### 3 Nutritional Challenges in Special Conditions and Diseases

#### 3.2 Iron Deficiency and Other Nutrient Deficiencies

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**Key Words**

- Micronutrient deficiencies
- Iron
- Anemia
- Eating disorders
- Chronic disease
- Iatrogeny

**Key Messages**

- Iron deficiency and anemia are the most widespread human deficiencies and produce reduced productivity and learning.
- Endemic deficiencies of vitamin A and zinc are associated with greater infectious morbidity in children.
- Eating disorders, clinical illness and iatrogenic causes are the bases of micronutrient deficiencies in clinical pediatrics.
- The combination of addressing the underlying causes and providing prudent supplementation with vitamins and/or minerals is essential to resolving micronutrient malnutrition.

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**Introduction**

Micronutrients (vitamins and minerals) are essential for human health, growth, and development. Humans evolved as hunter-gatherers, expending large amounts of energy to obtain sustenance from wild plants and hunted game. The evolutionary complementary feeding of infants involved pre-masticated meat. As such, humans evolved consuming large amounts of a micronutrient-rich food. The advent of the agricultural era placed reliance on nutrients primarily on a narrow selection of grains and tubers, exposing humankind to the risk of vitamin and mineral deficiencies. Table 1 illustrates the various mechanisms that can contribute to nutrient deficiencies [1].

**The Clinical Contexts of Micronutrient Deficiencies**

The various contexts within which micronutrient deficiencies can occur are outlined in table 2 [2]. Among the vitamins, deficiencies of vitamins A, D, C, B₆, B₁₂, thiamin, riboflavin, niacin, and folic acid can be encountered in free-living children in a public health context as a result of social or environmental adversity or abuse. Similarly, nutritional deficiencies of phosphorus, magnesium, iron, zinc, iodine, fluorine and selenium can occur in sectors of a free-living public. In a public health sense, deficiencies of micronutrients have recently been termed ‘hidden hunger’ because the nutrients responsible for the deficiency cannot be seen in the foods, and one might be consuming sufficient total energy and macro-nutrients, and still suffer a vitamin or mineral deficit [3].

Clinical deficiencies of vitamins E and K, pantothenic acid and biotin among vitamins, and
calcium, copper, selenium, molybdenum, chromium and manganese among minerals, have been documented only with severe disorders in pathophysiology or due to iatrogenic factors, or in some cases, with controlled experimental depletion in adult volunteers. The deficiencies of this group of nutrients do not represent a public health concern.

Specific Nutrient Deficiencies of Public Health Importance, Afflicting Those Consuming Poor Diets and under Environmental Stress

A selected cluster of six micronutrients merit in-depth mention and consideration as their prevention, mitigation, and therapy can represent a public health challenge.

Iron Deficiency and Iron Deficiency Anemia

Iron is the most important and challenging of the public health micronutrient deficiencies. It is estimated that from 2 to 5 billion of the world’s 6 billion inhabitants are iron-deficient, and from one third to one sixth of these have microcytic, hypochromic anemia attributable to iron deficiency. Iron deficiency has a series of functional consequences as outlined in table 3. These are common to the condition, whether or not it is associated with anemia. Hence, iron deficiency disorders can take a devastating toll on the fitness of both individuals and the communities of which they are a part [4].

Among the risk factors for iron deficiency are: reliance on iron-poor foods such as milk and dairy products (including human milk), rice, fruits, and fleshy vegetables; reliance on foods of low iron bioavailability, and blood-feeding parasites [5]. Iron deficiency is common in infants, in the second semester of infancy as well as in adolescence, due to rapid growth in boys and to the onset of menarche in girls.

The mechanisms of host defense against infection exclude iron from cells and sequester the

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<tr>
<th>Table 1. Mechanisms contributing to micronutrient malnutrition</th>
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<tr>
<td>Insufficient intake of nutrient in relation to requirements</td>
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<tr>
<td>Impaired intestinal nutrient absorption</td>
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<td>Diminished whole-body retention of nutrient</td>
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<td>Impaired cellular nutrient utilization</td>
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<td>Enhanced intrinsic destruction of nutrient</td>
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<th>Table 2. The scenarios and contexts for developing micronutrient malnutrition</th>
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<td><strong>Adverse social or environmental conditions</strong></td>
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<td>Poverty or displacement, which interfere with the access to food; disruptions in agriculture or trade, which interfere with the availability of food; unsanitary conditions or transmission of pathogens, which compromise the absorption or retention of nutrients</td>
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<td><strong>Eating disorders or abuse</strong></td>
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<td>Emotional disturbances related to food or intentional restriction or deprivation of food by caretakers</td>
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<td><strong>Clinical illnesses</strong></td>
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<td>Disease states with pathophysiological effects that impair the consumption, absorption, utilization or retention of nutrients</td>
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<td><strong>Iatrogenic factors</strong></td>
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<td>Inappropriate withholding of essential nutrients or prescription of medications with anti-nutritional effects</td>
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<th>Table 3. Functional consequences of iron deficiency</th>
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<td>Reduce cognitive development as measured by intelligence quotient</td>
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<td>Reduced attention span</td>
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<td>Poor learning and impaired scholastic performance</td>
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<td>Decreased exercise stamina</td>
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<td>Reduced muscular force and strength</td>
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<td>Impaired body temperature regulation</td>
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<td>Immune deficiencies involving macrophage and neutrophil phagocytosis, T-cell proliferation, and interleukin-2 responses</td>
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<tr>
<td>Depriving intracellular pathogens of the iron needed for proliferation and virulence and protecting the host from more severe consequences of infection</td>
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Iron Deficiency and Other Nutrient Deficiencies

Iron within cells into ferritin in an attempt to deprive pathogenic organisms of iron. For certain intracellular pathogens, iron deficiency of the host may confer relative protection.

**Hypovitaminosis A**

The most heralded consequences of vitamin A deficiency are night blindness (failure to adapt to vision in dim light) and xerophthalmia (ocular lesions that can lead to nutritional blindness). However, the most devastating manifestation is for marginal vitamin A deficiency, which is associated with an increased risk of mortality from common childhood infections and measles [6]. Worldwide, at any given time, less than 5 million children have a certain stage of xerophthalmia, whereas 130 million preschool children will have some degree of hypovitaminosis A. Risk factors include a predominantly plant-based diet, severe infections such as measles, AIDS and tuberculosis, recurrent gastrointestinal or respiratory infections, and poor hygienic living conditions [7].

**Iodine Deficiency Disorders**

Millennia of soil leaching has depleted most soils of iodine. During the 1990s, a major international public health effort raised the coverage of iodized salt from 20% to over 80%, improving iodine status worldwide. Yet, an estimated 285 million schoolchildren, worldwide, are at risk of suffering iodine deficiency disorders. In areas of the interior of central Africa, where the myxedematous form of goiter exists, an environmental scarcity of selenium has been suggested as the factor which produces profound hypothyroidism [8].

**Zinc Deficiency**

Zinc is virtually absent in fruits, vegetables and tubers, and the zinc content in legumes and whole grains is tightly bound by phytic acid, and not easily available for intestinal absorption. It has thus been postulated that zinc deficiency is widespread and responsible for some of the linear growth retardation in developing countries. Getting adequate zinc is especially challenging during the period of weaning, as virtually no unfortified complementary food can provide the recommended intakes for late infancy [9].

Zinc deficiency is associated with impaired immune function, and recent epidemiological studies indicate that child deaths from respiratory and gastrointestinal infections could be reduced by assuring adequate zinc nutrition in at-risk populations.

**Vitamin B<sub>12</sub> Deficiency**

Although it was thought to be a predominant condition of the elderly, recent surveys in Africa and Mesoamerica indicate high prevalences of low vitamin B<sub>12</sub> status [10]. A combination of dietary insufficiency with environmental factors impairing gastric (*Helicobacter pylori*) and intestinal (bacterial overgrowth) health contribute to this condition as a pediatric public health problem.

**Hyporiboflavinosis**

In actual numbers, it is probable that more children worldwide have a marginal riboflavin status (as indicated by abnormal values on a biochemical biomarker of riboflavin status, erythrocyte glutathione reductase activity coefficient) than even iron deficiency. Severe riboflavin deficiency with clinical manifestations is rare, and most often seen in the context of multiple micronutrient deficits.

**Micronutrient Deficiencies in Other Pediatric Contexts**

**Micronutrient Deficiencies in Eating Disorders**

Eating disturbances and disorders can contribute to serious micronutrient deficiencies [11]. This ranges from picky-eating and fear of fatness in younger children to overt anorexia nervosa and bulimia in adolescents. The addition of emetics and laxatives to control weight gain aggravates nutrient absorption and retention. Cases of in-
Reduced childhood micronutrient deficiencies have been recorded in children raised in cults with unorthodox vegetarian dietary practices.

**Chronic Clinical Disorders and Micronutrient Deficiencies**

Table 4 summarizes selected clinical disorders contributing to micronutrient deficiency. A series of nutrients that are wasted in the urine, including vitamin A and trace elements, will be lost in excess with systemic inflammatory responses, as seen in AIDS, tuberculosis, malaria and systemic parasitoses. Urinary nutrient wasting also occurs in certain renal diseases in which the glomeruli become porous, tubular reabsorption is impaired, or both.

The essential purpose of the alimentary tract is to obtain nutrients; therefore any digestive or absorptive disorders will compromise nutrient uptake [12]. Virtually all vitamins and minerals can be adversely affected by small bowel diseases. Blood loss leading to iron deficiency is common in inflammatory bowel disorders. Neuromuscular disorders interfere with proper chewing and swallowing, often limiting the quantity and variety of dietary intake.

Diabetes mellitus is associated with deficiency of a number of minerals. Magnesium, calcium and phosphorus can be wasted in chronic renal disease, as well as all water-soluble vitamins; fat-soluble vitamin levels in the circulation are frequently elevated. Chronic hemo- and peritoneal dialysis generally progressively deplete vitamins.

Acrodermatitis enteropathica and Menkes disease represent examples of congenital illnesses that affect the cellular transporters for zinc and copper, respectively. This results in total body depletion of zinc and the manifestations of severe zinc deficiency. The defect of copper transport in Menkes disease is not only in the gut but throughout the body, generating profound signs of copper depletion through impaired utilization of the metal.

**Iatrogenic Causes of Micronutrient Deficiencies**

Prescriptions and practices of clinical practitioners can contribute iatrogenic causes of micronutrient deficiencies. Improper formulation of infant formula, enteral feedings and parenteral infusions has produced deficiencies of vitamin E, zinc, copper, selenium, molybdenum and chromium, as well as chloride [13, 14]. A variant of this mechanism is the addition of a medication to a formula that destroys or inactivates a nutrient. Prolonged use of antibiotics, purging the intestinal flora, has contributed to vitamin K and biotin deficiency. Other medications interfere with the absorption or utilization of one or another micronutrient. Sulfasalazine, for example, interferes...
with folate absorption and metabolism. Antacids and acid-blocking drugs create pH and secretory conditions in the stomach and upper intestine. The roster of drug–nutrient interactions compromising micronutrient malnutrition is exhaustive, and cannot be covered in full here.

Conclusions

- Children commonly develop overt deficiencies of only certain vitamins (A, D, C, B₆, B₁₂, thiamin, riboflavin, niacin, folic acid) and minerals (phosphorus, magnesium, iron, zinc, iodine, fluorine and selenium)
- The practitioner must know the signs and symptoms and appropriate interpretation of hematological, biochemical and functional indices of vitamin and mineral deficiencies
- The appropriate prescription of the deficient nutrient, combined with attention to the underlying cause(s) of deficiency, should restore an adequate state of micronutrient nutrition

References