

## ZINC AND HEALTH: Current Status and Future Directions

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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:

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American Society for Clinical Nutrition  
Centers for Disease Control and Prevention  
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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 5:00p.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.

**ZINC AND HEALTH: Current Status and Future Directions  
An NIH Workshop**

**November 4-5, 1998  
Lister Hill Auditorium  
National Institutes of Health  
Bethesda, Maryland, USA**

**Sponsored by the Office of Dietary Supplements, NIH  
Co-Sponsors:**

**American Dietetic Association  
American Society for Clinical Nutrition  
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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**

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## **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

BREAK

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## **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 Neomate-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**

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### **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 PM     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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**SESSION VI**                     **Zinc in Growth and Specific Disease Entities**  
**Chair: Craig McClain, M.D.**  
**University of Kentucky, Lexington, KY**

- 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

Marianna K. Baum, Ph.D.  
University of Miami, School of Medicine  
Miami, FL

Jeremy M. Berg, Ph.D.  
Johns Hopkins University School of Medicine  
Baltimore, MD 21205-2105

Raymond K. Blanchard, Ph.D.  
University of Florida  
Gainesville, FL

Kenneth H. Brown, M.D.  
University of California, Davis  
Davis, CA

Ashley I. Bush, M.D., Ph.D.  
Harvard Medical School  
Charlestown, MA

Robert Colvin, Ph.D.  
Ohio University  
Athens, OH

Robert J. Cousins, Ph.D.  
University of Florida  
Gainesville, FL

Robert DiSilvestro, Ph.D.  
Associate Professor  
The Ohio State University  
Columbus, OH

Carol Fierke, Ph.D.  
Duke University  
Durham, NC

Pamela J. Fraker, Ph.D.  
Michigan State University  
East Lansing, MI

Christopher J. Frederickson, Ph.D.  
MicroFab Technologies, Inc.  
Plano, TX

D. Michael Hambidge, M.D.  
University of Colorado  
Denver, CO

Jeffrey L. Jackson, M.D.  
USUHS  
Bethesda, MD

Carl L. Keen, Ph.D.  
University of California, Davis  
Davis, CA

Janet C. King, Ph.D.  
Director  
USDA, ARS, WHNRC  
Presidio San Francisco, CA

Nancy F. Krebs, M.D.  
University of Colorado  
Denver, CO

Bo Lonnerdal, Ph.D.  
University of California, Davis  
Davis, CA

Ruth S. MacDonald, Ph.D.  
University of Missouri  
Columbia, MO

Wolfgang Maret, Ph.D.  
Harvard University  
Boston, MA

Craig McClain, M.D.  
University of Kentucky  
Lexington, KY

Eugenio Mocchegiani, Ph.D.  
Immunology Center INRCA  
Ancoha, Italy

Boyd L. O'Dell, Ph.D.  
University of Missouri  
Columbia, MO

Thomas V. O'Halloran, Ph.D.  
Northwestern University  
Evanston, IL

Dr. Bruce R. Pitt, Ph.D.  
University of Pittsburgh School of Medicine  
Pittsburgh, PA

Saul Powell, Ph.D.  
Winthrop University Hospital  
Mincola, NY

Lothar Rink, Ph.D.  
University of Lubeck School of Medicine  
Lubeck, Germany

Sunil Sazawal, Ph.D.  
Johns Hopkins School of Hygiene and Public  
Health  
Baltimore, MD

Marilyn E. Scott, Ph.D.  
McGill University  
Sainte-Anne de Bellevue, Quebec, Canada

Neil Shay, Ph.D.  
University of Illinois at Urbana Champaign  
Urbana, IL

Christine L. Tully, M.D.  
Dorn VA Medical Center  
Columbia, SC

Raul A. Wapnir, Ph.D., M.P.N.  
North Shore University Hospital  
Manhasset, NY

Meryl Wastney, Ph.D.  
Georgetown University Medical Center  
Washington, DC

Richard Wood, Ph.D.  
USDA Human Nutrition Research Center  
on Aging  
Boston, MA

Peter Zalewski, Ph.D.  
University of Adelaide  
The Queen Elizabeth Hospital  
Woodville, South Australia

Carl L. Keen, Ph.D.  
University of California, Davis  
Davis, CA

Janet C. King, Ph.D.  
USDA, ARS, WHNRC  
Presidio San Francisco, CA

Nancy F. Krebs, M.D.  
University of Colorado  
Denver, CO

## PLANNING COMMITTEE

Carolyn K. Clifford, Ph.D.  
National Cancer Institute Program  
Rockville, MD

Jerry Cott, Ph.D.  
National Institute of Mental Health  
Rockville, MD

Robert J. Cousins, Ph.D.  
University of Florida-Gainesville  
Gainesville, FL

Robert W. Eisinger, Ph.D.  
Office of AIDS Research  
Office of the Director  
Bethesda, MD

Robert Eiss, Ph.D.  
FIC, Fogarty International Center  
Bethesda, MD 20892

Nancy D. Ernst  
National Heart, Lung & Blood  
Bethesda, MD

Pamela J. Fraker, Ph.D.  
Michigan State University  
East Lansing, MI

Stephen C. Groft, Pharm.D.  
Office of the Director  
National Institutes of Health  
Bethesda, MD 20892-9120

Dr. Joan A. McGowan, Ph.D.  
National Institute of Arthritis and  
Skin Disease  
Bethesda, MD

Kenneth A. Gruber, Ph.D.  
National Institute on Deafness & Other

Communication Disorders  
Rockville, MD  
Carole Hudgings, Ph.D.  
National Institute of Nursing  
Bethesda, MD

Richard D. Irwin, Ph.D.  
National Institute of Environmental Health  
Bethesda, MD

Carl L. Keen, Ph.D.  
University of California  
Davis, CA

Jag H. Khalsa, Ph.D.  
National Institute on Drug Abuse  
Rockville, MD 20857

Lori Klein  
National Library of Medicine  
Bethesda, MD

Nancy F. Krebs, MD  
University of Colorado  
Denver, CO

Donna Krasnewich, M.D., Ph.D.  
National Human Genome Research Institute  
Bethesda, MD

Dr. Dennis Leszczynski  
Office of International Science  
Center for Scientific Review (CSR)  
Rockville, MD 20892

Bo Lonnerdal  
University of California  
Davis, CA

Kenneth May, Ph.D.  
National Institute of Diabetes & Digestive  
& Kidney Disease  
Bethesda, MD

Jean Pennington, Ph.D., R.D.  
NIDDK  
Bethesda, MD 20892-6600

Peter D. Preusch, Ph.D.  
National Institute of General Medical  
Bethesda, MD

Pamela Starke-Reed, Ph.D.  
National Institute of Aging, Biology  
of Aging  
Bethesda, MD  
Lois A. Salzman, Ph.D.  
NIDR  
Bethesda, MD

Charles R. Sherman, Ph.D.  
Office of the Director  
Bethesda, MD

Martina Vogel-Taylor, M.T.  
Office of Disease Musculoskeletal  
Bethesda, MD