

This Week's Citation Classic®

Prasad A S, Halsted J A & Nadimi M. Syndrome of iron deficiency anemia, hepatosplenomegaly, hypogonadism, dwarfism, and geophagia. *Amer. J. Med.* 31:532-46, 1961.

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A syndrome occurring in males, characterized by severe iron deficiency anemia, hypogonadism, dwarfism, hepatosplenomegaly, and geophagia, was observed in villages in Iran—here due to malnutrition. The possibility of zinc deficiency was considered as an explanation of hypogonadism and dwarfism. The predominantly wheat diet and geophagia most likely interfered with both iron and zinc absorption. [The *SCJ*® indicates that this paper has been cited in more than 320 publications.]

A Diet of Zinc or Clay

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In 1958, I finished my training in internal medicine and hematology under C.J. Watson at the University of Minnesota. My original plan was to return to India in an academic post. Unfortunately, I could not achieve this because I lacked British training. My problem was further compounded in that, as an exchange visitor, I could not stay in the US. Fortunately, Hobart A. Reimann, who had preceded Watson as chief of medicine at the University of Minnesota, had just been appointed visiting professor and chief of medicine at the Nemazee Hospital, which was affiliated with Pahlevi University in Shiraz, Iran. Reimann offered me an academic position at the Nemazee Hospital, and I accepted.

The Nemazee Hospital was structured on the pattern of an American hospital in every sense except that the research laboratory facilities were not up to par. The hospital mainly took care of rich Iranians. Fortunately, I also had access to Saadi Hospital, a city hospital where we encountered complicated clinical problems that affected poor Iranians. Chancellor Z. Ghorban of Pahlevi University had the vision to establish a medical center in Shiraz that would provide teaching and training programs for the

students on an American pattern. In light of that vision, he provided all possible support for my activities.

Very quickly, I became aware of an unusual, unreported clinical syndrome. This syndrome was characterized by marked hypochromic anemia due to iron deficiency, hepatosplenomegaly, dwarfism, lack of development of primary and secondary sexual characteristics, and a history of prolonged geophagia (clay eating). It turned out to be a common occurrence around Shiraz.

The entire range of clinical features of this syndrome was reversed following adequate nutrition and iron therapy for anemia. Thus, our studies led us to suggest for the first time that this syndrome was related to nutritional deficiency. Our later studies established that similar dwarfs in Egypt were deficient in both zinc and iron.¹

The habit of geophagia in Iran puzzled me a great deal for many years. In retrospect, one might speculate that since zinc deficiency results in neuro-sensory disorders (abnormal tastes and dark adaptation), perhaps a perversion of taste caused them to eat clay.² Once these dwarfs received adequate nutrition, they did not revert to geophagia after discharge from the hospital.

The initial clinical observations in Shiraz turned out to be very exciting. A significant proportion of the widespread growth retardation related to malnutrition seen in the Third World may indeed be related to zinc deficiency, which is easily correctable.

I received the Raulin Award—established in France and given by the International Society of Trace Elements Research in Humans at their Tokyo meeting in 1989. The award was established in honor of J. Raulin of Lyon, France, who showed 120 years ago that zinc was essential for the growth of microorganisms.³ It took almost 100 years to recognize its vital role in humans. I also received a Medal of Honor from the mayor of Lyon, in 1989, for my contributions in the field of zinc metabolism.

1. Prasad A S, Miale A, Farid Z, Sandstead H H & Schuler 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. (Cited 325 times.) [See also: Prasad A S. Zinc deficiency in humans. Citation Classic. *Current Contents/Clinical Medicine* 17(38):14, 18 September 1989 and *CC/Life Sciences* 32(38):14, 18 September 1989.]
2. Prasad A S. Clinical spectrum and diagnostic aspects of human zinc deficiency. (Prasad A S, ed.) *Essential and toxic trace elements in human health and disease*. New York: Liss, 1988. p. 3-53.
3. Raulin J. Etudes chimiques sur la vegetation. *Ann. Sci. Natur.—Bot. Biol. Veg.* 11:93-9, 1869.

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