Considerations in the Copper Deficient Patient

Patients at risk	♦ Gastrectomy/gastric surgery bypassing duodenum & between 100-200cm of jejunum (primary site for copper absorption) o Roux en y gastric bypass in particular with pts supplemented with zinc and no copper ♦ Excess zinc ingestion ♦ Parenteral nutrition without or insufficient copper added ♦ Enteral feeding o Inadequate copper content of formulas (Japan) o Jejunal access ♦ Nephrotic syndrome o Increased permeability of glomerulus to ceruloplasmin ♦ Alkaline therapy for renal tubular acidosis ♦ Menke's kinky hair disease o X-linked recessive multisystemic lethal disorder of copper metabolism ♦ Occipital horn disease o Occipital horn syndrome, formerly considered a variant of Ehlers-Danlos syndrome, an X-linked recessive connective tissue disorder; considered a milder variant of Menkes disease. ♦ Wilson's disease o Serum copper is low, which may seem paradoxical given that Wilson's disease is a disease of copper excess, however it is sequestered in the liver; 95% of plasma copper is carried by ceruloplasmin which is often low in Wilson's disease.
Signs / Symptoms	♦ Anemia - hypochromic-microcytic o Unresponsive to iron supplementation ♦ Neutropenia ♦ Leukopenia ♦ Osteoporosis ♦ Myeloneuropathy ♦ Myelodysplastic syndromes
Labs	♦ CBC w/ differential ♦ Also consider B6, Vitamin E, thiamine if myeloneuropathy present ♦ Serum copper o Can be lowered by: corticosteroids, corticotropin o Can be increased under a number of conditions due to increased concentrations of ceruloplasmin: oral contraceptive use, pregnancy, infections, inflammation, myocardial infarction, rheumatoid arthritis, dilated cardiomyopathy ♦ Ceruloplasmin

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	○ Acute phase protein--increases in acute or chronic infection, inflammatory states, malignancy, liver disease, myocardial infarction, oral contraceptive use ○ Lowered in: ▪ Nephrotic syndrome ▪ Menkes syndrome ▪ Wilson's disease ▪ Chronic hepatitis ♦ WBC w/ differential ○ Low neutrophil count ♦ Erythrocyte superoxide dismutase activity – not available at UVA ○ Not as specific as serum copper or ceruloplasmin concentration, although may be more sensitive ○ Increased activity in: alcoholism and Down's syndrome ♦ Cytochrome C oxidase activity - not available at UVA
Dosing	♦ RDA = adult men and women is 900µg/day ♦ Oral/enteral ○ Net amount absorbed increases as the amount in diet increases, but absorption is more efficient when intake is low. ○ 2 mg copper gluconate daily or every other day ○ 10 g pure cocoa powder (4 teaspoons) ▪ Some reports of tachycardia ♦ IV ○ 1.5-3 mg IV for how long x 3-5 days ○ In those refractory to IV repletion, consider that the IV copper may retain more if infused over a longer period of time like magnesium. ♦ Recheck serum copper in 4 weeks ○ Do not check too soon after beginning supplementation.
Considerations if deficient or refractory to repletion	♦ Inorganic copper is absorbed in the stomach and proximal duodenum under acidic conditions, while cuproprotein copper is absorbed below the level of the pancreatic duct (i.e., alkaline conditions) ○ Copper sulfate may not be well absorbed in alkaline medium ○ Copper gluconate ○ Copper ♦ If oral: ○ May alter bioavailability: phytates/fiber, stop PPI/H2 blockers, antacids, high dose vitamin C, zinc, iron, fructose ○ Zinc ▪ Zinc induces synthesis of metallothionein in the intestinal mucosa cells, but copper binds more avidly to metallothionein displacing zinc that will then be absorbed, while copper remains bound to

	metallothionein in the mucosa instead of entering the body. This copper is returned to the intestinal lumen with natural turnover of mucosal cells and excreted. ▪ Stop denture cream with zinc ▪ No zinc lozenges ▪ Do not exceed zinc to copper ratio of 10:1 – 30:1 can precipitate copper deficiency ♦ Do not take copper supplements with iron or zinc ♦ Ensure denture cream does not contain zinc ♦ IV fluids o Urinary copper losses were double those of orally fed individuals. This probably reflects the fact that in oral feeding copper reaches the liver first, where it is incorporated into ceruloplasmin and only then arrives at the kidneys as a nonfilterable complex. In intravenous feeding, part of the infused copper reaches the kidneys in a filterable form, and this is liable to be lost in the urine. • Shike M, Roulet M, Kurian R, et al. Copper metabolism and requirements in total parenteral nutrition. Gastroenterology. 1981;81:290-97.

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Specific Patient Populations—this is not an exhaustive list of cases in pubmed

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Note: For all the Japanese references below, copper deficiency was due solely as a result of inadequate copper in their commercial formulas. "In Japan, solutions used for enteral feeding have been classified prescription or nonprescription enteral nutrition by the government to control medical cost. The price of the nonprescription one is much cheaper than that of the prescription one. Therefore, many hospitals use the nonprescription one instead of the prescription one. However, nonprescription enteral nutrition solutions are prepared from a limited

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