Discovery of the importance of trace elements in nutrition began in the 19th century with the chemical analysis of elements in biological samples and the demonstration that certain elements were essential for growth of microorganisms, e.g., essentiality of zinc for Aspergillus niger (Raulin 1869). The clinical investigations of Stockman (1893, 1895a and 1895b) in women with “chlorosis” and the iron deprivation experiments of Cloetta (1897) in dogs, were the first to show that dietary deficiency and/or loss of a trace element (iron) from the body caused a specific disease (iron deficiency anemia). In light of the knowledge and medical practice of the time (Oslor 1892), their findings were revolutionary.

As reviewed by Underwood and Mertz (1987), understanding of the roles of trace elements in nutrition required the development of purified diets and methods of animal care that limit exposure to contaminants. In addition, new technologies were necessary for measurement of trace elements in biological samples. Veterinary and plant scientists led the way in discovery. They showed that low soil and plant content of specific trace elements such as cobalt, copper, selenium and zinc, and imbalances of certain trace elements such as manganese and copper, and zinc and copper cause disease. Their discoveries helped clinical scientists recognize functions of trace elements in humans and the effects of trace element deficiencies and excesses on human health. The papers presented at this symposium illustrate this process.

In the first paper, Levander (2000) describes his collaboration with Melinda Beck that led to their unprecedented discovery that passage of an avirulent strain of coxsackievirus B3 (CVB3/0) through selenium-deficient or vitamin E–deficient mice caused a change in the genomic structure of the virus so that it was identical to that of the virulent strain CVB3/03, except for one nucleotide, and was cardiovirulent in normal mice. Thus, diet of the host affected the pathogen itself. One wonders how such a phenomenon might contribute to the emergence of new pathogens.

In the second paper, Klevay (2000) reviewed research from 1928 to 1999 that established the essentiality of copper for a healthy cardiovascular system. Although it is clear that the lipid hypothesis fails to explain many phenomena associated with ischemic heart disease, the properties of few other protective or poisonous agents have been evaluated extensively. The dominance of the lipid hypothesis may have discouraged scientists lacking historical information from gaining the knowledge required to test alternatives. Because the U.S. diet seems to be low in copper, it is expected that the few investigators who are focused on relationships between copper nutriture and cardiovascular health will continue to find evidence of essentiality of copper for cardiovascular health.

In the third paper, Hetzel (2000) summarizes research over the past 30 years that established the essentiality of iodine for brain development and showed that maternal repletion with iodine during pregnancy prevents cretinism. The association between goiter and cretinism had been known since the mid-19th century, and prevention of goiter by iodine has been known since early in this century. In spite of this knowledge, iodine deficiency continued to be a major cause of morbidity in regions in which soil iodine is low. Research by Hetzel and co-workers and others provided the knowledge required for an International Consultative Group that works closely with the WHO and UNICEF to assist countries in the establishment of universal iodination of salt. Their goal is elimination of iodine deficiency brain damage by the year 2000.

In the fourth paper, Sandstead et al. (2000) review observations from the past 100 years that are relevant to the role of zinc in brain. Almost all of the evidence is from the past 40 years. In the past 30 years, adverse effects of zinc deficiency on brain function of experimental animals and humans were revealed. Progress in understanding mechanisms by which zinc affects brain function has been slower. Recent research has found repletion of zinc nutriture efficacious for cognition when administered with other potentially limiting micronutrients. Because clinical and laboratory signs of zinc nutriture are insensitive, one suspects that considerably more data will be necessary before health agencies will make the prevention of human zinc deficiency a priority.
LITERATURE CITED

Note: additional references for research papers in trace element nutrition may be found in *The Journal of Nutrition* online (www.nutrition.org); see “Supplemental Data” in the February 2000 issue


Stockman, R. (1895b) On the amount of iron in ordinary dietaries and in some articles of food. J. Physiol. 18: 484–489.