ZINC AND HEALTH: Current Status and Future Directions

A workshop sponsored by the NIH Office of Dietary Supplements.

November 4–5, 1998

Lister Hill Auditorium
National Institutes of Health
Bethesda, Maryland, USA

Co-Sponsors:
American Dietetic Association
American Society for Clinical Nutrition
Centers for Disease Control and Prevention
Department of Defense
Fogarty International Center
Food and Drug Administration/Center for Food Safety & Applied Nutrition
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INTRODUCTION TO THE WORKSHOP ON ZINC AND HEALTH: CURRENT STATUS AND FUTURE DIRECTIONS

The 1994 Congressionally mandated Office of Dietary Supplements was formally established at the end of November 1995, within the Office of the Director (OD) at the National Institutes of Health. Among the tasks for this office are:

“to explore more fully the potential role of dietary supplements as a significant part of the efforts of the United States to improve health care; … and to conduct and coordinate scientific research within the National Institutes of Health relating to dietary supplements .” (Public Law 103-417).

In June, 1996 in keeping with the focus on activity heightened by publication of Physical Activity and Health, A Report of the Surgeon General the Centennial Olympic Games, and the 1996 Paralympic Games, the ODS held its first major workshop, Dietary Supplements for Physically Active People. This Workshop, Zinc and Health, Current Status and Future Directions, is the second in the ODS series of major workshops which will present a state-of-the-art review of zinc as it relates to health. The last five years have seen a virtual explosion of interest and understanding of the spectrum of functions of zinc at sub-cellular levels. Zinc is a versatile trace element required as a cofactor by more than 300 enzymes in every organ of the body. Zinc supports the work of numerous proteins in the body—among them are the metalloenzymes, which are involved in a variety of metabolic processes. The zinc atom is so ubiquitous in cellular metabolism, that even minor impairment of an adequate supply is likely to have multiple biological and clinical effects. Given the central roles of zinc in cellular growth and differentiation, it is no surprise that the effects of zinc deficiency are pronounced in the rapid turnover of tissues and organs, especially the immune system. “Zinc is a prime candidate for attention at the close of this and the beginning of the next millennium.” D. Michael Hambidge, M.D. (personal communication, fall, 1998)

It is likely that identifying and correcting borderline nutritional zinc deficiency will offer widespread health benefits. Pharmacological doses of zinc may also be beneficial in certain circumstances and harmful in others. In the public health arena, the positive results of zinc supplementation trials on childhood morbidity and mortality in developing countries have been remarkable and offer promise as a low cost solution to specific health problems.

The goal of this workshop is to provide an overview of the biochemical, cellular, and nutritional requirements of zinc in health and disease. Attention will be focused on six key areas where zinc supplementation may play a role in the prevention, reduction or treatment of disease. The following topical areas will be addressed: zinc nutrition; zinc and the GI tract; immune system, antioxidant, and defense functions of zinc; zinc and cellular mechanisms; zinc and the central nervous system; and zinc in growth and specific disease entities. In addition, new and emerging roles of zinc in human health will be discussed, as well as new measurement and
assessment techniques available in the field of zinc research. A desired outcome for this meeting is the development of a research agenda that will identify key areas warranting further investigation. The value of, indeed the necessity for, well-designed, adequately controlled, randomized, and professionally executed intervention studies is of special importance with this particular micronutrient, given the lack of adequate biomarkers and the lack of specific clinical features of zinc deficiency.

The workshop will bring together leading experts in zinc research and clinicians from many scientific disciplines who will present a timely update and critical needs assessment on zinc and health to researchers, nutritionists, and public health advisors and policy makers. These scientists will present reviews of the current state of scientific knowledge regarding zinc nutriture, requirements, and function that will be applicable to many basic science, clinical and public health programs across the country.

In closing, copies of this program booklet will be available for downloading from the Office of Dietary Supplements web site at http://dietary-supplements.nih.gov as well as a copy of the Zinc and Health Bibliography prepared in conjunction with the National Library of Medicine. We would also like to acknowledge the assistance of Donna F. Allen of the ODS project staff for her editing and word processing of the program booklet, and the assistance of Kristine M. Scannell for production of the Zinc and Health Searchable Bibliography.

Rebecca B. Costello, Ph.D.

Bernadette M. Marriott, Ph.D.
GENERAL INFORMATION

Workshop sessions will be held in the Lister Hill Auditorium (Building 38A) National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland. Sessions will run from 8:00 a.m. to 5:00 p.m. on Tuesday. The telephone number for the message center is (301)-496-4062.

CAFETERIA

The cafeteria is located on the lower level, and is open daily form 7:00 a.m. to 3:00 p.m.

SPONSORS

The primary sponsor for this workshop is the NIH Office of Dietary Supplements, in conjunction with the American Dietetic Association and the American Society for Clinical Nutrition, the Centers for Disease and Prevention, Department of Defense, Food and Drug Administration/Center for the Fogarty International Center, and the Food Safety and Applied Nutrition, National Institute on Dental and Craniofacial Research, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Drug Abuse, National Institute of General Medical Sciences, and the Office of Research on Women’s Health at the NIH.
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An NIH Workshop

November 4-5, 1998  
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National Institute of Dental Research and Craniofacial Research  
National Institute of Diabetes and Digestive and Kidney Diseases  
National Institute on Drug Abuse  
National Institute of General Medical Sciences  
Office of Research on Women’s Health

Wednesday, November 4, 1998  8:00 AM-5:00 PM

8:00–8:15 AM  
Welcoming Remarks  
Bernadette M. Marriott, Ph.D.,  
Director, Office of Dietary Supplements

Opening Remarks - William R. Harlan, M.D.,  
Associate Director of Disease Prevention, NIH

Introduction of Chairs  
Rebecca B. Costello, Ph.D., Office of Dietary Supplements  
Co-Chairs:  
D. Michael Hambidge, M.D., University of Colorado, Denver, CO  
Robert J. Cousins, Ph.D., University of Florida, Gainesville, FL
**SESSION I**  
**Zinc Nutrition**  
Chair: Nancy F. Krebs, M.D.  
*University of Colorado, Denver, CO*

8:15–8:45 AM  
**Human Zinc Nutrition**  
D. Michael Hambidge, M.D.  
*University of Colorado, Denver, CO*

8:45–9:05 AM  
**Assessing Marginal Zinc Deficiency: Where Are We Now and Where Are We Going in the Future?**  
Richard Wood, Ph.D.  
*Tufts University, Boston, MA*

9:05–9:25 AM  
**Kinetics of Zinc Metabolism**  
Meryl Wastney, Ph.D.  
*Georgetown University, Washington, DC*

9:25–9:45 AM  
**Physiological Adjustments in Zinc Homeostasis With Changes in Need.**  
Janet C. King, Ph.D.  
*USDA, Agricultural Research Service, Western Human Nutrition Research Center, San Francisco, CA*

9:45–9:55 AM  
**Update: Zinc and Age-Related Eye Disease Study – Phase II**  
Rick Ferris, M.D.  
*National Eye Institute, N.I.H., Bethesda, MD*

9:55–10:15 AM  
Chair Summary, Panel Discussion and Questions

10:15–10:30 AM  
BREAKE

**SESSION II**  
**Zinc in the GI Tract**  
Chair: Bo Lonnerdal, Ph.D.  
*University of California–Davis, CA*

10:30–10:50 AM  
**Overview of Zinc Absorption and Excretion in the GI Tract**  
Nancy F. Krebs, M.D.  
*University of Colorado, Denver, CO*

10:50–11:10 AM  
**Dietary Factors Influencing Absorption of Zinc**  
Bo Lonnerdal, Ph.D.  
*University of California – Davis, CA*
11:10–11:30 PM  Integrative Aspects of Zinc Transporter Family  
Robert J. Cousins, Ph.D.  
*University of Florida, Gainesville, FL*

11:30–1:50 AM  Zinc Deficiency, Malnutrition and the GI Tract  
Raul Wapnir, Ph.D., M.P.H.  
*North Shore University Hospital, Manhasset, NY*

11:50–12:10 PM  Regulation of Intestinal Gene Expression by Dietary Zinc: Induction of Uroguanylin mRNA by Zinc Deficiency  
Ray Blanchard, Ph.D.  
*University of Florida, Gainesville, FL*

12:10–12:30 PM  Chair: Summary, Panel Discussion and Questions

12:30–1:30 PM  LUNCH

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**SESSION III**  Immune System, Antioxidant and Defense Functions of Zinc  
Chair: Pamela Fraker, Ph.D.  
*Michigan State University, East Lansing, MI*

1:30–1:50 PM  Zinc in the Immune System  
Pamela Fraker, Ph.D.  
*Michigan State University, East Lansing, MI*

1:50–2:10 PM  Zinc-Altered Immune Function and Cytokine Production  
Lothar Rink, M.D., Ph.D.  
*Institute of Immunology and Transfusion Medicine, Lubeck, Germany*

2:10–2:30 PM  Zinc in the Gastrointestinal Immune System: A Neomatode-Infected Mouse Model  
Marilyn E. Scott, Ph.D.  
*McGill University, Quebec, Canada*

2:30–2:50 PM  The Antioxidant Potential of Zinc  
Saul Powell, Ph.D.  
*Winthrop University Hospital, Mincola, NY*

2:50–3:05 PM  BREAK

3:05–3:25 PM  Zinc Metallothionein: A Link Between Cellular Zinc and Redox State
Wolfgang Maret, M.D.
*Harvard University, Boston, MA*

3:25–3:45 PM  Cellular Zinc Fluxes and the Regulation of Apoptosis/
Gene-directed Cell Death  
Peter D. Zalewski, Ph.D.
*University of Adelaide, Woodville, South Australia*

3:45–4:05 PM  Interaction of Metallothionein and Nitric Oxide  
Bruce R. Pitt, Ph.D.
*University of Pittsburgh School of Medicine, Pittsburgh, PA*

4:05–5:00 PM  Chair: Summary, Panel Discussion and Questions

**ADJOURN**
DAY 2
Thursday, November 5, 1998 8:00AM-5:00 PM

SESSION IV  Zinc and Cellular Mechanisms
Chair: Thomas V. O’Halloran, Ph.D.
Northwestern University, Evanston, IL

8:00–8:20 AM Cellular Chemistry of Zinc
Thomas V. O’Halloran, Ph.D.
Northwestern University, Evanston, IL

8:20–8:40 AM Primary and Secondary Zinc Deficiency on Factors Contributing to Abnormal Embryonic and Fetal Development
Carl L. Keen, Ph.D.
University of California–Davis, CA

8:40–9:00 AM Role of Zinc in Plasma and Membrane Function
Boyd L. O’Dell, Ph.D.
University of Missouri, Columbia, MO

9:00–9:20 AM Function and Mechanism of Zinc Metalloenzymes
Carol Fierke, Ph.D.
Duke University, Durham, NC

9:20–9:40 AM Zinc Finger Proteins
Jeremy Berg, Ph.D.
Johns Hopkins University, Baltimore, MD

9:40–10:00 AM Chair Summary, Panel Discussion and Questions

10:00–10:15 AM BREAK

SESSION V  Zinc and the Central Nervous System
Chair: Christopher J. Frederickson, Ph.D.
MicroFab Technologies, Inc., Plano, TX

10:15–10:35 AM Importance of Zinc in the CNS
Christopher J. Frederickson, Ph.D.
MicroFab Technologies, Inc., Plano, TX
10:35–10:55 AM  Zinc Transport and Synaptic Signaling
Robert Colvin, Ph.D.
*Ohio University, Athens, OH*

10:55–11:15 AM  Zinc and Altered Cognitive Function
Christine L. Tully, M.D.
*Dorn Veteran’s Medical Center, Columbia, SC*

11:15–11:35 AM  Alzheimer’s Disease, Amyloid Protein and Zinc
Ashley I. Bush, M.D., Ph.D.
*Massachusetts General Hospital, Charlestown, MA*

11:35–11:55 AM  Neurobiology of Zinc Influenced Eating Behavior
Neil Shay, Ph.D.
*University of Illinois, Urbana, IL*

11:55–12:15 PM  Chair Summary, Panel Discussion and Questions

12:15–1:00 PM  LUNCH

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<td><strong>Zinc in Growth and Specific Disease Entities</strong></td>
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<td>Chair: Craig McClain, M.D.</td>
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<td>University of Kentucky, Lexington, KY</td>
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1:00–1:20 PM  Clinical Consequences of Altered Immune Function During Zinc Deficiency
Sunil Sazawal, Ph.D.
*Johns Hopkins School of Hygiene and Public Health, Baltimore, MD*

1:20–1:40 PM  Zinc Supplementation and Children’s Growth: A Meta-Analysis of Intervention Trials
Kenneth Brown, M.D.
*University of California–Davis, CA*

1:40–2:00 PM  The Role of Zinc in Growth and Cell Proliferation
Ruth S. MacDonald, Ph.D.
*University of Missouri, Columbia, MO*

2:00–2:20 PM  Diabetes and Oxidative Disease
Robert DiSilvestro, Ph.D.  
_Ohio State University, Columbus, OH_

2:20–2:35 PM  
BREAK

2:35–2:55 PM  
**Zinc and HIV Disease**  
Marianna Baum, Ph.D.  
_University of Miami, Miami, FL_

2:55–3:15 PM  
**Therapeutic Applications of Zinc in HIV**  
Eugenio Mocchegiani, Ph.D.  
_Italian National Research Centres on Aging, Ancona, Italy_

3:15–3:35 PM  
**Zinc and the Common Cold**  
Jeffrey L. Jackson, M.D.  
_Uniformed Services University of Health Sciences, Bethesda, MD_

3:35–3:55 PM  
**Chair Summary, Panel Discussion and Questions**

3:55–4:55 PM  
**Summary, Opportunities, Challenges, and Future Directions**  
Chairpersons: Robert J. Cousins, Ph.D.-University of Florida  
D. Michael Hambidge, M.D.-University of Colorado

Each of the six session chairs will summarize the results from their respective sessions and discuss recommendations for future research development.
SPEAKERS

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