normal. This is almost always caused by zinc supplementation. This was a 32-year-old female who presented with anxiety and digestive symptoms. She had been taking 50 mg of zinc per day for about six months at the recommendation of a previous practitioner. In this case, you would want to advise the patient to stop the supplements and retest about 30 to 60 days later.

Marker	Value	Functional Range	Lab Range
Glucose	77	75 - 90	65 - 99
Hemoglobin A1c	5.6	4.4 – 5.4	4.8 - 5.6
Uric Acid	3.8	3.2 - 5.5	2.5 - 7.1
BUN	11	13 – 18	6 - 20
Creatinine	0.66	0.7 – 1.0	0.57 - 1.00
BUN/Creatinine Ratio	17	9 – 23	9 - 23
Sodium	140	135 – 140	134 - 144
Potassium	4.4	4.0 – 4.5	3.5 - 5.2
Chloride	100	100 – 106	97 - 108
C02	21	25 – 30	18 - 29
Calcium	9.4	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	6.9	6.9 – 7.4	6.0 - 8.5
Albumin	4.2	4.0 – 5.0	3.5 - 5.5
Globulin	2.7	2.4 – 2.8	1.5 - 4.5
A/G ratio	1.6	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.2	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	58	42 – 107	39 - 117
LDH	134	140 - 180	119 - 226
AST	18	10 - 23	0 - 40
ALT	12	10 - 20	0 - 32
GGT	4	5 - 21	0 - 60
TIBC	424	275 – 425	250 - 450
UIBC	315	175 - 350	150 - 375
Iron	109	40 – 135	35 - 155
Iron saturation	26	17 – 45	15 - 55
Ferritin	114	30 - 100	15 - 150
Vitamin B-12	298	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	26.3	35 - 60	30.0 - 100.0
Cholesterol, total	182	150 - 250	100 - 199
Triglycerides	56	50 – 100	0 - 149
HDL	76	55 – 85	> 39
LDL	95	0 - 175	0 - 99
T. Chol / HDL Ratio	2.4	< 3	0 - 4.4
Triglycerides / HDL Ratio	0.74	< 2	< 3.8

Marker	Value	Functional Range	Lab Range
CRP-hs	8	< 1.0	0.00 - 3.00
Homocysteine	7.2	< 7.0	0.0 - 15.0
TSH	1.740	0.5 – 2.5	0.45 - 4.500
T4, total	10.6	6.0 – 12	4.5 - 12.0
T3 Uptake	19	28 - 35	24 - 39
T3, Total	208	100 – 180	71 - 180
Copper	220		72 - 166
Zinc	111		56 - 134
Zinc / Copper Ratio	0.50	> 0.85	
Serum Methylmalonic Acid (MMA)	140	< 300	0 - 378
WBC	5.7	5.0 – 8.0	3.4 - 10.8
RBC	4.30	4.4 – 4.9	3.77 - 5.28
Hemoglobin	12.0	13.5 - 14.5	11.1 - 15.9
Hematocrit	36.7	37 - 44	34 - 46.6
MCV	85	85 – 92	79 - 97
MCH	27.9	27.7 – 32.0	26.6 - 33.0
MCHC	32.7	32 – 35	31.5 - 35.7
RDW	13.0	11.5 – 15.0	12.3 - 15.4
Platelets	385	150 – 415	150 - 379
Neutrophils	54	40 – 60	
Lymphocytes	29	25 – 40	
Monocytes	10	4.0 – 7.0	
Eosinophils	7	0.0 – 3.0	
Basophils	0	0.0 – 3.0	

The next patient is a 27-year-old female with chief complaints of salicylate and amine intolerances. She had a history of elevated aminotransferases, was on oral contraceptives, and also had celiac disease. Check out her copper. It was extremely high at 220, and her serum zinc was 111, which is in the upper end of the range, but because her copper was so high, her zinc-to-copper ratio was still very low at 0.5. Her T3 was high, total T3 at 208, above the lab range. Her CRP is elevated at 8. Her platelets were a little bit high at 385. Her B12, 25(OH)D, and magnesium were all low.

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Ceruloplasmin	**54.1**	**High**	mg/dL	16.0 - 45.0	02
Copper, Serum	**220**	**High**	ug/dL Detection Limit = 5	72 - 166	02

01 SO LabCorp San Diego Dir: Jenny Galloway, MD
13112 Evening Creek Dr So Ste 200, San Diego, CA 92128-4108
02 BN LabCorp Burlington Dir: William F Hancock, MD
1447 York Court, Burlington, NC 27215-3361
For inquiries, the physician may contact **Branch: 800-762-4344 Lab: 858-668-3700**

Tests Ordered
Copper, Urine

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Copper, Urine					
Copper, Urine	4		ug/L Detection Limit = 1	Not Estab.	01
	Please note reference interval change				
Creatinine(Crt),U	0.64		g/L Detection Limit = 0.10	0.30 - 3.00	01
Copper/Crt Ratio	6		ug/g creat	0 - 49	
Copper,Urine 24 Hr	8		ug/24 hr	3 - 35	

01 BN LabCorp Burlington Dir: William F Hancock, MD
1447 York Court, Burlington, NC 27215-3361
For inquiries, the physician may contact **Branch: 800-762-4344 Lab: 858-668-3700**

I retested her serum copper and also ran ceruloplasmin, and both were elevated, so her copper was again 220, and her ceruloplasmin was 54.1. Then I did a 24-hour urine copper test, and it was in the low-normal range.

Test	Wilson Disease	Copper Toxicity	Menkes Disease (Kinky Hair Syndrome)	Copper Deficiency
Copper, blood	Low but may be normal	High	Low	Low
Copper, serum free	High	High	Low	Low
Ceruloplasmin	Low but may be normal	High	Low	Low
Copper, urine	Very High	High	Low	Low
Copper, liver/hepatic*	Positive, depending on the site sampled, may be negative	High or normal	Low	Low

Now in Wilson's disease, the expected findings are high serum copper, low ceruloplasmin, and very high urine copper. In copper toxicity, we would expect to see high serum copper, high ceruloplasmin, and high urine copper, so with her numbers, I was kind of surprised to see her urine copper normal because her ceruloplasmin was high, and serum copper was high, and I was expecting copper toxicity, but that is not what we saw. Her serum copper and ceruloplasmin were high, but her urine copper was actually low-normal.

TEST	RESULT			
Array 5 – Multiple Autoimmune Reactivity Screen **	**IN RANGE (Normal)**	**EQUIVOCAL***	**OUT OF RANGE**	**REFERENCE** (ELISA Index)
Parietal Cell + ATPase			1.90	0.1-1.4
Intrinsic Factor		1.18		0.1-1.2
ASCA + ANCA			1.90	0.2-1.4
Tropomyosin	0.99			0.1-1.5
Thyroglobulin	0.97			0.1-1.3
Thyroid Peroxidase	0.93			0.1-1.3
21-Hydroxylase (Adrenal Cortex)			1.43	0.2-1.2
Myocardial Peptide			1.93	0.1-1.5
Alpha-Myosin	0.99			0.3-1.5
Phospholipid			1.92	0.2-1.3
Platelet Glycoprotein			1.33	0.1-1.3
Ovary/Testis ***			1.60	0.1-1.2
Fibulin			1.93	0.4-1.6
Collagen Complex			2.18	0.2-1.6
Arthritic Peptide			1.66	0.2-1.3
Osteocyte			2.61	0.1-1.4
Cytochrome P450 (Hepatocyte)			2.07	0.3-1.6
Insulin + Islet Cell		1.68		0.4-1.7
Glutamic Acid Decarboxylase 65			1.89	0.2-1.6
Myelin Basic Protein			1.90	0.1-1.4
Asialoganglioside			2.47	0.1-1.4
Alpha-Tubulin + Beta-Tubulin		1.11		0.4-1.4
Cerebellar			2.15	0.2-1.4
Synapsin			1.37	0.1-1.2

Again, I suspected that inflammation was present, so I ran Cyrex Array 5 and found that she had positive results for multiple antibodies, so this is a polyreactive antibody production pattern, which suggests significant autoimmunity and cross-reactivity, which leads to an elevation in nearly all antibody production. It's not that the patient is actually producing antibodies to all of these tissues, but some of these antibodies are cross-reacting with various tissues, so you see elevations. When you see something like this on Cyrex Array 5, you really need to look at immune dysregulation, and in my experience, there is almost always something such as CIRS, heavy metal toxicity, or chronic infection that leads to a pattern like this where you see so many antibodies that are elevated. She, indeed, failed VCS testing and the biotoxin illness survey that we give patients,

and we're currently testing her for the biomarkers for CIRS, and that, again, would not be uncommon in cases of these polyreactive antibody elevations.

Marker	Value	Functional Range	Lab Range
Glucose	88	75 - 90	65 - 99
Hemoglobin A1c	5.3	4.4 – 5.4	4.8 - 5.6
Uric Acid	4.8	3.7 – 6.0	3.7 - 8.6
BUN	12	13 – 18	6 - 20
Creatinine	1.07	0.85 – 1.1	0.76 - 1.27
BUN/Creatinine Ratio	11	8 – 19	8 - 19
Sodium	142	135 – 140	134 - 144
Potassium	4.6	4.0 – 4.5	3.5 - 5.2
Chloride	101	100 – 106	97 - 108
C02	25	25 – 30	18 - 29
Calcium	9.9	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.7	3.0 – 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	5.0	4.0 – 5.0	3.5 - 5.5
Globulin	1.9	2.4 – 2.8	1.5 - 4.5
A/G ratio	2.6	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.5	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	30	42 – 107	39 - 117
LDH	137	140 - 180	121 - 224
AST	16	10 - 25	0 - 40
ALT	11	10 - 26	0 - 44
GGT	10	5 - 29	0 - 65
TIBC	239	275 – 425	250 - 450
UIBC	94	175 - 350	150 - 375
Iron	145	40 – 135	40 - 155
Iron saturation	61	17 – 45	15 - 55
Ferritin	361	30 - 100	30 - 400
Vitamin B-12	582	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	84.7	35 - 60	30.0 - 100.0
Cholesterol, total	199	150 - 240	100 - 199
Triglycerides	45	50 – 100	0 - 149
HDL	78	55 – 85	> 39
LDL	112	0 - 175	0 - 99
T. Chol / HDL Ratio	2.6	< 3	0 - 5.0
Triglycerides / HDL Ratio	0.58	< 2	< 3.8

Marker	Value	Functional Range	Lab Range
CRP-hs	0.1	< 1.0	0.00 - 3.00
Homocysteine	13.8	< 7.0	0.0 - 15.0
TSH	1.650	0.5 – 2.5	0.45 - 4.50
T4, total	7.3	6.0 – 12	4.5 - 12
T3 Uptake	27	30 - 38	24 - 39
T3, Total	84	100 – 180	71 - 180
Copper	58		72 - 166
Zinc	136		56 - 134
Zinc / Copper Ratio	2.34	> 0.85	
Serum Methylmalonic Acid (MMA)	70	< 300	0 - 378
WBC	4.3	5.0 – 8.0	3.4 - 10.8
RBC	5.04	4.4 – 4.9	4.14 - 5.8
Hemoglobin	15.5	14 - 15	12.6 - 17.7
Hematocrit	45.3	40 - 48	37.5 - 51.0
MCV	90	85 – 92	79 - 97
MCH	30.8	27.7 – 32.0	26.6 - 33.0
MCHC	34.2	32 – 35	31.5 - 35.7
RDW	13.7	11.5 – 15.0	12.3 - 15.4
Platelets	212	150 – 415	150 - 379
Neutrophils	44	40 – 60	
Lymphocytes	44	25 – 40	
Monocytes	8	4.0 – 7.0	
Eosinophils	3	0.0 – 3.0	
Basophils	1	0.0 – 3.0	

The next patient is a 29-year-old male with chief complaint of GI issues, including bloating and constipation and depression and anxiety symptoms for most of his life. Serum copper is lab-low at 58. The range is 72 to 166. Serum zinc is lab-high at 136, in a range of 56 to 134. We also note this patient has iron overload. Iron saturation is 61 percent. Ferritin is 361, which is nearly out of the lab range. TIBC and UIBC are low. This could be consistent with Wilson's disease, which can present with iron overload as well as low serum copper.

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Soluble Transferrin Receptor	13.4		nmol/L	12.2 - 27.3	02
Ceruloplasmin	12.8	**Low**	mg/dL	15.0 - 30.0	02

Effective January 18, 2016 the reference interval
for Ceruloplasmin will be changing to:

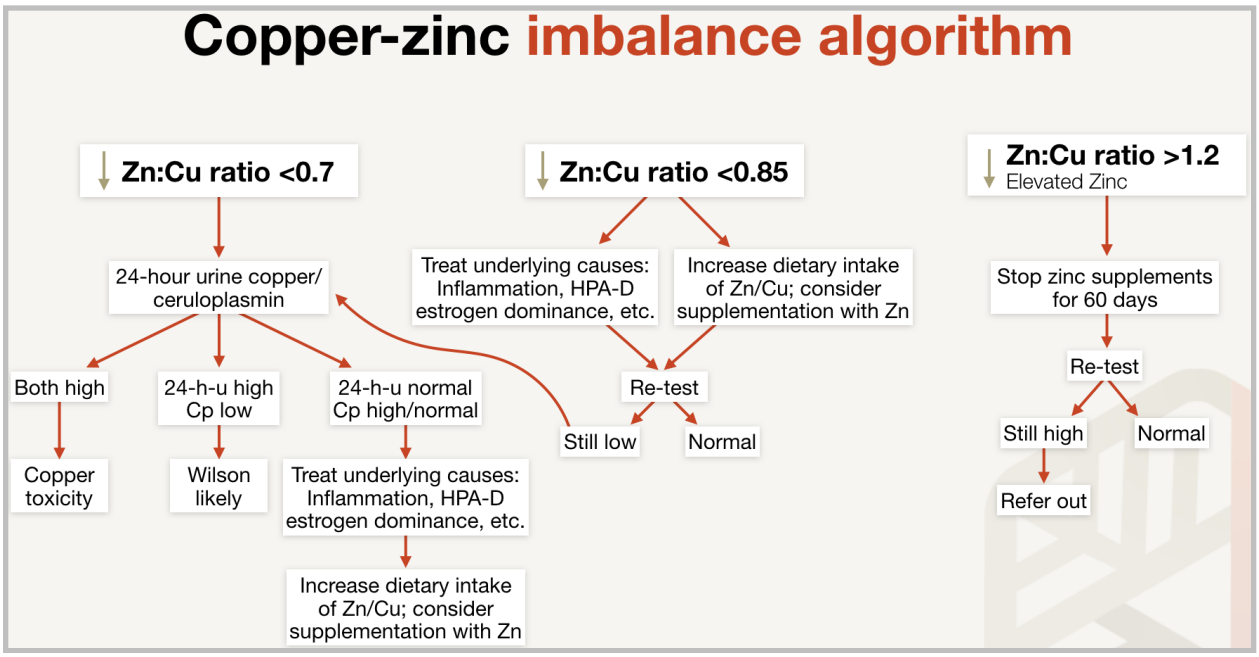
Male		
	0 - 30 days	Not Estab.
	1 - 6 months	11.0 - 31.0
	7 months - 12 years	18.0 - 35.0
	>12 years	16.0 - 31.0
Female		
	0 - 30 days	Not Estab.
	1 - 6 months	11.0 - 31.0
	>6 months	19.0 - 39.0

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Copper, Urine					
Copper, Urine	6		ug/L	Not Estab.	01
			Detection Limit = 1		
Creatinine(Crt),U	0.51		g/L	0.30 - 3.00	01
			Detection Limit = 0.10		
Copper/Crt Ratio	12		ug/g creat	0 - 49	
Copper,Urine 24 Hr	32		ug/24 hr	3 - 35	

I ran a ceruloplasmin test, and it was low, and urine copper is high-normal, so again, that perfectly fits what you would expect with Wilson's disease. I referred him to a specialist, and he was diagnosed with early-stage Wilson's disease.

Wilson's disease is a genetic abnormality inherited in an autosomal recessive manner that leads to impairment of cellular copper transport. It has a prevalence of approximately one case in 30,000 live births in most populations. Impaired biliary copper excretion leads to accumulation of copper in several organs, but most notably the liver, brain, and cornea. Over time, the liver is progressively damaged and eventually becomes cirrhotic. Clinical manifestations of Wilson's disease are predominantly hepatic, neurologic, and psychiatric, with many patients having a combination of symptoms.

However, some patients are completely asymptomatic in early stages or just have mild psychiatric symptoms such as anxiety and depression, which was the case with this patient. The majority of patients with Wilson's disease are diagnosed between the ages of five and 35 years, so he was pretty late on that spectrum, though this disorder has been diagnosed in younger patients and in patients as old as in their 70s. If Wilson's is untreated, it's universally fatal. However, the prognosis for patients who receive an early diagnosis and adhere to the treatment is pretty good. The earlier it is caught, the less copper is accumulated, and the better the prognosis, so it's really important to be aware of.



Let's talk about an algorithm for approaching zinc-copper imbalance. If the zinc-to-copper ratio is below 0.7, you would run a 24-hour urine copper and ceruloplasmin just to rule out Wilson's disease and frank copper toxicity, so if both are high, then that would be suggestive of copper toxicity. If 24-hour urine is high and ceruloplasmin is low, Wilson's disease is a definite possibility, and you want to refer out. If 24-hour urine is normal, and ceruloplasmin is high or normal, that could be inflammation, so you'd treat the underlying causes, then increase dietary intake of zinc and copper, and consider supplementation with zinc and then retest.

If the zinc-to-copper ratio is below 0.85 but above 0.7, you would treat the underlying causes, increase the dietary intake of zinc and copper, maybe consider supplementation with a lower dose of zinc, but that is only if the patient for whatever reason can't eat high-zinc foods, and then you would retest. If the ratio is still low, you do the same workup here according to where it falls, and then if it is normal, you're done. If the zinc-to-copper ratio is over 1.2, the first thing you do is ask the patient if he is taking zinc supplements. If he is, he stops zinc for 60 days. If he isn't taking zinc supplements and the ratio is high, then you have him significantly increase his intake of dietary copper, since the most likely cause is copper deficiency, and then you would retest. Depending on the value at that point, you can use this algorithm to determine what to do next.

Note that high levels of zinc in the absence of supplementation are pretty rare, and there are some case reports of genetic disorders causing this in children, and strangely, they present with symptoms of zinc deficiency, so if you see high zinc, you've increased dietary copper, and the patient is not taking zinc supplements, you may want to refer out to a specialist.

Given that elevated serum copper is usually a sign of inflammation rather than excess copper intake and could even mask copper deficiency, and given that copper deficiency can exacerbate inflammation, I believe that when the zinc-to-copper ratio is depressed and no signs of copper

toxicity are present, such as elevated ceruloplasmin or elevated 24-hour urine copper, the patient should increase his intake of dietary copper, but since we don't have an accurate marker for detecting the early stages of copper deficiency, the safest route is to increase only their dietary intake and not take copper supplements. The body has sophisticated mechanisms for regulating copper absorption and metabolism, and cases of toxicity from dietary intake are extremely rare.

Signs and symptoms of copper deficiency include fatigue, arthritis, joint pain, osteoporosis, low body temperature, anemia that is unresponsive to iron but responsive to copper, muscle soreness, hair thinning, bruising, and also neurodegenerative disease and cardiovascular disease. Populations that are at risk include babies who have been fed cow's milk formula, which is low in copper; premature infants; people with GI malabsorption issues; people with cystic fibrosis; and then people taking high-dose, meaning over 40 mg per day, of zinc.

USDA recommended Cu intake by population

Population	Amount (mcg)
Infants (0–6 months)	200
Children (7 months–13 years old)	220–700, depending on age
Adolescents (14–18 years old)	890
Adults	900
Pregnant women	1,000
Breastfeeding women	1,300

The USDA recommends the following intake of copper by population: 200 mcg for infants, 220 to 700 mcg for kids depending on their age, 890 mcg for adolescents, and then 900 mcg for adults, 1,000 for pregnant women, and 1,300 for breastfeeding women.

The upper limit for the intake of copper, as I mentioned, is currently 10 mg per day, but recent research suggests that it should be significantly higher. In one study after applying a safety factor of 10, extrapolating from animals to humans, the upper limit would be 49 mg per day, which is about five times higher than the present upper limit.