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CLINICAL, BIOCHEMICAL, AND NUTRITIONAL ASPECTS OF TRACE ELEMENTS

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EDITOR

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CLINICAL, BIOCHEMICAL, AND NUTRITIONAL ASPECTS OF TRACE ELEMENTS

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to my family

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Preface

As recently as twenty years ago deficiency of zinc in human subjects was considered improbable. Today it is being recognized with greater frequency every day under a variety of circumstances. During the decade of the seventies considerable progress was made in the field of trace elements. Three events led to those advances. The first was the recognition of the many biochemical roles of trace elements that had been reported since 1960. The second was the development of accurate and simple methodology with the use of atomic absorption spectrophotometry in the early sixties, which made it simple to assess the status of trace elements in human subjects. The third, and most important, event was the documentation that deficiency of trace elements in human subjects can occur under the most practical dietary conditions. That finding was of critical importance from the public health point of view in the world population. This is particularly true for zinc.

With respect to basic biochemical mechanisms of absorption and interactions of certain trace elements, there has been considerable progress since 1970. We have learned a great deal about the intestinal absorption of zinc, but such progress has not been made with respect to other elements. We have also learned of the many interactions that determine the requirement of trace elements. Although the progress has been substantial, we have not yet achieved agreement in regard to zinc-binding ligands that may play an important role in bioavailability.

We have yet to define the basic biochemical mechanisms of trace elements that would explain the clinical expression of their deficiencies. In some cases, we have made tremendous progress, but a complete understanding of the sequence of events that lead to deficiency symptoms remains to be elucidated.

In the clinical applications of trace elements, we have seen tremendous progress. For example, several forms of zinc deficiency have been identified, among them the severe zinc deficiency seen in acrodermatitis enteropathica and following total parenteral nutrition and the conditioned zinc deficiency associated with sickle cell disease and chronic uremia. It has also been posited that zinc deficiency has implications in patients with hypogeusia, and it is established that malnutrition is never an isolated protein-calorie deficiency but is always complicated by deficiency of other micronutrients, including the

trace elements. In addition, a recent report that, in China, Keshan disease, which frequently is fatal, is due to selenium deficiency and that a large number of Chinese children are being supplemented with selenium with excellent results is truly a remarkable advance. One must realize, however, that these observations need further confirmation and that more studies are needed to document the role of selenium deficiency in myocarditis.

Much of the stimulus for recent clinical interest in trace elements has come from the use of total parenteral nutrition. It is convincing to see evidences of pure deficiencies of zinc, copper, or chromium in patients who have received total parenteral nutrition without trace element supplementation. These examples serve as human models for the pure trace elements deficiency state that has been experimentally induced in laboratory animals. Recently, successful attempts have been made to induce mild deficiency of zinc in human volunteers, which further defines the mild end of the spectrum of this condition.

At the Conference on Clinical, Biochemical, and Nutritional Aspects of Trace Elements the possible role of trace elements as therapeutic agents was discussed. As an example, zinc may act as an antisickling agent that may prove to be beneficial for treatment and prevention of pain crisis in sickle cell disease. It is important, however, to differentiate between this therapeutic application and the nutritional zinc supplementation used for correction of deficiency states.

Various biochemical assay methods in current use may be useful in identifying deficiency states, if the tests are properly controlled. However, it is important to note that there is no single bioassay that would diagnose deficiency of trace elements. It may be possible to develop better diagnostic techniques, perhaps based on measurement of trace element-dependent functional proteins. It is well known, for example, that measurement of serum iron binding capacity and ferritin provides an excellent tool for assessment of body iron status. Perhaps similar tests will become available for measuring other trace elements.

Perhaps the most impressive and most promising development in the trace element field in recent years has been the recognition that trace elements may have an important role in immune functions. The influence of zinc on T lymphocytes, for example, appears to be well documented. The implications of this finding extend to other areas as well, such as development of malignancies, inasmuch as T natural killer cells appear to be zinc dependent.

One important point raised in this symposium concerns the question of whether certain individuals or populations have a genetic basis for requiring higher or lower levels of trace elements. Studies must be conducted to resolve this issue in order to define optimal requirements of trace elements in the human population. At present, human requirements of trace elements are at best an approximation only.

It appears that epidemiologists and toxicologists, who are concerned with heavy metals toxicity, face very much the same problem as those of us who are concerned with nutritional levels. The question of availability of heavy metals, the chemical nature of the heavy metal compounds, and their interactions with other nutrients all seem to play important roles with respect to toxic effects of heavy metals. We are now concerned with marginal toxicities, which are difficult to recognize and diagnose, just as the nutritionist, who is concerned with marginal deficiency of trace elements.

Deficiency syndromes for nickel have also been recognized in several animal species, and it is likely that nickel is important in human nutrition as well.

It is obvious that there are problems with the methodology of measuring trace elements that remain to be solved. Although much progress has been made in this area, the analytical techniques need more refinement if we are to obtain reproducible results within individual laboratories and universally.

In spite of these tremendous advances in the field of trace elements in recent years, serious nutritional deficiencies remain a problem, especially in developing countries. There have been only a few international efforts to overcome malnutrition complicated by a deficiency of one or the other trace elements. It is therefore very important, in our opinion, to look at trace elements nutrition in any given population. In fact, we have learned at this conference that protein is utilized inefficiently when there is a deficiency of zinc. Thus, zinc supplementation in the diets of growing children would be much less expensive and more efficacious than the various protein supplements that have been tried with limited success in several developing countries.

The subdivision of trace elements into essential and toxic categories is somewhat arbitrary. We all recognize that trace elements that are now considered toxic may in fact be essential. In this book, the trace elements categorized as essential are zinc, copper, chromium, selenium, manganese, nickel, tin, silicon, and vanadium. The essentiality and clinical importance of zinc and copper for human subjects are well established. Evidence indicates that chromium and selenium are probably clinically important, although distinct deficiency disorders of these two elements in human subjects are not well characterized. Furthermore, although manganese is known to participate in various enzymatic functions, its deficiency in human subjects has not been recognized, and there is no evidence that nickel, tin, silicon, and vanadium are, in fact, essential for human nutrition. These elements have been included only to stimulate future research in human subjects, inasmuch as animal studies have yielded very interesting data with respect to essentiality.

The elements here classified as toxic, lead, cadmium, and mercury, are known health hazards and are considered to be of great clinical importance throughout the world.

It is hoped that this book will provide stimulus for further research in the field of trace elements and will lead to the development of corrective measures that will solve the many problems related to trace elements in nutrition throughout the world. Physicians, nutritionists, and biochemists should find this book not only informative but also stimulating.

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Contents