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TRACE ELEMENTS in BIOLOGY and AGRICULTURE

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FOODS and nutrients are necessary for cell growth because of their function in generation or release of energy, building and repair of protoplasm, and regulation of metabolic processes. They are usually classified as: (*a*) an energy source, (*b*) a nitrogen source, (*c*) growth factors (organic compounds not synthesized by the organism and required usually in small amounts), and (*d*) mineral salt or inorganic nutrient.

A number of inorganic elements, or minerals, are required by all living forms for normal growth and reproduction. This is not true of all the elements of the periodic table, although most have been found in living cells. The minerals essential to life are generally divided into two classes: macronutrients, or major elements, needed in relatively large amounts, and the micronutrients, or trace elements, required only in small amounts.

For most organisms the macronutrient elements include sulphur, phosphorus, potassium, magnesium, calcium, and nitrogen. In addition, sodium and chloride are needed by animals and, according to recent experiments, probably by plants as well. The trace elements include iron, zinc, manganese, and copper. Molybdenum, boron, and vanadium are also needed by plants, and iodine, cobalt, and probably molybdenum by animals. Even though micronutrient elements are required in only extremely small quantities, they are no less important than the major elements.

The fact that the trace metals are needed in only small quantities indicates that they are functioning in some catalytic role, usually as part of an enzyme system. In this respect the function of trace elements is similar to that of the organic micronutrients, the vitamins. A known enzymatic role has been described for most of the trace elements. Exceptions are iodine, which is a component of the thyroglobulin molecule, and cobalt, which is part of the vitamin B_{12} molecule.

Although we can describe a specific function for most of the metals, as long as essential enzyme systems can be activated by a variety of elements we can expect nonessential metals to have a significant effect on the metabolism of plants and animals. There are many examples of multiple-metal effects on enzyme systems, some of the most striking of which are from the area of plant-animal relationship. Judging by the optimum concentration of an element for enzyme activity as well as the ratio of stimulatory and inhibitory metals present, it is evident that under physiological conditions some systems may be working at a maximum rate whereas others may be operating at less than 1 percent of maximum efficiency.

Obviously there must be some balance in the

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soil, in the plant, and in the animal which leads to a normal, healthy individual. However, the difficulty of determining the normal activator of a metabolic system and factors which will influence the rate of reaction in vivo is demonstrated by a number of recent experiments.

Is growth or yield an adequate criterion for determining whether the various metabolic systems are functioning at a level to give maximum benefit to the organism? Can we apply trace elements and other fertilizers to the soil and to the diets of animals until we obtain maximum crop yield or maximum growth rate and expect, at the same time, to receive maximum nutritional benefit for the organisms? There are several excellent examples which say we cannot. One might say that these are extreme and special cases. However, it is gradually becoming evident that visual symptoms of plant and animal deficiency are not necessary to prove deficiencies in the health and vigor of the organism. Deficiencies and excesses are a matter of degree, and plants, like animals, may become decidedly inferior in quality long before showing outward signs. Hence, yield or growth is no longer an adequate sign of health.

The next question is, what criteria can be used? From a physiological point of view, criteria must by necessity vary with the nature of the objective. If it is aroma in tobacco that is desired, then a plant that is slightly deficient in sulphur may be essential. If it is tensile strength and kink in wool, then the dietary level of copper may be one of the major factors. Many other examples could be cited.

What seems clear from numerous studies is that certain metabolic characteristics appear under conditions of varying trace-element supply and not merely in association with an overall reduction or increase in mass or quantity. In other words, each level of trace-element supply during growth produces a characteristic metabolic pattern irrespective of the yield. The enzymatic patterns are the real test. Enzyme concentration and activity are changing under all conditions of trace-element nutrition. These changes of enzymatic activity will certainly be of value in the early diagnosis of animal and plant diseases which are not apparent from growth studies, and, as Williams recently emphasized, each individual represents a special problem (*1*).

Several general patterns evolve from the physico-chemical and nutritional studies on the influence and mechanism of action of metals in enzyme systems. Although there are exceptions to these generalizations, it appears that those metals most closely associated with electron transferring systems are copper, iron, zinc, and molybdenum. Nonenzymatic studies have shown that these metals have the inherent capacity to function as electron mediators in oxidation-reduction reactions. The important biochemical questions are: (*a*) why is this capacity for catalyzing oxidation-reduction reactions accentuated in the presence of specific proteins, and (*b*) what is the nature of the linkages which allow specific coupling of these metal systems to others, which in turn allows the transfer of electrons along specific pathways? The pattern that seems to be emerging is that these metals are not required specifically for the combination of substrate to the catalytic protein but rather that they function primarily as "electron couplers" from one protein system to another.

Tabulated results of studies show that magnesium and, to a certain extent, manganese are required primarily for those reactions involving group transfer, in particular those in which phosphate participates. For example, to metabolize glucose it must be phosphorylated. Phosphate is transferred from adenosine triphosphate to glucose to form glucose-6-phosphate and adenosine diphosphate. Magnesium is required for this group transfer. In recent years it has become increasingly clear that enzymes participate intimately in group transfer by serving as the intermediate carrier. Magnesium plays a predominant role in promoting the formation of the enzyme-substrate complex and the resulting intermediate of the reaction. The presence of a pyrophosphate structure in many of the co-factors and substrates involved in group transfer suggests that a chelate structure with magnesium is probable.

The predominant metal in general enzymatic decarboxylation and hydrolysis reactions is manganese. To a lesser extent zinc and magnesium also are factors. At present there is no general agreement as to the primary mechanism of action of these metals. Some workers feel that they form an essential structure with the substrate and thus act to bring the substrate into combination with the protein. Others feel that the metal combines with the enzyme and functions primarily to accelerate and therefore to increase the concentration of an essential intermediate in the reaction. Manganese does not have strong inherent properties for catalyzing decarboxylation, whereas other metals, such as copper, which do not function as cofactors in enzymatic decarboxylation, are very effective in nonenzymatic reactions. The suggestion, therefore, that manganese functions in enzyme systems by forming chelate structures with the substrate lacks strong experimental support.

Conclusion

Emphasis in nutrition during the past 30 years has been on identification and establishment of absolute requirements of inorganic and organic nutrients for "normal" growth and development. Almost by necessity it was assumed that the animals in a population were all identical and therefore had the same nutritional requirements. It is now clear, however, that there are large individual variations in nutritional requirements. In addition, quantitative studies on various tissues indicate that small changes in the diet often lead to dramatic effects on enzyme systems. Thus studies in the future must emphasize the individual.

Nutritional individuality can be an important factor in human health and disease. Small changes in concentration of the trace elements in the diet, for example, will alter the concentration of metabolic intermediates and products formed by an individual. Growth alone, therefor, is not the only criterion that can be used for testing the adequacies of a diet.

REFERENCE

(*1*) Williams, R. J.: Biochemical individuality. New York, N. Y., John Wiley & Sons, Inc., 1956.

Allocation of Charity Funds for Research

The voluntary health agencies listed below in the United States raised $116,788,220 in 1956, according to the National Health Education Committee, Inc., New York City. In the same year, $20,918,-043 was allocated for research by the agencies.

Voluntary agency	Amount raised	Amount allocated for research
American Cancer Society	$27, 234, 612	$7, 735, 537
Damon Runyon Fund	984, 743	1, 006, 033
American Heart Association and affiliates	17, 755, 910	[1] 6, 100, 000
National Association for Mental Health	695, 054	[2] 149, 007
Arthritis and Rheumatism Foundation	2, 449, 396	467, 521
United Cerebral Palsy	8, 318, 000	538, 865
National Multiple Sclerosis Society	2, 007, 606	[2] 270, 805
Muscular Dystrophy Associations	4, 191, 109	1, 405, 415
National Council to Combat Blindness	257, 915	127, 954
National Society for the Prevention of Blindness	255, 902	47, 667
American Foundation for the Blind	666, 973	none
National Foundation for Infantile Paralysis	51, 971, 000	3, 069, 239
Total	116, 788, 220	20, 918, 043

[1] Not final. [2] National office figures only.