

was approximately one year delayed behind chronologic age; predicted adult height in 22 subjects was -1.24 SDS.

References

1. Wilson JH, Elledge SJ. *Science* 2002;297:1822-1823.
2. Yang H, et al. *Science* 2002;297:1837-1848.
3. Witt E, Ashworth A. *Science* 2002;297:534.
4. Wajnrajch MP, et al. *Pediatrics* 2001;107:744-754.

Second Editor's Comment: The phenomena described in the papers given as references are phenomenal. The first 3 references read as a package will permit any reader not informed about such matters to advance into the upper elementary levels, both in respect to understanding the physiology and pathophysiology of Fanconi Anemia, breast cancer, and to the interactions of genes and gene products.

Allen W. Root, MD

Robert M. Blizzard, MD

Serum Zinc in Infants and Preschool Children in the Jeddah Area: Effect of Diet and Diarrhea in Relation to Growth

Dr. Bahijri has written a thoughtful analysis of the etiology and effect of zinc deficiency on wasting and stunting of 728 children in 5 age groups (4-6, 6-<12, 12-<24, 24-<36, and 36-72 months). Using the concept of weight for height, the subjects were classified according to their grade of wasting, and using the concept of height for age, the subjects were classified according to their grade of stunting. The dietary, auxological, and chemical evaluations were carefully done in accord with the most modern standards and techniques. The study was undertaken to determine the prevalence of zinc deficiency in the Jeddah (Saudi Arabia) area among preschool age children, to see whether such a deficiency is a cause of retarded growth, to determine whether a relationship exists between height for age and serum zinc concentrations, and if possible to determine the causes of zinc deficiency.

The authors presented serum zinc levels in the various age groups for subjects: (1) without stunting and wasting, (2) with various grades of wasting, (3) with various grades of stunting, and (4) with both stunting and wasting. Many subjects in each group had zinc levels <10.4 $\mu\text{mol/L}$ which is frequently cited in the literature as the cut off for normalcy. However, the lowest mean serum zinc levels were found in the patients in the group with stunting and wasting. Whereas those who had neither stunting nor wasting had the highest levels. The older stunted children (group 3) had lower zinc levels than those found in the younger children. All patients with wasting (group 2) had hypozincemia.

The authors concluded that diarrhea rather than low dietary intake mostly accounts for the low zinc levels in infants (4-12 months). As the subjects passed the 24 month mark, diet deficiency became the presumed major cause of hypozincemia and this cause became more dominant as the etiology in the oldest age group (36-72 months).

The importance of zinc in biology is well reviewed, including that zinc is known to influence cell division, growth and development, as well as sexual maturation. It is needed also as a membrane stabilizer, and is

essential for the integrity of the immune system. More than 100 enzymes require zinc as a cofactor, and zinc seems to be involved in the proper storage and release of insulin, growth and repair of tissues, wound healing, ability to taste food, production of prostaglandins, mineralization of bone, blood clotting, function of vitamin A, and functions of the thyroid hormones.

Not commonly known, an important predisposing factor for zinc deficiency is the extensive use of cereal protein which limits the availability of zinc due to high phosphate and phytate content. The recommended dietary allowance of the Food and Nutrition Board and the National Academy of Sciences in the United States is 15 mg/day for adult males and 12 mg/day for adult females, with higher recommended levels during pregnancy and lactation. Requirements for infants and children are relatively high in relation to body size because of increased requirements for physical growth.

The best sources for zinc in the diet are meat and fish; the bioavailability of zinc from animal products is considered to be greater than that from plants. Diarrhea is associated with zinc deficiency and low serum zinc concentration. Suggestions have been made that growth retardation commonly seen in children in developing countries is related to zinc nutritional deficiency.

Unfortunately, it was not feasible to interpret the direct effect of zinc deficiency on wasting or stunting although a significant majority of subjects with wasting and/or stunting had severe deficiency. The author summarized: "The result of this work shows a high incidence of low serum zinc levels among Jeddah-area infants and young preschool children, which is associated with diarrhea and wasting in the first two years of life, and generally low dietary intake, wasting and/or stunting in older children. Zinc supplementation is recommended for certain categories of subjects to improve appetite and hence dietary intake, immunocompetence, and anthropometric measurements."

Bahijri SM. *Annals of Saudi Medicine* 2002;21:324-329.

First Editor's Comment: A complete reprint of this article will be sent to those who request it by e-mail to rblizzard@compuserve.com.

Unfortunately in nearly all studies of this type it is difficult to separate cause and effect. For example, does malnutrition or illness produce wasting and/or stunting accompanied by zinc deficiency or is the zinc deficiency etiologic in malnutrition and/or illness and/or stunting and/or wasting? In spite of this excellent study, the answer to this question remains an enigma. Moreover, zinc supplementation seems indicated to a much greater extent than currently in use.

Robert M. Blizzard, MD

Second Editor's Comment: Recently Brown et al published a meta-analysis of randomized controlled trials of the effects of supplemental zinc on the growth and serum concentrations of prepubertal children. A total of 33 studies were compiled demonstrating that zinc supplementation produced a significant positive height response and an increase in serum zinc levels. Growth responses were greater in those children with low weight for age and low height for age. This paper was reviewed in *Growth, Genetics & Hormones* in 2002 (Vol. 18, No. 4) and the importance of recognizing the value of zinc nutrition in "at risk" populations was emphasized.

However the note of caution noted below by Dr. Tarim should be kept in mind.

Fima Lifshitz, MD

Reference

1. Brown KH, et al. *Am J Clin Nutr* 2002;75:1062-1071.

Letter to the Editor:

I would like to add a precaution before suggesting zinc supplementation to anyone with nutritional growth retardation who lives in places where zinc deficiency may be prevalent. Iron deficiency which may co-exist with zinc deficiency may be aggravated during zinc therapy because these two minerals may block the intestinal absorption of each other.¹ Consequently, iron deficiency may also worsen growth retardation. Therefore, I suggest excluding iron deficiency, which is easier to diagnose than zinc deficiency, before initiating zinc supplementation.

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Reference

1. Lifshitz F, et al. Nutritional Growth Retardation. In: Lifshitz F, ed. *Pediatric Endocrinology 3rd Edition*. New York: Marcel Dekker, 1996:103-120.

Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus

Because multiple laboratory tests are used in the diagnosis and management of this disease, the quality of the scientific evidence supporting the use of these assays varies. Therefore, an expert committee drafted evidence-based recommendations for the use of laboratory analysis in patients with DM. An external panel of experts (DB Sacks, DE Bruns, DE Goldstein, NK Maclaren, JM McDonald and M Parrott) reviewed a draft of the guidelines, which were modified in response to the reviewers' suggestions, and other steps were taken to gain a consensus of expert opinions. The guidelines, as published in *Clinical Chemistry*, consist of an Executive Summary of one page providing specific recommendations based on data published or expert consensus. Several analyses are of minimal clinical value at the present time and measurement of them is not recommended. The entire article is 42 pages. Those clinicians treating diabetics should at least scan the article and closely scrutinize the Executive Summary.

Highlights of the Executive Summary are now presented:

Glucose should be measured in an accredited laboratory to establish the diagnosis of DM and to screen high-risk individuals. Blood should be drawn after an overnight fast. Glucose should be measured in plasma. If plasma cannot be separated from cells within 60 minutes, a tube with glycolytic inhibitor should be used. On the basis of biological variation, glucose analysis should have analytical imprecision less than 3.3%, bias less than 2.5%, and total error less than 7.9%.

The OGTT is not recommended for the routine diagnosis of type 1 or 2 DM. The key limitation of the OGTT is its poor reproducibility. It is recommended for establishing the diagnosis of gestational DM.

Because of the imprecision and variability among glucose meters, they should not be used to diagnose DM and have limited value in screening. Noninvasive glucose analyses cannot be recommended at present as replacements for plasma glucose or measurements by an accredited laboratory. Glycated hemoglobin (GH_b) should be measured at least biannually in all patients with DM. US laboratories should use GH_b assays certified by the National GH Standardization Program