

# Practical Considerations for Parenteral Trace Elements (Copper, Selenium, Zinc)

The provision of copper, selenium, and zinc is an important aspect of parenteral nutrition to ensure delivery of essential nutrients. This practice tool addresses practical considerations related to these essential nutrients and is intended to optimize clinical practice and patient outcomes.

Topic		Copper	Selenium	Zinc
Normal Function, Pharmacokinetics, Lab Values, and Monitoring	<b>Physiologic Function</b>	<ul style="list-style-type: none"> <li>Iron metabolism</li> <li>Connective tissue maturation</li> <li>Neurotransmission</li> <li>Energy production</li> </ul>	<ul style="list-style-type: none"> <li>Glutathione, iodine, and thyroid metabolism</li> <li>Cardiac functioning</li> <li>Cell growth and apoptosis</li> <li>Serves as an antioxidant</li> <li>Insulin-mimetic properties</li> </ul>	<ul style="list-style-type: none"> <li>Cellular metabolism</li> <li>Glucose metabolism and insulin secretion</li> <li>Immune function</li> <li>Wound healing</li> <li>Protein synthesis</li> <li>Sex organ development</li> </ul>
	<b>Site of Absorption</b>	Duodenum, proximal small intestine, stomach (minimal)	Duodenum	Duodenum, proximal jejunum
	<b>Significant Routes of Elimination</b>	Bile, intestine, renal	Renal, some fecal losses	Intestine
	<b>Select Monitoring Parameters<sup>1,2,3</sup></b>	<ul style="list-style-type: none"> <li>Serum copper<sup>4</sup> and serum ceruloplasmin</li> <li>*Free Copper = (Total serum copper in mcg/dL) – (Ceruloplasmin in mg/dL x 3)</li> <li>Urine copper</li> <li>Superoxide dismutase activity</li> </ul>	<ul style="list-style-type: none"> <li>Serum selenium</li> <li>Glutathione peroxidase (plasma and red blood cell)</li> <li>Thyroid function tests</li> </ul>	<ul style="list-style-type: none"> <li>Serum zinc</li> <li>Alkaline phosphatase</li> <li>Copper status for patients on zinc supplementation</li> <li>Add oral/enteral before zinc supplementation</li> <li>Consider checking vitamin A level</li> </ul>
Deficiency	<b>Causes and At-Risk Populations (Consider Dose Increase – See Dosing Section)</b>	<ul style="list-style-type: none"> <li>Long-term PN without copper</li> <li>Burns</li> <li>Continuous renal replacement therapy</li> <li>Gastric resections, bariatric surgery, short bowel syndrome, malabsorption disorders, high GI losses</li> <li>Prolonged enteral zinc supplementation</li> </ul>	<ul style="list-style-type: none"> <li>Long-term PN without selenium</li> <li>Breastfed infants of mothers with poor nutrition/low selenium levels</li> <li>Continuous renal replacement therapy</li> <li>Enterocutaneous fistulae</li> <li>Maple Syrup Urine Disease</li> <li>Phenylketonuria</li> <li>Prematurity</li> <li>Proximal small bowel resection or malabsorption disorders</li> </ul>	<ul style="list-style-type: none"> <li>Long-term PN without zinc</li> <li>Alcoholism</li> <li>Breastfed infants of mothers with poor nutrition/low zinc levels</li> <li>Burns</li> <li>Immune disorders</li> <li>Liver disease</li> <li>Pregnancy</li> <li>Prematurity</li> <li>Renal disease</li> <li>Short bowel syndrome, malabsorption disorders, high GI losses</li> </ul>
	<b>Signs and Symptoms</b>	<ul style="list-style-type: none"> <li>Bone pain</li> <li>Impaired wound healing</li> <li>Iron deficiency (secondary)</li> <li>Myelopathy</li> <li>Neutropenia, leukopenia, anemia, and/or pancytopenia</li> <li>Optic neuropathy</li> <li>Skin and hair depigmentation</li> <li>Osteoporosis</li> </ul>	<ul style="list-style-type: none"> <li>Alopecia</li> <li>Ataxia</li> <li>Cardiomyopathy</li> <li>Decreased thyroid function</li> <li>Growth retardation</li> <li>Reproductive failure</li> <li>Myopathy</li> </ul>	<ul style="list-style-type: none"> <li>Acrodermatitis enteropathica</li> <li>Alopecia</li> <li>Altered taste and smell</li> <li>Decreased immune function</li> <li>Delayed sexual maturation</li> <li>Diarrhea</li> <li>Growth retardation</li> <li>Impaired wound healing</li> <li>Night blindness</li> </ul>

GI, gastrointestinal; PN, parenteral nutrition

<sup>1</sup> Defer labs during periods of acute illness and inflammation. Consider obtaining inflammatory markers (e.g., CRP (c-reactive protein)).

<sup>2</sup> Frequency of monitoring is patient specific; however, generally 4 weeks after dose change and then every 1-3 months once stable.

<sup>3</sup> Refer to institution- and age-specific ranges for normal values.

<sup>4</sup> Serum copper concentration does not correlate with copper balance.

	Topic	Copper	Selenium	Zinc
Toxicity	<b>Causes and At-Risk Populations</b> <i>(Consider dose decrease – see Dosing section)</i>	<ul style="list-style-type: none"> <li>Hepatobiliary impairment</li> <li>Wilson’s Disease</li> </ul>	<ul style="list-style-type: none"> <li>Renal insufficiency</li> </ul>	
	<b>Signs and Symptoms</b>	<ul style="list-style-type: none"> <li>Abdominal pain</li> <li>Blue-green GI output</li> <li>Bradycardia</li> <li>Growth failure</li> <li>Hemolysis</li> <li>Hypercholesterolemia</li> <li>Hypotonia</li> <li>Liver failure</li> <li>Metallic taste</li> <li>Neurologic impairment</li> <li>Peripheral edema</li> <li>Photophobia</li> <li>Renal failure</li> </ul>	<ul style="list-style-type: none"> <li>Anorexia</li> <li>Dyspepsia</li> <li>Fatigue</li> <li>Garlic aroma of breath</li> <li>Hair and nail loss</li> <li>Hypersalivation</li> <li>Hypopigmentation</li> <li>Peripheral neuropathy</li> <li>Rash</li> <li>Seizures</li> </ul>	<ul style="list-style-type: none"> <li>Abdominal pain</li> <li>Anemia</li> <li>Anorexia</li> </ul>
Dosing Considerations	<ul style="list-style-type: none"> <li>Parenteral dosing of copper, selenium, and zinc can be found in the <i>Appropriate Dosing for Parenteral Nutrition: ASPEN Recommendations</i> at <a href="https://nutritioncare.org/PNDosingRecommendations">nutritioncare.org/PNDosingRecommendations</a>.</li> <li>Prior to considering a dose increase or dose reduction for deficiency or toxicity, respectively, ensure proper monitoring is performed.</li> <li>Trace element laboratory parameters should be deferred during periods of acute illness or inflammation. Consider obtaining inflammatory markers (e.g., CRP (c-reactive protein)).</li> <li>Individual patient trace element status should direct dosing decisions.</li> <li>High concentrations of trace elements may alter PN compatibility and stability; ensure PN admixture is compatible and stable when compounding and prior to administration.</li> </ul>			

GI, gastrointestinal

## Product Availability

Single Product Availability	
<b>Copper</b>	Cupric chloride injection, USP 0.4 mg/mL <sup>†</sup>
<b>Selenium</b>	Selenious acid injection, USP 6 mcg/mL <sup>†</sup> Selenious acid injection, USP 60 mcg/mL <sup>†</sup>
<b>Zinc</b>	Zinc sulfate injection, USP 1 mg/mL <sup>†</sup> Zinc sulfate injection, USP 3 mg/mL <sup>†</sup> Zinc sulfate injection, USP 5 mg/mL <sup>†</sup>

<sup>†</sup> Manufacturer: American Regent

\* Manufacturer: Pfizer/Hospira

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Multiple Trace Element Product Availability <sup>1</sup>	
<b>Neonatal/ pediatric &lt;10 kg</b>	Multrys™ (trace elements injection 4*, USP) <sup>†</sup> 1mL= zinc 1000 mcg, copper 50 mcg, manganese 3 mcg, selenium 6 mcg
<b>Pediatric, adolescents, adults &gt;10 kg</b>	Tralement™ (trace elements injection 4*, USP) <sup>†</sup> 1mL = zinc 3 mg, copper 0.3 mg, manganese 55 mcg, selenium 60 mcg

<sup>†</sup> Manufacturer: American Regent

<sup>1</sup> For neonates, infants and children, weight-based dosing is imperative. Refer to manufacturer package labeling as well as *Appropriate Dosing for Parenteral Nutrition: ASPEN Recommendations* at [nutritioncare.org/PNDosingRecommendations](https://nutritioncare.org/PNDosingRecommendations).

### References:

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2. *JPEN J Parenter Enteral Nutr.* 2019;43 Suppl 1:S5-S23.
3. *Clin Nutr.* 2018 Dec;37(6 Pt B):2354-2359.
4. *JPEN J Parenter Enteral Nutr.* 2004;28(6):S39-70.
5. *The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum, 2nd Ed.* Silver Spring, MD: ASPEN; 2015.
6. *The A.S.P.E.N. Adult Nutrition Support Core Curriculum, 3rd Ed.* Silver Spring, MD: ASPEN 2017.
7. *Nutr Clin Pract.* Feb 2015, 30 (1) 44-58.
8. *Clin Biochemistry.* 1995 28(6): 561 – 566.
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