

Handbook on the Toxicology of Metals

Handbook on the Toxicology of Metals

Third Edition

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Preface

The *Handbook on the Toxicology of Metals* is a comprehensive review dealing with the effects of metallic elements and their compounds on biological systems. Special emphasis has been laid on the toxic effects in humans, although toxic effects in animals and biological systems *in vitro* are also discussed whenever relevant. As a basis for a better understanding of the potential for adverse effects on human health, information is also given on sources, transport, and transformation of metals in the environment and on certain aspects of the ecological effects of metals.

The first edition of the handbook appeared in 1979, and was followed by a second edition in 1986. The work rapidly fulfilled the aims of the editors and became a standard reference work for physicians, toxicologists, and engineers in the fields of environmental and occupational health. There has been a long interval between the 2nd edition and the present one, but the aims of this third edition are basically the same as those of the previous editions, i. e., to provide easy access to basic toxicological data and also give more in-depth treatment of some information, including a general introduction to the toxicology and risk assessment of metals and their compounds.

As with the previous editions, writing the 3rd edition of this book has been a part of the activities within the Scientific Committee on the Toxicology of Metals under the International Commission on Occupational Health, and the editors are happy that the work to make a third edition has been given a high priority among members. In some cases, we have been honored to include authors from outside of this committee. The chapter authors have, as far as possible, been the same as those who wrote the second edition, but in many cases, we were happy to introduce new colleagues.

Since the publication of the 2nd edition, a wealth of data has appeared, and several of the chapters dealing with specific metals have been completely rewritten; others have undergone a comprehensive updating. In order to not expand the present book and make it much larger than the second edition, which was published in two volumes, some of the general chapters have been merged and shortened, and the present book is published in one volume

in a larger format. For the interested reader who searches more detailed information on specific topics, each chapter contains a large number of relevant references also to recent reviews whenever these are available.

The development of modern devices in society demand new chapters which reflect the present concerns of the use of new materials, such as semiconductors in electronic devices, metallic nanotechnology devices, and platinum- and palladium-based catalytic converters.

The increasing use of biomarkers in occupational and environmental health has made it necessary to add a new chapter on biological monitoring and biomarkers. Immunotoxicology is an expanding field, and considerable achievements have been made in recent years. A chapter on "immunotoxicology of metals" has therefore been included. Immunological and genetic findings provide, in some cases, good explanations for the differences in susceptibility to development of disease from exposure to metals. Principles for prevention of the toxic effects of metals and risk assessment are important chapters, somewhat expanded, and a new chapter on a related topic "Essential Metals: Assessing Risks from Deficiency and Toxicity" brings up-to-date knowledge into this 3rd edition.

Before the manuscript of this 3rd edition could be finalized, our co-editor and friend Professor Lars Friberg died. He was the main editor of the two first editions of this handbook, and his ideas constituted the basis for the present edition. His stringent analytical views were invaluable, and his expertise and knowledge are greatly missed. We will also remember him as a loyal, generous, and warm friend, and hope that this book will be a lasting tribute to his memory.

The editors acknowledge each contributor to this book for their devotion and enthusiasm and for having prioritized the work to make the 3rd edition of *Handbook on Toxicology of Metals* available to the reader.

Gunnar F. Nordberg
Bruce A. Fowler
Monica Nordberg

Foreword: Outlook

Metals – a new old environmental problem

“Toxic metals” are one of the oldest environmental problems. Today, there are new dimensions of the problem, such as the production of metals in developing countries, leading to occupational exposure and exposure to the general public through the ambient air, drinking water, food, and consumer products. High technology development has also resulted in new products that need more metals in, for example, electronics, fuel cells and car exhaust technology. E-waste, together with drug waste, are new waste problems. The use of metals like gallium, indium, and germanium, which are used in semiconductors has increased steadily over the last 25 years. The e-Waste problem is further augmented by the export of electronic waste from developed to developing countries. Nanotechnology can also lead to unforeseen problems caused by consumer products and combustion of material based on nanoparticles.

Arsenic is a common toxic element which produces clinical disease in India and Southeast Asia from drinking water. This region is also experiencing growing use in semiconductor production. High concentrations of arsenic in drinking water also occur in South America and the U.S. Arsenic is a good example showing how old knowledge is forgotten or ignored, creating new problems. In a number of developing countries, this problem is further exacerbated by expanding human populations and the overexploitation of ground water.

Environmental health problems—and successes stories from the toxicology of metals—have been highlighted in the EEA report on Environment and Health 2005. Some of the key conclusions concerning toxic metals are:

- A number of chemicals are potentially carcinogenic. Approximately 500 metals are classified as carcinogens and are not legally allowed to reach the consumer. They may, however, reach the environment via diffuse sources, for example, in accidental cases. Arsenic in drinking water and cadmium from diffuse

sources are environmental contaminants of special concern, because of increasing environmental exposure and their established carcinogenicity.

- Radon exposure is the best documented environmentally related cause of cancer, but is localized in geographical areas where radon precursors (uranium) occur naturally in the ground. Uranium can also contaminate drinking water, leading to kidney injuries.
- Mercury at concentrations that are sometimes observed in the environment is well known to have neurodevelopmental effects, for example, attention problems, reduced learning ability, and slightly reduced IQ in children. Measures are now being taken in Europe to reduce, *inter alia*, prenatal mercury exposure in order to ensure that tolerable daily intakes for pregnant women are not exceeded.
- Lead is an established neurodevelopmental toxicant to humans. Mild mental retardation of children 0-4 years of age in the WHO-Europe region resulting from lead exposure accounts for 4.4% of DALYs (disability adjusted life years). Recent studies on the effects of lead in humans suggest that a “safe” exposure level currently cannot be established. More data on lead exposure of European citizens are necessary and are currently being collected. A ban on leaded petrol has been very successful in lowering blood lead levels in children, which clearly indicates a reduced exposure.
- The global distribution of “new” metals used in automobile catalytic converters to reduce hydrocarbon pollution is clearly shown in the Arctic. Concentrations of platinum, palladium, and rhodium in ice and snow in Greenland have increased rapidly since the 1970; the same trend has been observed in Germany.
- The cadmium contamination of agricultural land has increased during the 20th Century in Europe, leading to exposure from vegetables. Suspicions of kidney and skeleton injuries exist in Europe.

- The effects of combined, long-term and cumulative exposures to *Mixtures of Metals* from diffuse sources might be under-estimated (sometimes called the “cocktail effect”). Research in this area needs to develop methods and models to analyze exposures and pathways to disease from *Combinations of Toxic Metals*.

21st Century approaches for 21st Century problems

The shift in focus from legislation for stationary sources to diffuse sources is clearly demonstrated in European Union (EU) legislation, exemplified with directives on integrated pollution prevention and control, Eco-Management and Audit Scheme, European Eco-label, and Integrated Product Policy looking at all phases of a products’ life-cycle and taking action where it is most effective. The precautionary principle is also an important starting point.

However, the problems of the 21st century need tools developed in the 21st century. The issue of environment and health is characterized by multicausality with different strengths of association. This means that the links between exposures and their health consequences depend on the environmental pollutants and diseases being considered, but are also influenced by factors such as genetic constitution, age, nutrition and lifestyle, and socio-economic factors, such as poverty and level of education. Important elements of exposure and risk assessment are the estimation of the body burden of chemicals, combined exposures from multiple sources (food, air and water) and the timing of exposures. Preventive measures require the development of proactive risk assessment and management replies that can contribute to the formulation of adequate responses, not at least consider the costs of action and non-action.

Given the complexities and uncertainties relating to environmental health issues, a new participatory framework for risk assessment and risk management is developing, involving a broader framing of scientific assessment of risks, uncertainties, and ignorance, and

options for action, communication, monitoring, and evaluation of the effectiveness of actions. Approaches, systems, and services are required to support many different types of actors and other afflicted individuals, not just the policymakers. At a symposium organized by the Scientific Committee on the Toxicology of Metals, International Commission on Occupational Health, a number of these approaches for toxic metals and metalloids were discussed, along with the ongoing need for international collaboration. This “Symposium on Risk Assessment of Metals,” hosted by the European Environment Agency in Copenhagen, Denmark, June 13-14, 2005 was sponsored by FORMAS, (Sweden) and co-sponsored by the Agency for Toxic Substances and Disease Registry (USA). This conference brought together a number of international experts on the toxicology of metals to review, discuss, and critique chapters for the *Handbook on the Toxicology of Metals* so that the most relevant and up-to-date information will be available for the production of this important reference work.

Research, knowledge, assessments, and monitoring

Environmental research is a prerequisite for evidence-based policymaking, assessing new knowledge and early warnings. The production of the handbook is one assessment example. The project has also highlighted biomarkers and biological monitoring as an important tool to identify and quantify the exposure, predict health effects, sensitive populations, and perhaps also diagnose a disease. Bio-monitoring is also an effective mean to evaluate the target setting and other policy interventions. However, it raises ethical questions that must be addressed.

Copenhagen 13th June 2005

European Environment Agency
Jacqueline Mc Glade

FORMAS
Lena Sennerby
Forsse

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- Gallium and Semiconductor Compounds
- Palladium
- General Chemistry, Sampling, Analytical Methods,
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- Arsenic
- Gallium and Semiconductor Compounds
- Essential Metals: Assessing Risks from Deficiency and
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