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Toxicology Excellence for Risk Assessment

Thursday, March 20
1:00 PM – 4:30 PM

Friday, March 21
9:00 AM – 3:30 PM

Seattle Sheraton Hotel
1400 6th Avenue
Seattle, Washington 98101

For additional information please contact Dr. Gay Goodman by email at ggoodman@kleinfelder.com or by phone at 206-284-4820.

US EPA is contributing a portion of the travel funds for speakers.

SYMPOSIUM

PERCHLORATE EXPOSURES, IODINE MODULATION OF EFFECT, AND EPIDEMIOLOGIC ASSOCIATIONS: IMPLICATIONS FOR RISK ASSESSMENT

An Ancillary Program of the Annual Meeting of the Society of Toxicology

Dedicated in fond memory of Professor Monte Greer

OVERVIEW

Speakers will present new data, new analyses, and other recent work from observational and experimental studies in humans on the relationship between perchlorate exposures and thyroid function. One speaker will review recent findings on natural perchlorate in the hydrologic cycle. The physiological relevance of natural perchlorate will be discussed. The role of iodine nutrition in raising the threshold for perchlorate effects will be addressed. Evidence for and against the attribution of causality to a given epidemiologic association will be examined. Substantial time is allotted for audience-interactive discussion. The program will close with a consensus-building session.

Program Committee: Gay Goodman (chair), Michael L. Dourson, and Robert A. Howd.

Speakers: Yona Amitai, Benjamin C. Blount, Lewis E. Braverman, John P. Gibbs, Gay Goodman, Robert A. Howd, Steven H. Lamm, Elizabeth N. Pearce, and David A. Stonestrom.

Discussant: Gregory A. Brent

Prof. Amitai is the lead investigator of ongoing epidemiologic studies of thyroid function and neurodevelopment in infants and young children within three Israeli suburbs that differed with respect to the concentration of perchlorate in the drinking water [Amitai et al. 2007. Gestational exposure to high perchlorate concentrations in drinking water and neonatal thyroxine levels. Thyroid 17: 843-850]. Dr. Amitai will present published and unpublished results from the Israeli study.

Dr. Blount has applied sophisticated analytical methods to the measurement of background perchlorate exposure in the US population. He was the principal author of an epidemiologic study which reported associations between background urinary perchlorate and serum thyroxine in a national survey of US women, with stronger associations found for the subset with urinary iodine < 100 µg/L [Blount et al. 2006. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ. Health Perspect. 114: 1865-1871].

Prof. Braverman is distinguished by his record of clinical and observational research in thyroidology, including studies addressing the thyroid outcomes of altered iodine status. He has acted as principal or co-investigator for a number of studies addressing perchlorate health effects in humans. Recently he reviewed clinical and occupational perchlorate studies [Braverman 2007. Clinical studies of exposure to perchlorate in the United States. Thyroid 17: 819-822].

Prof. Brent, a clinical thyroidologist whose research interests include regulation of sodium-iodide symporter gene expression, was a member of the 2003-2005 NAS/NRC Committee to Assess the Health Implications of Perchlorate Ingestion. Prof. Brent will participate via Web link.

Dr. Gibbs was the lead investigator of the first occupational health study of thyroid function in ammonium perchlorate workers. Subsequently he organized a series of population studies to evaluate thyroid function in neonates and schoolchildren from three Chilean cities that differed with respect to the concentration of perchlorate in the drinking water [Téllez Téllez et al. 2005. Long-term environmental exposure to perchlorate through drinking water and thyroid function during pregnancy and the neonatal period. Thyroid 15: 963-975]. Dr. Gibbs will present unpublished urinary iodine data from the Chilean study and an analysis of these data.

Dr. Goodman has been contributing to knowledge of perchlorate toxicology and health risks since 1998. She was the co-investigator (with Prof. Monte Greer as the principal investigator) of the Greer study, a clinical exposure study that is the cornerstone of current US EPA and Cal/EPA regulatory policy [Greer et al. 2002. Health effects assessment for environmental perchlorate contamination: The dose response for inhibition of thyroidal radioiodine uptake in humans. Environ. Health Perspect. 110: 927-937]. Dr. Goodman will present unpublished urinary iodine data from the Greer study and an analysis of individual perchlorate sensitivity as a function of iodine status.

Dr. Howd played a key role in the development of the California Public Health Goal (PHG) for perchlorate, supervising the work of Dr. David Ting. Recently, Dr. Howd co-authored an analysis of perchlorate/thyroid hormone associations in the NHANES data set examined by Blount et al. (2006), in which other inhibitors of iodide uptake were included as covariates [Steinmaus et al. 2007. Impact of smoking and thiocyanate on perchlorate and thyroid hormone associations in the 2001-2002 National Health and Nutrition Examination Survey. Environ. Health Perspect. 115: 1333-1338].

Dr. Lamm has published widely on thyroid function in perchlorate-exposed populations. He was the lead author of one of the two occupational health studies in ammonium perchlorate workers and has collaborated with Prof. Braverman on clinical studies of perchlorate exposure in volunteers. Recently, Dr. Lamm took the lead in analyzing possible perchlorate/thyroid hormone associations in the NHANES dataset examined by Blount et al. (2006) [Lamm et al. 2007. Perchlorate, thyroxine, and low urine iodine association not seen with low creatinine-adjusted urine iodine among women of childbearing age. Thyroid 17(s1): S-51 (doi:10.1089/thy.2007.1519, Program Number 22)].

Prof. Pearce has contributed much of what is known about breast milk perchlorate levels and their possible relationship to iodine status in US women. She was the lead author of a recent epidemiologic investigation of thyroid function in perchlorate-exposed pregnant women of varying iodine status resident in three European cities [Pearce et al. 2007. Thyroid function is not affected by environmental perchlorate exposure in first trimester pregnant women. Thyroid 17(s1): S-133 (doi:10.1089/thy.2007.1519, Program Number 275)].

Dr. Stonestrom, an acknowledged expert in unsaturated-zone (vadose-zone) hydrology, conducts collaborative research on naturally occurring perchlorate, nitrate, and other salts in arid and semi-arid regions [Rao et al. 2007. Widespread natural perchlorate in unsaturated zones of the southwest United States. Environ. Sci. Technol. 41: 4522-4528 (10.1021/es062853i S0013-936X(06)02853-7)].

PARTICIPANT AFFILIATIONS

Yona Amitai, MD, MPH – Director, Department of Mother, Child & Adolescent Health, Ministry of Health, Jerusalem; Associate Professor of Pediatrics, Hebrew University-Hadassah, Jerusalem, Israel.

Benjamin C. Blount, PhD – Research Chemist, Centers for Disease Control and Prevention, Atlanta, GA.

Lewis E. Braverman, MD – Professor of Medicine, Section of Endocrinology, Diabetes, and Nutrition, Boston University School of Medicine and Medical Center, Boston, MA.

Gregory A. Brent, MD – Chief, Endocrinology and Diabetes Section, VA Greater Los Angeles Healthcare System; Professor of Medicine and Physiology, David Geffen School of Medicine, UCLA, Los Angeles, CA.

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Elizabeth N. Pearce, MD – Asst. Professor of Medicine, Section of Endocrinology, Diabetes, and Nutrition, Boston University School of Medicine, Boston, MA.

David A. Stonestrom, PhD – Research Hydrologist, U.S. Geological Survey, Menlo Park, CA.

PROGRAM

Thursday, March 20, 1:00 PM – 4:30 PM

Iodine Modulation of Thyroid Function: Influence of Perchlorate and Other Structurally Related Anions

Chair: Robert Howd

1:00-1:25 Benjamin Blount: Background urinary perchlorate and statistical analysis of its association with serum levels of TSH and T4 in men and women sampled in the National Health and Nutrition Examination Survey (NHANES): The influence of gender and iodine status.

1:25-1:50 Steven Lamm: Statistical analysis of association between urinary perchlorate and serum levels of TSH and T4 in women sampled in the National Health and Nutrition Examination Survey (NHANES): The importance of creatinine adjustment when using spot urines to establish iodine status.

1:50-2:15 Robert Howd: Statistical analysis of association between urinary perchlorate and serum levels of TSH and T4 in women sampled in the National Health and Nutrition Examination Survey (NHANES): Consideration of iodine status, smoking, and thiocyanate.

2:15-2:45 Break.

2:45-3:10 Lewis Braverman: Thyroid function in long-term clinical and occupational exposures to perchlorate: Iodine homeostasis at work.

3:10-3:35 Gay Goodman: New data from the Greer study: The influence of iodine status and gender on the dose-response for perchlorate inhibition of thyroidal iodide uptake in human volunteers.

3:35-4:30 Q&A and audience-interactive discussion.

PROGRAM, *continued*

Friday, March 21, 9:00 AM – 11:15 AM

Fetal and Early-Life Perchlorate Exposures and Outcomes

Chair: Michael Dourson

9:00-9:15 Elizabeth Pearce: Breast milk perchlorate and iodine in a cohort of lactating Boston-area women: Lack of statistical evidence for an effect of perchlorate on breast milk iodine or colostrum iodine.

9:15-9:45 Yona Amitai: Serum T4 levels and neurodevelopmental test scores in Israeli infants from neighborhoods with markedly different perchlorate concentrations in drinking water: Lack of statistical evidence for an effect of drinking-water perchlorate on thyroid function or neurodevelopment.

9:45-10:15 John Gibbs: Statistical analysis of association between urinary perchlorate and serum levels of TSH and T4 in mothers and newborns from three Chilean cities with markedly different perchlorate concentrations in drinking water: Does categorization by iodine status affect outcome?

10:15-10:30 Elizabeth Pearce: Statistical analysis of association between urinary perchlorate and serum levels of TSH and free T4 during the first trimester of pregnancy in women from Wales, Italy, Argentina, and California: Lack of evidence for a perchlorate effect, irrespective of iodine status.

10:30-10:45 Q&A.

10:45-11:15 Break.

PROGRAM, *continued*

Friday, March 21, 11:15 AM – 3:30 PM

Natural Perchlorate Sources, New Studies, and Other New Information: Implications for Risk Assessment

Chair: Gay Goodman

11:15-11:45 David Stonestrom: Natural perchlorate in the hydrologic cycle: Review of recent findings.

11:45-12:15 Speakers and session chairs: Moderated discussion of the question: "What can we deduce about the physiological relevance of historical exposures to natural perchlorate?"

12:15-12:30 Gregory Brent (via Web link). Comments on the information presented. Discussion of the question: "Does the new information call for reexamination of the no-effect level and/or uncertainty factor recommended by the NAS/NRC committee?"

12:30-1:45 Catered lunch followed by Q&A and audience-interactive discussion.

1:45-2:00 Break.

2:00-2:30 Speakers and session chairs: Moderated discussion of the question: "What is the role of iodine nutrition in determining perchlorate health risks?"

2:30-3:30 Consensus-building session with audience participation. Moderated discussion of the question: "What does the new information imply for the assessment of perchlorate health risks?"

3:30 Adjourn.