NUTRITION AND ENVIRONMENTAL HEALTH:

The Influence of Nutritional Status on Pollutant Toxicity and Carcinogenicity

Edward James Calabrese

Volume II: Minerals and Macronutrients

A Volume in Environmental Science and Technology: A Wiley-Interscience Series of Texts and Monographs Edited by Robert L. Metcalf and Werner Stumm

Nutrition and Environmental Health

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Volume 2
MINERALS AND MACRONUTRIENTS

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To My Wife Mary

Series Preface

Environmental Science and Technology

The Environmental Science and Technology Series of Monographs, Textbooks, and Advances is devoted to the study of the quality of the environment and to the technology of its conservation. Environmental science therefore relates to the chemical, physical, and biological changes in the environment through contamination or modification, to the physical nature and biological behavior of air, water, soil, food, and waste as they are affected by man's agricultural, industrial, and social activities, and to the application of science and technology to the control and improvement of environmental quality.

The deterioration of environmental quality, which began when man first collected into villages and utilized fire, has existed as a serious problem under the ever-increasing impacts of exponentially increasing population and of industrializing society. Environmental contamination of air, water, soil, and food has become a threat to the continued existence of many plant and animal communities of the ecosystem and may ultimately threaten the very survival of the human race.

It seems clear that if we are to preserve for future generations some semblance of the biological order of the world of the past and hope to improve on the deteriorating standards of urban public health, environmental science and technology must quickly come to play a dominant role in designing our social and industrial structure for tomorrow. Scientifically rigorous criteria of environmental quality must be developed. Based in part on these criteria, realistic standards must be established and our technological progress must be tailored to meet them. It is obvious that civilization will continue to require increasing amounts of fuel, transportation, industrial chemicals, fertilizers, pesticides, and countless other products; and that it will continue to produce waste products of all descriptions. What is urgently needed is a total systems approach to modern civilization through which the pooled talents of scientists and engineers, in cooperation with social scientists and the

medical profession, can be focused on the development of order and equilibrium in the presently disparate segments of the human environment. Most of the skills and tools that are needed are already in existence. We surely have a right to hope a technology that has created such manifold environmental problems is also capable of solving them. It is our hope that this Series in Environmental Sciences and Technology will not only serve to make this challenge more explicit to the established professionals, but that it also will help to stimulate the student toward the career opportunities in this vital area.

Robert L. Metcalf
Werner Stumm

Preface

This book is the second of a two-volume set concerned with the influence of nutritional status on pollutant toxicity and/or carcinogenicity. While Volume I dealt with the interactions of the vitamins with toxic substances, Volume II details the role of the minerals, protein, fats, carbohydrates, and specific amino acids, as well as fiber and synthetic antioxidants on the adverse effects of pollutants.

This two-volume set comprises the first major synthesis of the general area of nutrition and environmental health. It is intended to be a comprehensive and detailed evaluation of the extent to which nutrients interact with toxic substances in the environment. This volume is organized by nutrient so that each nutrient is given a chapter or a section within a chapter if there is only limited information available on that topic. Within each chapter, the various pollutant interactions with that nutrient are discussed. For example, there are separate chapters on calcium, copper, iron, selenium, and so on. Within each of these chapters there are discussions of how that particular nutrient affects the toxicity of, say, cadmium, fluoride, lead, or nitrosamines, depending on the situation. In general, the pollutants are divided into two categories—inorganic and organic—and then discussed in an alphabetic setting in order to provide a consistent and organized scheme. Furthermore, chapters that have a summary section at the end provide an integrated discussion to a complex series of nutrient-pollutant interactions and an indication of the biomedical significance of the previously discussed findings, as well as a sense of direction for further research. Summary sections were not provided for those sections (i.e., Chapter 6, "Other Minerals" and Chapter 12, "Synthetic Antioxidants") in which the research base is too limited.

This book is not only a comprehensive and critical review of the published literature concerning the role of nutritional status on pollutant toxicity, it is also designed to provide numerous viable and socially relevant research hypotheses for individual investigators to

pursue and/or government personnel within research and developmental departments to consider in the formulation of priority allocations.

Governmental regulatory personnel who are concerned with the task of establishing criteria for the development of standards for chemical toxicants should find these volumes of critical interest. In essence, these books provide a vast amount of information on individuals who may be at increased risk to develop adverse effects from pollutant exposures. For whether or not these so-called high-risk groups are specifically protected by standards, they must at least be considered during the standard derivation process.

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Amherst, Massachusetts
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Contents

1 Calcium

A. INORGANIC SUBSTANCES

1. Cadmium

That dietary factors may affect the toxicity of cadmium is well known (Table 1). Considerable research efforts have been directed toward elucidating the influence of various nutrients including ascorbic acid, iron, and zinc on the toxicity of cadmium (Supplee, 1961, 1963; Fox and Fry, 1970; Petering et al., 1971; Maji and Yoshida, 1974; Ragan, 1977; Levander, 1978). An early observation that calcium levels in the diet would modify the toxicity of cadmium was provided by Worker and Mogicovsky (1961), who noted that chickens fed a diet low in calcium and vitamin D exhibited an increased cadmium uptake via the gastrointestinal tract. In the years since this report, there has been a growing concern over the potential interrelationship of calcium and cadmium because (1) cadmium is known to cause demineralization (including decalcification) of bone in both animal models and humans; and (2) cadmium is known to be a cause of hypertension in animal models, while hard water (i.e., water with high levels of calcium) is thought to protect against the development of cardiovascular disease. The following section will show how low levels of dietary

Table 1. Relationships between Cadmium and Essential Nutrients

Nutrient	Dietary Intake of Individual Nutrients		
	Normal[a]	Deficiency[b]	Excess[c]
Zinc	+	+	+
Iron	+	+	+(Fe^{2+})
Manganese	+	?	?
Copper	+	+	+
Selenium	+	?	+
Calcium	+	+	?
Ascorbic Acid	?	?	+
Vitamin D	?	+	?
Protein	?	+	+

[a]+ Cadmium affects metabolism and/or function of the nutrient, ? No relationship has been established.

[b]+ A deficiency of the nutrient increases the severity of cadmium toxicity.

[c]+ An excess of the nutrient decreases the toxicity of cadmium.

Source: Spivey-Fox, M.R. (1974). Effect of essential minerals on cadmium toxicity. A review. *J. Food Sci.* **39**:322.

calcium enhance the tissue retention and presumably the toxicity of dietary cadmium, as well as how cadmium alters calcium metabolism and how this may be related to the development of osteomalacia.

Influence of Low Levels of Dietary Calcium on Cadmium Retention. Numerous researchers have evaluated the influence of low and normal levels of dietary calcium on the retention of cadmium in a variety of species including the chicken (Worker and Mogicovsky, 1961; Kobayashi et al., 1971; Koo et al., 1978), mice (Suzuki et al., 1969), rats (Itokawa et al., 1973; Pond and Walker, 1975; Washko and Cousins, 1975, 1976; Kello et al., 1979; Hamilton and Smith, 1978), and golden hamsters (Miller et al., 1975), with the predominant research being with the rat model. Although several studies concerning calcium-cadmium interactions preceded the 1970s (Worker and Mogicovsky, 1961; Suzuki et al., 1969; Fleishman et al., 1968), most of the research has been of a very recent nature, getting strong impetus from the reports on cadmium-induced Itai-Itai disease in Japan, which was characterized by osteomalacia with renal tubular damage in women. These women were also found to have diets low in calcium and