TRACE ELEMENTS AND IRON IN HUMAN METABOLISM

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SPRINGER SCIENCE+BUSINESS MEDIA, LLC

Library of Congress Cataloging in Publication Data

Prasad, Ananda Shiva.
Trace elements and iron in human metabolism.

(Topics in hematology)
Includes bibliographies and index.
1. Trace element metabolism. 2. Iron metabolism. I. Title. II. Series. [DNLM: 1. Trace Elements – Metabolism. 2. Iron – Metabolism. QU130.3 P911t]
QP534.P7 612'.3924 78-13446
ISBN 978-1-4684-0795-2

ISBN 978-1-4684-0795-2 ISBN 978-1-4684-0793-8 (eBook)
DOI 10.1007/978-1-4684-0793-8

Originally published by Plenum Publishing Corporation in 1978
Softcover reprint of the hardcover 1st edition 1978

TO MY FAMILY

FOREWORD

Each year, it becomes more apparent that trace elements play an important role in human metabolism. The concept is no longer new. The literature on the subject is voluminous.

Dr. Prasad, who has been interested in this field for many years, has undertaken the enormous task of bringing our knowledge together in a comprehensive fashion. This monograph should prove very informative and extremely useful to everyone who is concerned with human disease and with the maintenance of good health. His coverage of the subject is broad. Because of the importance of iron, in addition to "trace" elements, in human metabolism and nutrition, a chapter dealing with iron has been included.

Maxwell M. Wintrobe, M.D.

PREFACE

It has been known for several decades that many elements are present in living tissues, but it was not possible to measure their precise concentrations until recently. They were therefore referred to as occurring in "trace" amounts, and this practice led to the use of the term "trace elements." Although techniques now available are such that virtually all trace elements can be determined with reasonable accuracy, the designation "trace elements" remains in popular usage.

During the past two decades, remarkable advances have taken place in the field of trace-element research. Although deficiencies of iron and iodine in man have been known for many years, it is only recently that the essentiality of zinc and copper in human metabolism and nutrition has been recognized. Thirty-five years ago, carbonic anhydrase was recognized to be the only enzyme requiring zinc, but now there are approximately seventy related metalloenzymes known for which zinc is needed. The essential role of zinc in growth and development and its basic role in deoxyribonucleic acid (DNA) synthesis have been established only in the past decade.

Recent developments demonstrate that zinc therapy may have a widespread role in various disease processes associated with conditioned deficiency of zinc. Indeed, zinc therapy for patients with acrodermatitis enteropathica has now become a lifesaving measure. It is also becoming clear that besides nutritional deficiency of zinc, conditioned deficiency of this element due to several disease states is probably not uncommon. Awareness of this possibility is likely to uncover many other clinical conditions in which zinc therapy may prove to be beneficial.

Zinc appears to have a fundamental anticalcium action at the cell-membrane level. This mechanism could account for the inhibitory action of zinc on a number of cells, including inflammatory cells and platelets. If this

is true, zinc may have potential as an antiinflammatory agent in a variety of diseases, one of which would be rheumatoid arthritis.

The essential role of copper in collagen synthesis, the role of chromium in glucose tolerance factor, the presence of selenium as an integral part of the enzyme glutathione peroxidase of human red cells, and the important role of manganese in the metabolism of cartilage clearly suggest that these elements have vital functions to perform in human metabolism. A proper understanding of their biochemical roles and the application of such knowledge to human diseases could predictably have a great impact on the future practice of medicine.

In this book, all elements known to be essential for man, such as iron, iodine, zinc, copper, manganese, selenium, chromium, and fluoride, with the exception of cobalt, have been included. The only known function of cobalt in man appears to be related to its presence in the vitamin B_{12} molecule. For this reason, this element is not discussed. A short discussion on the role of newer trace elements has been included, inasmuch as future research may implicate these elements in human health and disease. Although magnesium is usually not considered to be a trace element, its biochemical role in enzymatic functions is similar to that of other trace elements. For this reason, it has been included here.

A considerable number of essential trace elements occupy positions in the periodic table between atomic numbers 23 and 34. This atomic-number interval includes two elements, gallium and germanium, for which no vital roles have been described so far. Future studies may uncover essential functions for these two elements.

Toxic elements important for man, such as cadmium, lead, and mercury, are also covered in this book. Recent studies indicate that the toxicity of cadmium and lead may be due to their adverse effects on zinc metalloenzymes. The toxicity of mercury may be diminished by supplementation with selenium in experimental animals. These observations emphasize the interactions of various elements and suggest possible means by which the toxicity of certain metals may be ameliorated. Competition for similar binding sites between zinc and copper, iron and copper, and iron and manganese is a well-known phenomenon. A thorough knowledge of these interactions may provide yet another means by which storage disorders such as Wilson's disease and hemochromatosis may be managed in the future. It is important, however, that one look at these leads very critically and not be indiscriminate in the medical usage of various trace elements in disease conditions.

Physicians, biochemists, nutritionists, and medical researchers should find this book useful, inasmuch as standard textbooks, generally speaking, have thus far not focused on these newer developments in the field of trace elements. It is hoped that an awareness of the metabolic functions of trace

elements may lead to better management of some of the diseases associated with their abnormalities.

I wish to thank Dr. Maxwell M. Wintrobe for his helpful suggestions. Ms. Karen Harrington, Clare Giska, Emily Quigley, and Maha Fakhouri provided secretarial help for which I am very grateful. I also wish to thank Doug Door, who checked many references in the library.

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