

# Blood Chem Zinc-Copper Imbalance Review

Serum copper and serum zinc are poor markers for dietary intake of copper and zinc.

## NUMEROUS NON-NUTRITIONAL FACTORS INFLUENCE ZINC AND COPPER SERUM LEVELS

- Zinc in serum goes down in oxidative stress and inflammation.
- Copper is elevated in the inflammatory response in a wide range of conditions.

## HIGH COPPER-TO-ZINC RATIO: CAUSE OR EFFECT?

- Blood copper level correlates strongly with the marker of inflammation C-reactive protein, yet substantially increasing copper intake doesn't increase CRP.
  - This suggests that elevated blood copper is likely a symptom of inflammation rather than its cause.
  - This could explain why high copper is a risk factor for heart attack
- Some studies suggest that copper deficiency worsens inflammation.
- Finally, prolonged use of zinc supplements may cause secondary copper deficiency.

## SERUM COPPER AND ZINC DO NOT DETECT MILD TO MODERATE DEFICIENCY OR EXCESS

- Serum copper levels are now considered to be rather worthless for determining copper deficiency or copper overload.
- Serum copper and ceruloplasmin concentrations are useful to diagnose Menkes and Wilson's diseases and moderate-to-severe copper deficiency. However, these markers are not sensitive enough to detect changes of a lesser magnitude.
- They also act as acute-phase proteins and increase during inflammation, pregnancy, aging, and a number of diseases.
- Serum zinc is a better than serum copper and may be the best of all available zinc biomarkers.
- Vegetarians may require 50 percent more zinc than omnivores.

## SIGNS AND SYMPTOMS OF COPPER DEFICIENCY

- Bone malformation during fetal/childhood development
- Osteoporosis
- Impaired melanin synthesis

- Poor immune function
- Cardiovascular disease
- Altered cholesterol metabolism
- Iron deficiency anemia

**POPULATIONS THAT ARE AT RISK FOR COPPER DEFICIENCY 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
- People taking high-dose, meaning over 40 mg per day, of zinc.

**KEY TAKEAWAYS**

- A high copper-to-zinc ratio may indicate inflammation, HPA-D, estrogen dominance, or pregnancy, not necessarily excess copper or inadequate zinc intake.
- A high copper-to-zinc ratio is associated with numerous chronic inflammatory diseases.
- Presence of high serum copper or low serum zinc does not always warrant zinc supplementation, and it may even be harmful.
- Serum copper values are just a starting point and should never be used in isolation. If serum copper is elevated or decreased, use markers such as ceruloplasmin, 24-hour urine copper, ALT, AST, and possibly liver biopsy to clarify the diagnosis.

**FUNCTIONAL ZINC-TO-COPPER RANGE IS 0.85–1.2.**

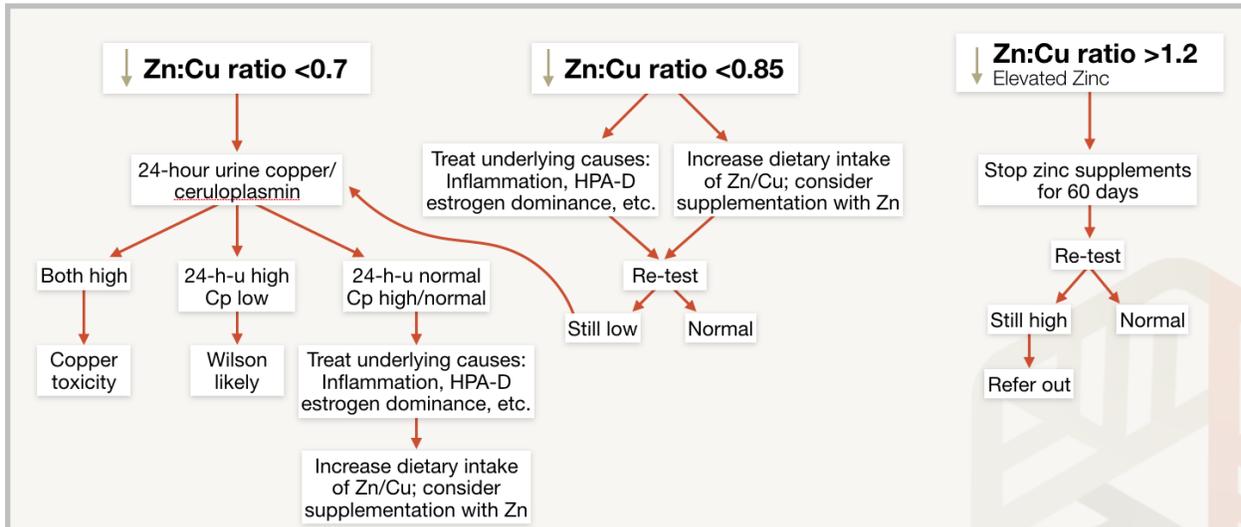
Marker	Lab Range	Functional Range
<b>Zinc</b>	56–134	64–126
<b>Copper</b>	72–166	81–157

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

## WILSON'S DISEASE

- Can present with iron overload as well as low serum copper.
- Ceruloplasmin is low, and urine copper is high or high-normal.
- Genetic, autosomal recessive, disorder that leads to impairment of cellular copper transport.
- Impaired biliary copper excretion leads to accumulation of copper in several organs, most notably the liver, brain, and cornea. Progressive liver damage leads to cirrhosis.
- Clinical manifestations of Wilson's disease are predominantly hepatic, neurologic, and psychiatric. However, some patients are completely asymptomatic in early stages or just have mild psychiatric symptoms such as anxiety and depression.
- The earlier it is caught, the less copper is accumulated, and the better the prognosis.

## COPPER-ZINC IMBALANCE ALGORITHM



High zinc levels in the absence of supplementation are rare, and the patient may need referral 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 and not take copper supplements.

## HIGHEST DIETARY SOURCES OF COPPER

Food	Amount (mg per 200 cal)
<b>Clam</b>	39
<b>Beef/lamb/goose liver</b>	14-17
<b>Oysters</b>	13
<b>Fresh basil</b>	3
<b>King crab</b>	2
<b>Sesame butter</b>	1
<b>Ham</b>	1
<b>Cashews</b>	1
<b>Octopus</b>	1
<b>Chestnuts</b>	1
<b>Chicken liver</b>	1
<b>Whitefish</b>	1

## ZINC

- Since we don't have a reliable biomarker, especially for marginal deficiency when serum zinc levels are low, it is difficult to determine whether it is from inflammation, marginal deficiency, or both.
- Given that zinc supplements can cause copper deficiency, copper deficiency is possibly more common than acknowledged, and there are no reliable markers for detecting mild copper deficiency. I believe that getting zinc from food rather than supplements is best in most cases.

## POPULATIONS AT RISK FOR ZINC DEFICIENCY

- Vegetarians, who require up to 50 percent more zinc than omnivores because of the nutrient inhibitors in plant-based foods
- People with GI malabsorption, including celiac and IBD
- Children and adolescents
- Pregnant and breastfeeding women
- Elderly
- Alcoholics

Signs and symptoms of zinc deficiency include poor neurological function, weak immunity, diarrhea, allergies, autoimmunity, thinning hair, intestinal permeability, acne, and rashes.

## HIGHEST DIETARY SOURCES OF ZINC

<b>Food</b>	<b>Amount (mg per 200cal)</b>
<b>Oyster</b>	265
<b>Veal liver</b>	17
<b>King crab</b>	16
<b>Lobster</b>	10
<b>Beef, chuck</b>	10
<b>Lamb, shank</b>	10
<b>Endive</b>	9
<b>Beef, brisket</b>	9
<b>Mushrooms, crimini</b>	8
<b>Broccoli rabe</b>	7
<b>Bison, ground</b>	6

High zinc intake, 40 to 50 mg of supplements, 10 mg of diet, has been shown to cause copper deficiency, so the upper limit for zinc is 40 mg per day, combined with supplements and food.

## WHO SHOULD SUPPLEMENT?

- Vegetarians and vegans, or those that can't eat foods rich in zinc or copper
- People with significant zinc and copper deficiency
  - Low serum copper is expected in Wilson's disease, so you need to test 24-hour urine copper and ceruloplasmin before you consider copper supplementation.
- People with GI absorption issues

When you do supplement, I recommend supplementing with both nutrients to reduce the risk of toxicity of one nutrient or inducing deficiency of the other.

## RECOMMENDED ZINC DOSAGE

Population	Amount (mg)
Low background intake	Up to 30 mg/d
Moderate background intake	Up to 15 mg/d
Maintenance dose	10–15 mg/d

Retest serum zinc levels after 60 to 90 days. Once therapeutic goal is achieved, I suggest dropping supplementation and advising patients to get zinc from food. Vegetarians/vegans may need a maintenance dose of 10 to 15 mg of zinc per day. Best form is zinc glycinate.

## RECOMMENDED COPPER DOSAGE

Population	Amount (mg)
Low background intake	6–8 mg/d
Moderate background intake	2–4 mg/d
Maintenance dose	1–2 mg/d