Editorial

Zinc is an essential micronutrient for living organisms from the unicellular level to the vertebrate species. Its recognition for human public health and clinical medicine, however, dates back only six decades to the middle of the last century. As is illustrated in each of the four contributions, zinc is a unique nutrient insofar as the assessment of zinc status in individuals and populations is so elusive, due to the absence of reliable biomarkers. According to Dr. Michael Golden, zinc is a type II nutrient; these are nutrients that cannot be retained and stored in the body, such that it is requisite to have a constant daily uptake to replace losses. In other species, the first reaction to a zinc-deficient diet is for the organism to go into conservation mode and defend the amount of zinc in the body; this process is accompanied by a profound loss of appetite and a cessation in growth. For humans, in whom eating is not only a response to hunger but also a social and cultural norm, individuals continue to eat a zinc-poor diet, adding a unique dimension to the biology of zinc depletion in our species.

An impressive amount of basic science regarding this mineral has been generated over the past six decades. Noel W. Solomons leads off the series of articles with an attempt at a succinct distillation of findings from physical and organic chemistry, physiology and metabolism from recent literature, which seeks to link, where possible, the known functions and actions of zinc with the clinical and epidemiological fundamentals of zinc nutrition. An important mechanistic understanding of zinc absorption

and transport, in terms of transporters and binding proteins, has developed. Examples are evident in insulin secretion of pancreatic islet cells and in the regulation of both elements of the lymphocyte system. These cellular and molecular insights further elucidate and explain the manifestations of inadequate zinc nutrition in clinical disorders and economically deprived populations.

Implications of zinc in clinical pediatrics are reviewed by Nancy F. Krebs. She covers the circumstances in which zinc deficiency on a dietary basis can occur, as in the ill-advised restriction of children's diets and the unique maternal genetic circumstance of low zinc concentrations in breast milk. Linking basic science to clinical dermatology and gastroenterology, Dr. Krebs describes the genetic disorder of zinc malabsorption, acrodermatitis enteropathica (AE). Among the important insights are the facts that only half of the AE cases have the classical mutation in the ZIP gene and that situations of atypical and mild AE are more common than generally recognized. The clinician needs to be vigilant about acquired (secondary) zinc deficiency in low birth weight and prematurity, gastrointestinal diseases, such as celiac disease, hepatic disorders, and cystic fibrosis. Confounded by the unreliability of zinc status biomarkers, a practical approach to proactive supplementation is outlined. Finally, with respect to the common cold, it seems that zinc lozenges can reduce symptoms when consumed in a timely manner at an appropriate dose, although their efficacy in otitis media is still uncertain.

Mary Edith Penny provides a comprehensive, impartial and insightful review of the original literature and extensive systematic reviews and meta-analyses related to zinc supplementation trials to address issues ranging from short stature to susceptibility to diarrhea and respiratory infections and to infectious mortality in childhood.

She also covers evidence related to therapeutic efficacy in acute and persistent diarrhea, which is accepted as reliable, and in lower respiratory infections and tuberculosis, for which the evidence is not conclusive. Among the more definitive findings is the safety of usual supplementation doses of oral zinc ranging from 5 to 20 mg daily in children. Any of the soluble zinc salts used in research and routine interventions are, in fact, effective as supplements. There are situations in which there is robust evidence for efficacy, as in reducing the duration of diarrheal episodes, but the magnitude of shortening is measured in hours, not days. Dr. Penny usefully confronts the heterogeneity among the findings of zinc supplementation trials for all purposes, and skillfully addresses the nuances related to age of the child, geographical setting, dosage and duration of zinc supplementation and initially circulating zinc concentration.

Insofar as zinc supplementation has many beneficial effects, delivery of the nutrient as a fortifying agent in a staple food for infants or children has been examined by a series of investigators in both developed and developing countries. A working group from the Aga Khan Univer-

sity in Karachi, Pakistan, led by Prof. Zulfiqar A. Bhutta, has prepared a systematic review of the meager contributory literature, constituting a total of 11 evaluable published reports, to see what the state of knowledge regarding efficacy of zinc fortification is at this time. They conclude that zinc fortification within a variety of food items has generally, but not universally, increased circulating levels of zinc as compared to an appropriate control group. Evidence for fortifications' conveying other putative benefits of additional dietary zinc for improved linear growth and increased disease resistance, which might be expected on the basis of supplementation trials, cannot yet be found in the research experience available in the literature. The authors propose some rationales for the inconsistencies in the findings to date and lay out suggestions for future research approaches to resolve the inconsistencies and further advance the suitable zinc fortification of staple foods in a public health context.

After vitamin A, iron and iodine, zinc is arguably the next most important nutrient of public health interest, reputed to be capable of reducing global child mortality by 4% overall. As such, no one in clinical or community pediatrics can ignore zinc. The present contributions attempt to reveal both the beauty marks and the warts across the surface of our growing – but as yet incomplete – understanding of zinc in pediatric medicine and public health.

Noel W. Solomons