Manual on Vitamin A Deficiency Disorders (VADD)
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Volume Editors

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76 figures, 4 in color, and 55 tables, 2012
Bibliographic Indices. This publication is listed in bibliographic services, including Current Contents® and PubMed/MEDLINE.

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Drug Dosage. The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

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Distribution rights of the English Edition, print and ebook in selected countries – S. Karger AG, Basel, Switzerland
www.karger.com
Printed in Switzerland on acid-free and non-aging paper (ISO 9706) by Reinhardt Druck, Basel
ISSN 0084–2230
e-ISSN 1662–3975
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The Sight and Life Manual on Vitamin A Deficiency Disorders (VADD) is now appearing in its 3rd edition. Although our scope has broadened from ‘sight’, a single focus on vitamin A, to ‘life’, a multiple micronutrient focus, we believe that vitamin A remains sufficiently important and interesting for us to dedicate a whole book to this nutrient.

This book not only draws on the latest scientific research and expert insights, but also benefits greatly from the work of previous generations of scientists and policy-makers. As a result, it is almost impossible to acknowledge all those who have contributed their expertise. Key sources include, among others, journal articles, policy statements, reports, fact sheets, guidelines, reference books, websites and – of course – the data and research to be found in Sight and Life Magazine itself.

We would like to take this opportunity to acknowledge the support we have experienced during the last couple of years in preparing the 3rd edition of this book. There are many people to acknowledge who have been associated with this project. We would therefore like to start with apologies to those who we may have omitted to mention. Extraordinary thanks go to Svenia Sayer-Ruehmann and Anne-Catherine Frey from the Sight and Life team for their skilful technical support, without which this publication would have never been completed. Further, our Sight and Life interns Laurence Curty and Sarah Diouf both merit special mention. We continue to appreciate Yvonne Bearne for her proofreading, and the Burger Druck team for laying out the book. We also wish to thank the World Health Organization for its kind permission to reprint the vitamin A deficiency world maps. Last but not least, Royal DSM deserves our special appreciation for its continuous support of Sight and Life; in particular, we would also like to thank Stephan Tanda, Chairman of the Sight and Life Steering Committee, for writing his encouraging foreword to this volume.
This Third Edition of the *Sight and Life* Manual on Vitamin A Deficiency Disorders (VADD) is likely to be the last. This is not because there is nothing more to learn about the subject. It is because in recent years there has been a major shift in the approach to the control of vitamin and mineral deficiencies (VMD) or multi-micronutrient deficiencies (MMD) – including VADD. This is largely due to the fact that it is now well recognized that VMD tend to occur together rather than on their own – a tendency that is most likely explained by the fact that most micronutrients are found in the same classes of foodstuffs, especially fruit, vegetables, fish and meat. Until recently, it was general practice to identify and combat the most serious forms of deficiency, usually of a single micronutrient. Prominent among these have been vitamin A, iron, iodine, zinc and folate. Today, although there remains a great deal to be learned about the individual roles and functions of most micronutrients in human nutrition, interest is increasingly focused on their interrelationship, especially as micronutrient intervention programs are on the increase and many are in the process of being scaled-up.

The recognition of the interconnected relationship of the micronutrients is further highlighted by the disbanding of the International Vitamin A Consultative Group (IVACG) and International Nutritional Anemia Consultative Group (INACG), which were set up more than thirty years ago to assist in the control of specific nutritional deficiencies. They have been replaced by the all encompassing Micronutrient Forum (MF), which held its first scientific meeting in April 2007. It is no exaggeration to say that hundreds of nutrition-related scientists, whose knowledge and research efforts were virtually confined to a single micronutrient, will now have to broaden their area of expertise and research. Rightly or wrongly, the demands of the time do not seem to permit the luxury of extreme specialization. Henceforth source materials like this manual will also need to focus more on VMD in general. *Sight and Life* sees this as a key role for itself in the future as we continue to evolve to ensure that we make a valuable contribution.

The Third Edition has not surprisingly increased considerably in size and includes three new chapters. The first of these is specifically titled ‘Foreground’ (as opposed to Background), in order to emphasize, from the start, that the focus of the Manual is on the control of VADD and that this objective should be kept in mind throughout the book. Chapter 2 illustrates how essential and versatile the vitamin A molecules are – together with their close relatives found in nature, the carotenoids. Without them human life, vision, growth and development would not be possible. The bioavailability of carotenoids has become so important that it now requires its own chapter (Chapter 5). In addition, the effect that the acute phase response (APR) has on serum retinol levels is of such significance that, after an introduction to the issue in Chapter 7, it remains a prominent feature in several subsequent chapters. As so often in the field

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**Preface**

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of VMD, the work on APR has been pioneered in relation to VADD, but its effect in relation to other micronutrient deficiencies has received little attention and much more research is necessary.

This edition also includes in Chapter 12 the latest available data on the global occurrence of VAD from the World Health Organization (WHO). Attention is drawn to the inability, over the past several years, to determine accurate prevalence figures for the number of blind persons living in any given country or region of the world or within any vulnerable group etc., due to the decision to no longer report non-blinding xerophthalmia and blinding xerophthalmia separately. As a consequence, while data on other causes of blindness are becoming increasingly precise, vitamin A deficiency blindness is included under the heading of 'other causes of childhood blindness' – something which should be rectified in view of its importance and public health impact.

In Memoriam
Martin Frigg, 1943–2010

While this third edition of the Sight and Life Manual on Vitamin A Deficiency Disorders was in preparation, we received news of the sad death of Martin Frigg, Director-General of Sight and Life from 1994 to 2005. Although Martin did not contribute to the present volume, it would not exist without his invaluable editorial work on the previous two editions.

We gratefully acknowledge Martin's past contribution and deeply lament his passing.

The Editors

Medicine is often considered to be both a science and an art. In reality it is neither, although it employs both science and art to meet its ends. It is better understood as a human endeavor dedicated to the prevention and cure of disease and the alleviation of suffering. Diseases, like the civilizations that suffer from them, rise and fall, occasionally without the cause(s) or the true effects of the measures employed against them being known. Amongst those diseases attributed to an inadequacy of nutrients in the diet, vitamin A deficiency was shown to hold a prominent place in the middle of the 20th century. At that point, it was the most common cause of blindness in young children worldwide. Within several decades, as a result of research that led to interventions, severe blinding vitamin A deficiency (xerophthalmia) had been brought under control to a large extent. However, at around the same time it was recognized that the problem had several other concerning elements:

- Vitamin A deficiency at a subclinical and so often unnoticed level is extremely widespread in developing countries;
- Even at this subclinical level, it has a significant adverse effect on morbidity and mortality rates;
- Other groups besides young children, such as pregnant and lactating women and school-age children, are also highly susceptible to vitamin A deficiency;
- Vitamin A and both pro- and non-pro-vitamin A carotenoids are increasingly being recognized as playing an important role in diseases which affect all age groups throughout the world, including age-related macular degeneration, cancer, metabolic syndrome and cardiovascular disease; and finally,
- New terminology is now generally accepted for the expanded and enhanced role that vitamin A is now recognized to play – vitamin A deficiency disorders (VADD).

Although many micronutrients are intimately involved in human health and the relationship between the micronutrients is increasingly important, the pioneer in vitamin deficiency research, vitamin A, remains an important and interesting research field. We trust that this Third Edition of the Vitamin A Manual will add to the body of literature that contributes towards interventions that ultimately ensure sustainable and significant improvements in human nutrition, health and well-being.

Donald McLaren
Klaus Kraemer
Foreword

A Powerful Commitment

Hidden hunger is the number one cause of death in the world, killing more people than AIDS, malaria and tuberculosis combined. The term describes the malnutrition that results from a lack of essential vitamins and minerals. Malnutrition and hunger in combination currently cause the deaths of 3.5 million children under the age of five every year. The achievement of no fewer than six out of the eight United Nations Millennium Development Goals is contingent on the elimination of hidden hunger.

Among the vitamins essential for healthy growth and development, vitamin A plays a key role. It was the recognition of the link between vitamin A deficiency and blindness in malnourished populations that inspired the founding of Sight and Life in 1986 and, indeed, gave the humanitarian initiative its name.

Since that time much has been learned about the characteristics and effects on the human physiology of a wide range of vitamins and minerals. Moreover, scientists have come to appreciate as never before the complex interactions of these micronutrients. A great deal of original research remains to be done, but the way forward is clear: the elimination of hidden hunger worldwide can only be achieved if scientists, policymakers, non-governmental organizations and the private sector join forces to defeat this public health scourge.

Sight and Life has an important role to play in this effort. It is the role of a committed advocate. Sight and Life maintains close and productive relationships with policymakers, other non-governmental organizations, researchers and private sector organizations to advocate targeted policies and effective programs that bring measurable benefits to some of the world’s poorest and most disadvantaged people. Sight and Life achieves this by invoking an array of approaches. These range from publishing authoritative works such as this volume through disseminating up-to-the-minute information and insights via Sight and Life Magazine to staging conferences and workshops, as well, of course, as funding original research work and field programs on the ground.

The role of Sight and Life is therefore to analyze what is good and what is new in the micronutrient arena but also to be aware of what is tried and tested so that it can effectively advocate good policy- and program-making. I know from my work with them that the Sight and Life team are passionate about the work they do and deeply dedicated to ensuring a sustainable and significant improvement in the health and well-being of some of the world’s poorest and most vulnerable people.

DSM fully supports Sight and Life. In our partnership with the World Food Programme (WFP), which has been running since 2007, Sight and Life plays a key role. It is DSM’s belief that together DSM and WFP can make a difference to the lives of millions of people. Improving nutrition
means improving lives: it means breaking the vicious circle of poverty and hunger and malnutrition which leads to suffering, disease and underachievement.

We believe that by improving people's lives in this way we can make a major contribution to unleashing the untapped human and economic potential of many countries around the globe. As our CEO Feike Sijbesma has often said of DSM, we cannot be successful, nor can we call ourselves successful, in a society that fails. This powerful corporate and personal commitment was recognized in October 2010 when the United Nations Association of New York awarded Feike Sijbesma the prestigious 2010 Humanitarian of the Year award for his outstanding commitment to corporate social responsibility (CSR) and in particular for DSM’s partnership with the United Nations World Food Programme.

It is an honor of which all of us at DSM are deeply proud. And we will be proud to continue our efforts to improve the lives of millions of people who so urgently need our help.

Stephan Tanda
Member of the DSM Managing Board
with responsibility for DSM's Nutrition cluster of businesses