ENVIRONMENTAL METAL POLLUTANTS, REACTIVE OXYGEN INTERMEDIARIES AND GENOTOXICITY

Molecular Approaches to Determine Mechanisms of Toxicity

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by

Maria E. Ariza
University of Arizona
Arizona Cancer Center

Gautam N. Bijur
Behavioral Neurobiology
University of Alabama at Birmingham

Marshall V. Williams
Department of Medical Microbiology & Immunology
The Ohio State University

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PREFACE

Humans are exposed daily to low concentrations of metals that are released into the environment by both natural and industrial processes. Recently, concerns have been raised about the acute and/or chronic exposure of humans to concentrations of these metals that are below the threshold levels established by various federal regulatory agencies. Because some of these metals are accumulated in various tissues, over time this may result in the accumulation of a significant body burden. This could increase the risk of developing a variety of diseases later in life at a time when thresholds for such effects may already be reduced by the processes of aging. Such possibilities could only further compromise the quality of life in the senior population and could contribute to the rising cost of health care in this country.

Studies that have been conducted to determine the possible risks associated with exposure to relatively non-toxic concentrations of environmental metals have been hampered by a lack of appropriate models and a lack of funding. It has also been difficult for researchers to demonstrate a correlation between the exposure of humans or animals to low concentrations of environmental pollutants and disease.

This book examines the recent technological advances in the areas of molecular biology, biochemistry, and computer enhanced image analyses that provide researchers with the tools to begin elucidating the mechanisms by which environmental metal pollutants cause DNA damage.

Several recent studies indicate that environmental metal pollutants may cause the deterioration of biological molecules through an oxidative mechanism. Our recent studies have shown that two environmental metal pollutants, lead and mercury, induce genotoxic DNA damage and that these metals are mutagenic by virtue of their ability to induce reactive oxygen intermediates in cells. However, lead and mercury do not induce reactive oxygen intermediates by the classical Fenton reaction, but rather by the activation of cellular enzymes (superoxide dismutase and xanthine oxidase) that produce superoxide anion and hydrogen peroxide.

One of the goals of this book is to demonstrate that the acute and chronic exposure of humans to environmental metal pollutants at concentrations below the threshold values recommended by federal protection agencies may pose a potential health hazard, since these metals induce the formation of reactive oxygen imtermediates in cells. A second objective is to describe the mechanisms by which environmental metal pollutants induce reactive oxygen intermediates in cells. A third objective is to describe the processes by which these reactive oxygen intermediates that are induced by environmental metal pollutants are genotoxic (mutagenic). Last, the authors will discuss the ways that these reactive oxygen intermediates induced by environmental metal pollutants can have a role in aging, carcinogenesis and certain neurovascular and cardiovascular diseases.

The authors will demonstrate that certain environmental metal pollutants are genotoxic (mutagenic), describing the role of reactive oxygen intermediates in causing the DNA damage induced by environmental metal pollutants and discussing the possible role that metal-induced reactive oxygen intermediates may have in human disease. The discussion of environmental metal pollutants will be limited to arsenic, cadmium, chromium, cobalt, lead, mercury, nickel, and zinc, all of which have been associated with causing disease in either animals or humans. These metals represent the most common environmental metal pollutants. Relevant studies on copper and iron will also be included, since these are the most commonly studied transition metals.