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Prasad A S, Miale A, Farid Z, Sandstead H H & Schulert A R. Zinc metabolism in patients with the syndrome of iron deficiency anemia, hepatosplenomegaly, dwarfism, and hypogonadism. *J. Lab. Clin. Med.* 61:537-49, 1963.

[Depts. Medicine and Biochemistry and Div. Nutrition, Vanderbilt Univ., Nashville, TN and Medical Dept., US Naval Medical Research Unit, No. 3, Cairo, Egypt]

The first conclusive evidence that zinc deficiency in humans occurred was presented in this article. This conclusion was based on the following: The zinc concentration in plasma, red cells, and hair was decreased, and ^{65}Zn studies revealed that the plasma zinc turnover rate was greater, the 24-hour exchangeable pool was smaller, and the excretion of ^{65}Zn in stool and urine was less in the zinc-deficient dwarfs than in the control subjects. [The *SCI*® indicates that this paper has been cited in over 315 publications.]

Zinc Deficiency in Humans

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I received my training in internal medicine and hematology at the University of Minnesota under Dr. C.J. Watson. After completion, I joined Dr. Hobart A. Reimann, visiting professor and chief of medicine at the Nemazee Hospital of Pahlevi University, Shiraz, Iran.

Soon after my arrival in Shiraz, Dr. James A. Halsted (a Fulbright Professor) brought to my attention a 21-year-old male at Saadi Hospital (a city hospital), Shiraz, who looked like a 10-year-old boy. In addition to severe growth retardation and iron deficiency anemia, he had hypogonadism, hepatosplenomegaly, rough and dry skin, mental lethargy, and geophagia. He ate only bread and consumed one pound of clay daily. We soon discovered that this unusual syndrome was common in Iran.[1] His iron deficiency anemia was without blood loss. I, therefore, reasoned that the total amount of available iron in the diet was insufficient. However, it was difficult to explain growth retardation, hypogonadism, and skin changes on the basis of tissue iron deficiency. I considered the possibility of zinc deficiency and speculated that factors responsible for decreased dietary availability of iron in these patients might also have decreased the availability of zinc. This factor has been now recognized and is an organic phosphate compound, phytate, which is present in high amounts in cereal proteins.

In 1961 I joined the Departments of Biochemistry and Medicine at Vanderbilt University, Nashville, Tennessee, under Dr. W.J. Darby, and moved to US Naval Medical Research Unit, No. 3, Cairo, Egypt. I shared with Dr. Darby my speculation that zinc deficiency in the Middle East was prevalent and was responsible for widespread growth retardation.

My team consisted of Drs. H.H. Sandstead, A.R. Schulert, A. Miale, and Z. Farid. We established for the first time that indeed zinc deficiency in humans occurred in the Middle East.[2,3] Our subsequent studies showed that zinc supplementation resulted in gain in height (five to six inches per year), increase of genitalia to normal size, and development of secondary sexual characteristics within 12-24 weeks in all patients.[4]

A decade of skepticism followed. The controversy finally ended in 1974 when the Food and Nutrition Board of the National Research Council included zinc for the first time in the recommended dietary allowances.

Following the discovery of the importance of zinc in humans, the greatest impact felt was on the role of zinc in human nutrition. Although initially zinc deficiency in humans was considered to be a rare phenomenon, it is now estimated that millions of people in developing countries may in fact have zinc deficiency. Conditioned deficiency of zinc in various diseased states has been now recognized and our recent studies suggest that a mild deficiency of zinc affecting cell mediated immune functions may be common even in the US.[5] Nearly 200 enzymes are now known to be regulated by zinc, and it is now recognized to be involved in gene expression. (See, for example, references 5 and 6.)

My unique experience in the Middle East led to an exciting career in research and I am continuing to remain heavily involved with various clinical, biochemical, and immunological studies related to zinc metabolism. For my contributions in this field, I have received the American Medical Association Goldberger Award, the Robert H. Herman Award, the American College of Nutrition Award, and the Gopalan Oration Gold Medal Award from India. I have been selected to receive the Raulin Award from France at the International Society of Trace Element Research meeting in Tokyo, Japan, August 28-September 1, 1989.

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2. **Prasad A S, Miale A, Farid Z, Sandstead H H & Schulert A R.** Zinc metabolism in patients with syndrome or iron deficiency anemia, hepatosplenomegaly, dwarfism, and hypogonadism. *J. Lab. Clin. Med.* 61:537-49, 1963. (Cited 315 times.)
3. **Prasad A S, Miale A, Farid Z, Sandstead H H, Schulert A R & Darby W J.** Biochemical studies on dwarfism, hypogonadism, and anemia. *Arch. Intern. Med.* 111:407-28. 1963. (Cited 240 times.)
4. **Sandstead H H, Prasad A S, Schulert A R, Farid Z, Miale A, Bassilly S & Darby W J.** Human zinc deficiency, endocrine manifestations and response to treatment. *Amer. J. Clin. Nutr.* 20:422-42, 1967. (Cited 215 times.) [See also: **Sandstead H H.** Citation Classic. *Current Contents/Life Sciences* 32(16):17, 17 April 1989.]
5. **Prasad A S, Meftah S, Abdullah J, Kaplan J, Brewer G J, Bach J F & Dardenne M.** Serum thymulin in human zinc deficiency. *J. Clin. Invest.* 82:1202-10, 1988.
6. **Evans R M & Hollenberg S M.** Zinc fingers: gilt by association. *Cell* 52:1-3, 1988.

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