

is treated with a parenteral dose of 10 mg. For patients with chronic malabsorption, 1–2 mg/d should be given orally or 1–2 mg per week can be taken parenterally. Patients with liver disease may have an elevated prothrombin time because of liver cell destruction as well as vitamin K deficiency. If an elevated prothrombin time does not improve during vitamin K therapy, it can be deduced that this abnormality is not the result of vitamin K deficiency.

Toxicity Toxicity from dietary phyloquinones and menaquinones has not been described. High doses of vitamin K can impair the actions of oral anticoagulants.

MINERALS

See also Table 96e-2.

CALCIUM

See Chap. 423.

ZINC

Zinc is an integral component of many metalloenzymes in the body; it is involved in the synthesis and stabilization of proteins, DNA, and RNA and plays a structural role in ribosomes and membranes. Zinc is necessary for the binding of steroid hormone receptors and several other transcription factors to DNA. Zinc is absolutely required for normal spermatogenesis, fetal growth, and embryonic development.

Absorption The absorption of zinc from the diet is inhibited by dietary phytate, fiber, oxalate, iron, and copper as well as by certain drugs, including penicillamine, sodium valproate, and ethambutol. Meat, shellfish, nuts, and legumes are good sources of bioavailable zinc, whereas zinc in grains and legumes is less available for absorption.



Deficiency Mild zinc deficiency has been described in many diseases, including diabetes mellitus, HIV/AIDS, cirrhosis, alcoholism, inflammatory bowel disease, malabsorption syndromes, and sickle cell disease. In these diseases, mild chronic zinc deficiency can cause stunted growth in children, decreased taste sensation (*hypogeusia*), and impaired immune function. Severe chronic zinc deficiency has been described as a cause of hypogonadism and dwarfism in several Middle Eastern countries. In these children, hypopigmented hair is also part of the syndrome. Acrodermatitis enteropathica is a rare autosomal recessive disorder characterized by abnormalities in zinc absorption. Clinical manifestations include diarrhea, alopecia, muscle wasting, depression, irritability, and a rash involving the extremities, face, and perineum. The rash is characterized by vesicular and pustular crusting with scaling and erythema. Occasional patients with Wilson's disease have developed zinc deficiency as a consequence of penicillamine therapy (Chap. 429).

Zinc deficiency is prevalent in many developing countries and usually coexists with other micronutrient deficiencies (especially iron deficiency). Zinc (20 mg/d until recovery) may be an effective adjunctive therapeutic strategy for diarrheal disease and pneumonia in children ≥ 6 months of age.

The diagnosis of zinc deficiency is usually based on a serum zinc level $<12 \mu\text{mol/L}$ ($<70 \mu\text{g/dL}$). Pregnancy and birth control pills may cause a slight depression in serum zinc levels, and hypoalbuminemia from any cause can result in hypozincemia. In acute stress situations, zinc may be redistributed from serum into tissues. Zinc deficiency may be treated with 60 mg of elemental zinc taken by mouth twice a day. Zinc gluconate lozenges (13 mg of elemental zinc every 2 h while awake) have been reported to reduce the duration and symptoms of the common cold in adults, but study results are conflicting.

TABLE 96e-2 DEFICIENCIES AND TOXICITIES OF METALS

Element	Deficiency	Toxicity	Tolerable Upper (Dietary) Intake Level
Boron	No biologic function determined	Developmental defects, male sterility, testicular atrophy	20 mg/d (extrapolated from animal data)
Calcium	Reduced bone mass, osteoporosis	Renal insufficiency (milk-alkali syndrome), nephrolithiasis, impaired iron absorption, thiazide diuretics	2500 mg/d (milk-alkali)
Copper	Anemia, growth retardation, defective keratinization and pigmentation of hair, hypothermia, degenerative changes in aortic elastin, osteopenia, mental deterioration	Nausea, vomiting, diarrhea, hepatic failure, tremor, mental deterioration, hemolytic anemia, renal dysfunction	10 mg/d (liver toxicity)
Chromium	Impaired glucose tolerance	<i>Occupational:</i> Renal failure, dermatitis, pulmonary cancer	Not determined
Fluoride	\uparrow Dental caries	Dental and skeletal fluorosis, osteosclerosis	10 mg/d (fluorosis)
Iodine	Thyroid enlargement, $\downarrow T_4$, cretinism	Thyroid dysfunction, acne-like eruptions	1100 $\mu\text{g/d}$ (thyroid dysfunction)
Iron	Muscle abnormalities, koilonychia, pica, anemia, \downarrow work performance, impaired cognitive development, premature labor, \uparrow perinatal maternal death	Gastrointestinal effects (nausea, vomiting, diarrhea, constipation), iron overload with organ damage, acute and chronic systemic toxicity, increased susceptibility to malaria, increased risk association with certain chronic diseases (e.g., diabetes)	45 mg/d of elemental iron (gastrointestinal side effects)
Manganese	Impaired growth and skeletal development, reproduction, lipid and carbohydrate metabolism; upper body rash	<i>General:</i> Neurotoxicity, Parkinson-like symptoms <i>Occupational:</i> Encephalitis-like syndrome, Parkinson-like syndrome, psychosis, pneumoconiosis	11 mg/d (neurotoxicity)
Molybdenum	Severe neurologic abnormalities	Reproductive and fetal abnormalities	2 mg/d (extrapolated from animal data)
Selenium	Cardiomyopathy, heart failure, striated muscle degeneration	<i>General:</i> Alopecia, nausea, vomiting, abnormal nails, emotional lability, peripheral neuropathy, lassitude, garlic odor to breath, dermatitis <i>Occupational:</i> Lung and nasal carcinomas, liver necrosis, pulmonary inflammation	400 $\mu\text{g/d}$ (hair, nail changes)
Phosphorus	Rickets (osteomalacia), proximal muscle weakness, rhabdomyolysis, paresthesia, ataxia, seizure, confusion, heart failure, hemolysis, acidosis	Hyperphosphatemia	4000 mg/d
Zinc	Growth retardation, \downarrow taste and smell, alopecia, dermatitis, diarrhea, immune dysfunction, failure to thrive, gonadal atrophy, congenital malformations	<i>General:</i> Reduced copper absorption, gastritis, sweating, fever, nausea, vomiting <i>Occupational:</i> Respiratory distress, pulmonary fibrosis	40 mg/d (impaired copper metabolism)