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.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Copper</th>
<th>Selenium</th>
<th>Zinc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiologic Function</td>
<td>Iron metabolism</td>
<td>Glutathione, iodine, and thyroid metabolism</td>
<td>Cellular metabolism</td>
</tr>
<tr>
<td></td>
<td>Connective tissue maturation</td>
<td>Cardiac functioning</td>
<td>Glucose metabolism and insulin secretion</td>
</tr>
<tr>
<td></td>
<td>Neurotransmission</td>
<td>Cell growth and apoptosis</td>
<td>Immune function</td>
</tr>
<tr>
<td></td>
<td>Energy production</td>
<td>Serves as an antioxidant</td>
<td>Wound healing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insulin-mimetic properties</td>
<td>Protein synthesis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sex organ development</td>
</tr>
</tbody>
</table>

**Normal Function, Pharmacokinetics, Lab Values, and Monitoring**

**Physiologic Function**
- Iron metabolism
- Connective tissue maturation
- Neurotransmission
- Energy production
- Glutathione, iodine, and thyroid metabolism
- Cardiac functioning
- Cell growth and apoptosis
- Serves as an antioxidant
- Insulin-mimetic properties
- Cellular metabolism
- Glucose metabolism and insulin secretion
- Immune function
- Wound healing
- Protein synthesis
- Sex organ development

**Site of Absorption**
- Duodenum, proximal small intestine, stomach (minimal)
- Duodenum
- Duodenum, proximal jejunum

**Significant Routes of Elimination**
- Bile, intestine, renal
- Renal, some fecal losses
- Intestine

**Select Monitoring Parameters**
- Serum copper and serum ceruloplasmin
  - Free Copper = (Total serum copper in mcg/dL) – (Ceruloplasmin in mg/dL x 3)
- Urine copper
- Superoxide dismutase activity

**Causes and At-Risk Populations**
- Long-term PN without copper supplementation
- Burns
- Continuous renal replacement therapy
- Gastric resections, bariatric surgery, short bowel syndrome, malabsorption disorders, high GI losses
- Prolonged enteral zinc supplementation

**Deficiency**
- Bone pain
- Impaired wound healing
- Iron deficiency (secondary)
- Myelopathy
- Neutropenia, leukopenia, anemia, and/or pancytopenia
- Optic neuropathy
- Skin and hair depigmentation
- Osteoporosis

**Signs and Symptoms**
- Alopecia
- Ataxia
- Cardiomyopathy
- Decreased thyroid function
- Growth retardation
- Reproductive failure
- Myopathy
- Acrodermatitis enteropathica
- Alopecia
- Altered taste and smell
- Decreased immune function
- Delayed sexual maturation
- Diarrhea
- Growth retardation
- Impaired wound healing
- Night blindness

Gi, gastrointestinal; PN, parenteral nutrition

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

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

3. Refer to institution- and age-specific ranges for normal values.

4. Serum copper concentration does not correlate with copper balance.
### Toxicity

<table>
<thead>
<tr>
<th>Topic</th>
<th>Copper</th>
<th>Selenium</th>
<th>Zinc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes and At-Risk Populations (Consider dose decrease – see Dosing section)</td>
<td>Hepatobiliary impairment</td>
<td>Renal insufficiency</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Signs and Symptoms</td>
<td>Abdominal pain</td>
<td>Anorexia</td>
<td>Anorexia</td>
</tr>
<tr>
<td></td>
<td>Blue-green GI output</td>
<td>Dyspepsia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bradycardia</td>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Growth failure</td>
<td>Garlic aroma of breath</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hemolysis</td>
<td>Hair and nail loss</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypercholesterolemia</td>
<td>Hypersalivation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypotonia</td>
<td>Hypopigmentation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Liver failure</td>
<td>Peripheral neuropathy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metallic taste</td>
<td>Rash</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neurologic impairment</td>
<td>Seizures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peripheral edema</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Photophobia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal failure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Dosing Considerations

- Parenteral dosing of copper, selenium, and zinc can be found in the Appropriate Dosing for Parenteral Nutrition: ASPEN Recommendations at nutritioncare.org/PNDosingRecommendations.
- Prior to considering a dose increase or dose reduction for deficiency or toxicity, respectively, ensure proper monitoring is performed.
- Trace element laboratory parameters should be deferred during periods of acute illness or inflammation. Consider obtaining inflammatory markers (e.g., CRP (c-reactive protein)).
- Individual patient trace element status should direct dosing decisions.
- High concentrations of trace elements may alter PN compatibility and stability; ensure PN admixture is compatible and stable when compounding and prior to administration.

### Product Availability

#### Single Product Availability

<table>
<thead>
<tr>
<th>Element</th>
<th>Description</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper</td>
<td>Cupric chloride injection, USP</td>
<td>0.4 mg/mL*</td>
</tr>
<tr>
<td>Selenium</td>
<td>Selenious acid injection, USP</td>
<td>6 mcg/mL†</td>
</tr>
<tr>
<td>Selenium</td>
<td>Selenious acid injection, USP</td>
<td>60 mcg/mL†</td>
</tr>
<tr>
<td>Zinc</td>
<td>Zinc sulfate injection, USP</td>
<td>1 mg/mL†</td>
</tr>
<tr>
<td>Zinc</td>
<td>Zinc sulfate injection, USP</td>
<td>3 mg/mL†</td>
</tr>
<tr>
<td>Zinc</td>
<td>Zinc sulfate injection, USP</td>
<td>5 mg/mL†</td>
</tr>
</tbody>
</table>

#### Multiple Trace Element Product Availability

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal/ Pediatric &lt;10 kg</td>
<td>MultrysTM (trace elements injection 4*, USP)†</td>
<td>1 mL = zinc 1000 mcg, copper 50 mcg, manganese 3 mcg, selenium 6 mcg</td>
</tr>
<tr>
<td>Pediatric, Adolescents, Adults &gt;10 kg</td>
<td>TralementTM (trace elements injection 4*, USP)†</td>
<td>1 mL = zinc 3 mcg, copper 0.3 mg, manganese 55 mcg, selenium 60 mcg</td>
</tr>
</tbody>
</table>

* Manufacturer: Pfizer/Hospira
† Manufacturer: American Regent

### Disclaimer

This content has been developed for use by healthcare professionals to inform other clinicians and/or patients/caregivers. ASPEN is making this content available for informational purposes only. This content is not based on ASPEN Board Approved documents and should not be confused with ASPEN clinical guidelines as it was not developed according to ASPEN guideline processes. Recommendations provided here do not constitute medical or other professional advice and should not be taken as such. To the extent that the information presented here may be used to assist in the care of patients, the primary component of quality medical care is the result of the professional judgment of the healthcare professionals providing care. The information presented here is not a substitute for the exercise of professional judgment by healthcare professionals. Circumstances and patient specifics in clinical settings may require actions different from those recommended in this document; in those cases, the judgment of the treating professional should prevail. Use of this information does not in any way guarantee any specific benefit in outcome or survival. This tool is intended to supplement, but not replace, professional training and judgment.

## References


© Copyright 2023 American Society for Parenteral and Enteral Nutrition | 11/27/23