

**SUNDAY EARLY AFTERNOON** OCT. 17, 1999 1:00 – 2:20 PM**SESSION I. Opening, Welcome & Overview**Co-Chairs: **Joan Cranmer, PhD and William Slikker, Jr., PhD**

- 1:00 PM** **Opening the Conference**  
Joan Cranmer, PhD  
Conference Chair, University of Arkansas for Medical Sciences
- 1:05** **Welcome - On Behalf of the Host Institutions**  
Betty Lowe, MD ~ Associate Dean for Children's Affairs  
University of Arkansas for Medical Sciences  
Senior Vice President / Medical Director, Arkansas Children's Hospital  
President, American Academy of Pediatrics (1993 – 94)
- 1:10** **Theme, Rationale and Overview of the Conference:  
Children's Health - from Molecule to Community  
and Back Again**  
Joan M. Cranmer, PhD

**SESSION II. Tutorials**Chair: **William Slikker, Jr., PhD**

The objective of this session is to provide scientific background for the more detailed sessions to follow. Tutorials will delineate basic principles of neuroanatomy and neurobiology of the developing organism. An overview of the principles of developmental neurotoxicology will build on this established anatomical/biological scientific base. These basic principles will be translated into specific susceptibilities in children. The tutorials will provide a unifying framework and rationale for the entire conference.

- 1:20** **Principles of Developmental Neuroanatomy and Neurobiology**  
Stanley Barone, PhD ~ US Environmental Protection Agency
- 1:40** **Principles of Developmental Neurotoxicology**  
William Slikker, Jr., PhD ~ National Center for Toxicological Research
- 2:00** **Specific Unique Susceptibilities of the Fetus, Infant, Child  
and Adolescent**  
Cynthia Bearer, MD, PhD ~ Case Western Reserve University

Note: In-depth reprints or books of the above tutorials are available in the Exhibit area.

**2:20** **Break and Set-up for Session III****SUNDAY LATE AFTERNOON** OCT. 17, 1999 2:25 – 6:15PM**SESSION III. Developmental Neurotoxicity of Lead: Model Example of an Interdisciplinary Approach**Co-Chairs: **Deborah Cory-Slechta, PhD & Herbert Needleman, MD**

This session is devoted to understanding the behavioral consequences of developmental lead exposure, the advances in understanding neurochemical and biochemical mechanisms of specified behavioral deficits and the long-term adverse consequences of such exposures. Issues such as the period of developmental exposure, reversibility, biphasic effects, and future research directions will be addressed.

- 2:25** **Introduction and Overview**  
Session Co-Chairs
- 2:30** **Molecular Neurochemical Mechanisms of Pb Exposure**  
Jan Suszkiw, PhD ~ University of Cincinnati
- 3:00** **Molecular Mechanisms of Pb and Synaptic Vesicle Proteins**  
Johnathan Pevsner, PhD ~ Kennedy Krieger Research Institute
- 3:30** **Refreshment Break**
- 3:45** **Glutamatergic Mediation of Plasticity**  
Steven Lasley, PhD ~ University of Illinois
- 4:15** **Dopaminergic and Glutamatergic Basis of Lead-Induced Cognitive Deficits**  
Deborah Cory-Slechta, PhD ~ University of Rochester Medical School

- 4:45** **Developmental Lead Exposure and Prefrontal Function in Children**  
Bruce Lanphear, MD, MPH ~ University of Cincinnati  
Richard Canfield, PhD ~ Cornell University
- 5:15** **Developmental Neurotoxicity and its Long-Term Ramifications**  
Herbert Needleman, MD ~ University of Pittsburgh
- 5:45** **Open Discussion and Itemization of Research Needs**  
Discussion Leaders: Co-Chairs
- 6:15** **Adjourn for Reception and Buffet Dinner**

**6:30 – 9:00 PM**  
**Welcoming Reception  
and Buffet Dinner**

**MONDAY MORNING** OCT. 17, 1999 8:15 AM – 12 NOON**7:45 – 8:15 Continental Breakfast****SESSION IV. Mechanisms of Developmental Neurotoxicology: Molecular and Cellular Targets**Co-Chairs: **Lucio Costa, PhD and Michael Aschner, PhD**

In this session we will examine selective mechanisms underlying neuronal and glial injury. Attention will be given to identifying specific models of injury in which fundamental biochemical and cellular mechanisms have been described. Mechanisms of neural patterning, neurotransmitter development, the role of apoptosis, effects of xenobiotics on second messenger signaling pathways and the involvement of oxidative stress in CNS injury will be examined. Where appropriate, inference will be made to the effects of various neurotoxicants (e.g., metals, pesticides, therapeutics, endocrine disruptors) on developmental processes, and their sequelae. We also will examine two cellular processes which are central to development, specifically, cellular adhesion and reorganization of the cytoskeleton. Both processes undergo critical modifications during development. Speakers will address how disturbances of these processes can result in structural and functional abnormalities of the nervous system.

- 8:15** **Introduction and Overview**  
Session Co-Chairs
- 8:20** **LTP, CaM Kinase, Cellular Mechanisms of Learning**  
Tomás Guilarte, PhD ~ Johns Hopkins University
- 8:45** **The Zinc Finger Domain of Proteins is Targeted by Heavy Metals**  
Nasser H. Zawia, PhD ~ Meharry College
- 9:10** **Second Messenger Systems**  
Lucio Costa, PhD ~ University of Washington
- 9:35** **Oxidative Stress, Excitotoxicity and Neurodegeneration**  
Mark Mattsson, PhD ~ University of Kentucky
- 10:00** **Refreshment Break**
- 10:15** **Neuron Interaction: Molecular Targeting by Developmental Neurotoxins**  
Michael Aschner, PhD ~ Wake Forest University School of Medicine
- 10:40** **Neural Cell Adhesion Molecules: Targets for Developmental Neurotoxicants**  
Cynthia Bearer, PhD ~ Case Western Reserve University
- 11:05** **Cyclic Nucleotides, Calmodulin, Calmodulin-Regulated Proteins, Cell Signaling, Cell Death**  
To be Invited
- 11:35** **Open Discussion and Itemization of Research Needs**  
Session Chairs
- 12:00 PM** **Adjourn for Lunch (on Your Own)**

**SESSION V: A Comparison of the Neurobehavioral Domains Affected by Methylmercury or PCBs: Can it Help us Interpret Studies with Exposure to Both?**

Co-Chairs: **Deborah C. Rice, PhD and Christopher DeRosa, PhD**

*This session will focus on comparing and contrasting the neurological and behavioral consequences of developmental exposure to PCBs and methylmercury (MeHg). Epidemiological studies in which developmental exposure was to MeHg, PCB's or a combination will be discussed and underlying behavioral/neurological processes identified. The relevant epidemiological studies can be conceived as a continuum of exposure, with exposure to only MeHg at one end and exposure to PCB and similarly-acting organochlorines on the other end. In between are studies in which exposure was to both agents to varying degrees. In addition, there is an extensive experimental animal literature on the behavioral effects of both agents. This wealth of information allows us to attempt to decipher which effects observed in some of the epidemiological studies may be the consequence of MeHg exposure, PCB exposure, or their interaction.*

- 1:15 **Introduction and Overview**  
Deborah Rice, PhD ~ US Environ Protection Agency
- 1:20 **Correspondence between Experimental and Epidemiological Endpoints of Neurotoxicity**  
Christopher DeRosa, PhD ~ Agency for Toxic Substances and Disease
- 1:50 **Experimental Effects of Methylmercury and PCB's: What do They Tell us About Expected Effects in Humans?**  
Christopher Newland, PhD ~ Auburn University
- 2:20 **Methylmercury Effects: Minamata/Iraq/Seychelles**  
Kathryn Mahaffey, PhD ~ US Environmental Protection Agency
- 2:50 **Refreshment Break**
- 3:05 **Methylmercury/PCB's: Faroe Islands/Brazil**  
Deborah Rice, PhD ~ US Environ Protection Agency
- 3:35 **PCBs/Methylmercury: The Oswego Study**  
Paul Stewart, PhD ~ SUNY Oswego
- 4:05 **PCB Effects: The Dutch Study**  
Svanti Patandin, MD, PhD ~ Rotterdam, The Netherlands (invited)
- 4:35 **Open Discussion and Itemization of Research Needs**  
Discussion Leaders: Co-Chairs
- 5:00 **Break and set-up for Presentation and Panel Discussion**

**SESSION VI. Special Presentation**

Chair: **Bob Sonawane, PhD**

Presentation

**“Overview of Newest Federal Child-Health Initiatives”**

**William Farland, PhD**

Director, National Center for Environmental Assessment  
Office of Research and Development  
US Environmental Protection Agency

**Newest Federal and Foundation Child Health Initiatives: Goals, Research Needs and Funding Opportunities.**

**Personal Interaction:** Representatives of many of the Sponsoring Organizations and others will attend the Social Evenings and Poster/Workshop sessions and be available to talk with Participants. **Materials:** Agencies, Foundations and other NGOs will have representatives and background materials available in the exhibit area during the Poster Session.

5:45 **Adjourn for Conference Country Cookout on the Riverfront**

**SESSION VII. Developmental Neurotoxicology in Children: Framing the Problem**

Co-Chairs: **Lynn Goldman, MD, MPH & Cynthia Bearer, MD, PhD**

*Child environmental health experts will present a comprehensive picture of the public health significance of developmental disabilities for children and their future success, epidemiology of developmental disability and evidence for impacts of developmental neurotoxicants on children, the state of the art of measurement of exposure, biomarkers, and endpoints, risk assessment, policy, prevention and intervention. This session should set the stage for discussions between toxicologists and epidemiologists about how to move forward to develop the research and tools that are needed to better address the problem of identifying developmental disabilities in children as a result of exposure to environmental agents.*

- 8:30 **Framing the Problem**  
Lynn Goldman, MD, MPH ~ Johns Hopkins University
- 8:55 **Children's Exposure**  
Richard Jackson, MD, MPH ~ National Center for Environmental Health / Centers for Disease Control
- 9:20 **Mechanisms Underlying Children's Susceptibility to Environmental Toxicants: Relevant Principles for Developmental Toxicology and Risk Assessment**  
Elaine Faustman, PhD, DABT ~ University of Washington
- 9:45 **Biomarkers of Exposure and Effect in Children**  
Cynthia Bearer, MD, PhD ~ Case Western Reserve University
- 10:05 **Use of Biomarkers (Caffeine Breath Test and Others) to Predict PCB/PCDF and Dioxin Neurotoxicity**  
George Lambert, MD ~ University of Medicine and Dentistry of NJ
- 10:25 **Refreshment Break**
- 10:40 **Fundamentals of Exposure Assessment in Humans: Cumulative & Aggregate Databases & Toxicokinetic Models (Demo in Workshop Session)**  
Christine Chaisson, PhD ~ Chaisson Inc
- 11:00 **Diagnosis, Prevention and Intervention of Developmental Neurotoxicology in Children (Demo in Workshop Session)**  
Rob Amler, MD, MS ~ Agency for Toxic Substances and Disease or TBA
- 11:20 **Measurement: Pediatric Cognitive / Neurobehavioral Test Batteries (Demo in Workshop Session)**  
Merle Paule, PhD ~ National Center for Toxicological Research
- 11:45 **Discussion, Closing Remarks, Goals for Afternoon Session**  
Cynthia Bearer, MD, PhD ~ Case Western Reserve University

**SESSION VII. Developmental Neurotoxicology in Children: Framing the Research Agenda**

Co-Chairs: **Bernard Weiss, PhD and George Lambert, MD**

- 1:30 **Framing the Research Agenda**  
Bernard Weiss, PhD
- 1:40 **Rates and Impact of Developmental Disabilities in the US**  
Colleen Boyle, PhD ~ Centers for Disease Control and Prevention
- 2:00 **Correlation between Exposures and Effects Risk Assessment and Policy Implications**  
Phil Landrigan, MD, MSc ~ Mt Sinai School of Medicine
- 2:20 **Outcome of Recent Related Children's Research Meetings**  
Bernard Weiss, PhD ~ University of Rochester School of Medicine  
Phil Landrigan, MD, MSc ~ Mt Sinai School of Medicine
- 2:50 **Role of the Clinician: The Green Book of the American Academy of Pediatrics**  
Ruth Etzel, MD, PhD ~ Chair, Committee on Environmental Health, AAP
- 3:10 **Open Discussion and Itemization of Research Needs “Building a Research Agenda for Children's Environmental Health in the New Millennium”**  
Discussion Leader: Lynn Goldman, MD

**SESSION IX. Poster Session and Workshops**

**Poster Session**

**Co-Chairs: To Be Invited**

Presentation of papers from poster and informal discussion is a highlight of this meeting. Free communications from poster on any topic of neuroscience + toxicology are welcome. All papers presented from poster or platform are invited for publication in the Special Issue of Neurotoxicology devoted to this conference.

**4:00 - 6:00 PM**

**Posters Attended and Discussed**

Selection of Student Awardees will be made during this time. \$1000 in cash awards and plaques will be presented on Wednesday.

Poster Presenters: Please mount your poster on Sunday on the poster board with the same number as your abstract. Posters should be up by 12:00 Noon Monday. Please take posters down by 12:30 PM Wednesday.

**Workshop A:**

**Pediatric Cognitive/Neurobehavioral Test Batteries**

**Co-Chairs: Merle Paule, PhD and TBA**

4-6 batteries in current use will be set-up for "on-hands" demonstrations. A brief background presentation from the podium will proceed the demos. Detailed write-ups will be included in the Abstract Book. Summaries will be set-up in "poster fashion."

**BARS Nonverbal Test for Indigenous Peoples**

Kent Anger, PhD or TBA

**Complex Brain Function Test ("The Nickel Game")**

Merle Paule, PhD ~ NCTR & UAMS/ACH, Little Rock, AR

**Pediatric Environmental Neurobehavioral Test Battery (PENTB)**

ATSDR Contractee

**The CANTAB Neuropsychological Test Battery (Seychelles)**

Deborah Cory-Slechta, PhD and/or Becky Brockel, PhD

**Tests of Motor, Sensory-Motor and Sensory Function (Seychelles)**

Bernard Weiss, PhD and/r Randy Pittelli

**Oswego Developmental Test Battery**

Paul Stewart, PhD and/or Tom Darville, PhD

**Workshop B:**

**Models of Exposure Assessment in Humans: Cumulative and Aggregate Databases and Toxicokinetic Models**

Prenatal, Perinatal, Postnatal and Lifelong Toxicokinetic and Risk Assessment Computer Models will be set-up for hands-on demonstrations.

**Workshop C:**

**How to Conduct an FOB**

A Video Tape Presentation of How to Conduct a Functional Observational Battery (FOB) will be shown. Scientists familiar with the proper conduct of a FOB will be available to answer questions.

Virginia Moser, PhD ~ US Environmental Protection Agency

**WEDNESDAY MORNING OCT. 20, 1999 8:15 AM - 12:30 PM**

7:45 - 8:15 AM ~ Continental Breakfast

**SESSION X: Hot New Topics in Developmental Neurotoxicology: Novel and Changing Perspectives**

**Co-Chairs: William Slikker, Jr., PhD and Kevin Crofton, PhD**

Developmental neurotoxicant risk assessment approaches need to be continually updated to meet new regulatory challenges. Examples of scientifically-based decision making will be drawn from the review of new therapeutic agents as well as environmental chemicals. The balancing of benefits and risks will be examined with examples of newly approved therapeutic agents. The novel application of knowledge bases to enhance the predictive capability of risk assessment approaches for endocrine disruptors

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will also be presented. New strategies for understanding the mode of action of potential endocrine disrupters and the application of this information to identify classes of agents for further study will be discussed.

**8:15 Introduction and Overview**

Session Co-Chairs

**8:30 Developmental Neurotoxicology of Therapeutics: Survey of Novel Recent Findings**

William Slikker, Jr, PhD ~ National Center for Toxicological Research/FDA

**8:50 Developmental Neurotoxicity of Endocrine Disruptors: Focus on Estrogens**

Bern Schwetz, DVM, PhD ~ National Center for Toxicological Research/FDA

**9:10 Developmental Neurotoxicity of Endocrine Disruptors: Focus on Thyroid**

Kevin Crofton, PhD ~US Environmental Protection Agency

**9:30 Free Communications** ~ selected from submitted abstracts

**10:00 Open Discussion and Itemization of Research Needs**

Session Co-Chairs

10:15 - 10:30 AM Refreshment Break

**WEDNESDAY MORNING OCT. 20, 1999 10:30 AM - 12:30 PM**

**SESSION XI. Roundtable: Do the EPA Developmental Neurotoxicity Guidelines Detect Human Developmental Neurotoxicity?**

**Chair: Hugh Tilson, PhD**

The objective of this session is to promote discussion concerning the sensitivity and applicability of EPA's Developmental Neurotoxicity Testing Guidelines. Questions have been raised about the completeness of the battery to assess the full range of developmental effects seen in humans and the frequency with which the battery has actually been required for testing chemicals by the Agency. The content of the testing battery and the results of a retrospective study to determine the sensitivity of the battery relative to measures of neurotoxicity in adult animals, as well as measures of developmental and reproductive toxicity will be presented. Panel participants will be asked to provide their perspectives concerning the adequacy of the test battery to detect human developmental neurotoxicants. Participants will also be asked for recommendations concerning the addition or deletion of various components of the current test battery.

Presentation

**"A Retrospective Analysis of EPA's Developmental Neurotoxicity Testing Battery"**

**Sue Makris, PhD**

Office of Pesticides, Prevention and Toxic Substances  
US Environmental Protection Agency

Panel Discussants:

- Cynthia Bearer, MD, PhD ~ Case Western Reserve University
- Alan Hoberman, PhD ~ Argus/Primedica
- Carole Kimmel, PhD ~ NCEA/ORD/EPA
- Sue Makris, PhD ~ OPPT/ORD/EPA
- John O'Donoghue, PhD ~ Eastman Kodak Company
- Deborah Rice ~ NCEA/ORD/EPA
- David Wallinga, MD ~ Natural Resources Defense Council

**SESSION XII: Presentation of Student Awards**