Chapter 20

The Diagnosis of Zinc Deficiency

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Introduction

The very large number of indices that have, from time to time, been evaluated, promulgated and, with experience, discarded as methods of assessing the zinc status of a subject is true testimony to the difficulties involved (Solomons 1979; Kirchgessner and Roth 1981; Golden and Golden 1985). None of the methods currently used can be recommended, with the possible exception of the monitoring of responses to zinc supplementation with plasma zinc estimation in conjunction with clinical evaluation.

The remarkable report by Beach et al. (1982) clearly shows the extraordinary extent of the difficulties involved, if all the features of zinc deficiency are to be properly ascribed. These authors fed pregnant mice a moderately zinc-deficient diet from day 7 of gestation until parturition. After birth, the pups were cross-fostered to normally nourished mice. They showed depressed immune function for at least 6 months. This is at least understandable; however, the second and the third generation mice, all of which were fed absolutely normal diets, continued to manifest reduced immunocompetence. This finding is staggering in its implications. If the same holds true for humans, as for these mice, you may have a compromised immune system because your grandmother took a zinc-deficient diet during her pregnancy! You would thus have a manifestation of zinc deficiency. I cannot conceive, at the moment, of the mechanism involved; I am also quite confident that no test so far devised, or even contemplated, will specifically identify this defect as being due to zinc deficiency. Clearly, our studies and ideas about zinc nutrition are at an early and conceptually naive stage.
Zinc Deficiency – The Diagnostic Problem

Water, water, everywhere, nor any drop to drink.
(Coleridge, *The Ancient Mariner*)

The most notable feature of both mild and severe experimental zinc deficiency, which is crucial to any appreciation of tests to assess zinc status, is that there is almost no reduction in the tissue concentration of zinc, even in overt, severe, symptomatic zinc deficiency (Williams and Mills 1970; Kirchgessner et al. 1976; Aggett et al. 1983). Muscle and white cell zinc are stubbornly preserved. There is a small decrease in liver and pancreatic zinc in prolonged, profound deficiency. The only tissue with an unequivocal reduction in zinc is bone. This is not a very useful diagnostic feature for human studies, particularly as the zinc sequestered in bone is neither readily available nor exchangeable, so that zinc deficiency can be present without any change in bone zinc and vice versa. However, even in very severe zinc deficiency, the quantitative reduction in total body zinc is small. There is still plenty of zinc on an absolute basis and the change in the zinc concentration in the tissues of metabolic importance is trivial.

It seems that the paradoxical observation of suffering from overt zinc deficiency and yet having a normal tissue zinc concentration is a particularly difficult feature of zinc deficiency for researchers to come to terms with. For example, Thompson (1985) argued that the pigs studied experimentally by Aggett et al. (1983), which had been put on a zinc-deficient diet, had stopped growing, had developed all the classical features of zinc deficiency and were reported to be preterminal and yet had normal concentrations of zinc in their white cells and muscle, could not, therefore, be zinc deficient (sic). Thompson (1985) stated that “the white cells are showing that the animals were not short of zinc, but that, if the diet were continued, the level would eventually fall and then the animals might be truly deficient”.

Certainly, the clinicians who looked after these debilitated animals had no doubt about the diagnosis and would disagree fundamentally with Dr. Thompson’s interpretations in the light of their experience that adding zinc alone to the diets of these animals restored their health completely to normal and stopped them from dying. Surely it is not in question that they were in fact suffering from actual zinc deficiency, and only from zinc deficiency, despite the normal levels of tissue zinc. It is equally undeniable that there is a major conceptual problem when we try to understand the nature of zinc deficiency. Such an understanding is essential before we can devise tests to determine which individuals are actually suffering from zinc deficiency. We also require techniques capable of differentiating between such zinc-deficient subjects and those showing changes in zinc metabolism due to factors totally unrelated to zinc nutriment. The nature of the response to a deficiency of zinc is at the heart of the problem.