

TWENTY-SECOND INTERNATIONAL NEUROTOXICOLOGY CONFERENCE

“Environment and Neurodevelopmental Disorders”

September 11-14, 2005 • Sheraton Imperial Hotel & Conference Center • Research Triangle Park, North Carolina, USA

NEAR-FINAL PROGRAM

Sunday Afternoon 11 Sept 2005 1:30 – 6:30 PM

1:00 PM Registration Opens

1:30 – 8:30 PM NIEHS Town Meeting & Public Forum

Featuring Open Dialogue with the Director of NIEHS & Short Talks by Experts on

- *neurodevelopmental disorders over the lifespan*
- *issues of specific concern to North Carolinians*

5:30 PM..... “Meet, Greet and Eat”

Informal discussion. Networking. Camaraderie. Visit Exhibits.

Free food and refreshments provided for NIEHS Town Meeting participants and Neurotoxicology Conference participants in a comfortable informal social setting.

Sunday 11 Sept 2005 5:30 PM... “Meet, Greet & Eat”

Free and open to the public and all Conference participants & guests

**5:30
“Meet, Greet & Eat”**

Refreshments & Buffet (Cash Bar)

Sunday Evening 11 Sept 2005 6:30 PM – 8:30 PM

I. OPENING OF THE CONFERENCE

Conference Chair: Joan M. Cramer, PhD, ATS
22nd International Neurotoxicology Conference

6:30 – 8:30 PM

Advocacy Session / Public Forum

SESSION II. NEUROTOXICANTS AND LEARNING AND DEVELOPMENTAL DISABILITIES: TRANSLATING THE SCIENCE INTO EDUCATION AND PUBLIC POLICY

Session Co-Chairs: Elise Miller, MEd
J. Peterson Myers, PhD

Theme: The conference will start with a public forum on the latest science linking neurotoxicants to learning and developmental disabilities (LDDs) and the need to educate health-affected constituencies about these issues and to foster stronger policy to protect children's environmental health.

Researchers are often reluctant to become involved in educating the general public about technical subjects or the intersections of science and public policy for fear that such activities will take them away from more important work or raise questions about their objectivity. This session will highlight why researchers can and need to play an important role in helping to translate science into stronger public policy. After an overview of the science and related policies, including examples of how the precautionary principle can be implemented in this context, panelists will describe model environmental health programs initiated by learning and developmental disabilities organizations. This public forum is open

not only to researchers and scientists, but to educators, administrators, parents of children with LDDs and anyone else who is concerned about environmental contributors to the apparent rise in LDDs.

Presentations

Overview of Emerging Science on Neurotoxicants in Relation to Learning and Developmental Disabilities

Ted Schettler, MD, MPH ~ Science and Environmental Health Network

Ted Schettler is the science director of the Science and Environmental Health Network and co-chair of the Human Health and Environment Project of Greater Boston Physicians for Social Responsibility. Dr. Schettler is co-author of *Generations at Risk: Reproductive Health and the Environment*, which examines reproductive and developmental health effects of exposure to a variety of environmental toxicants. He is also co-author of *In Harm's Way: Toxic Threats to Child Development*, which discusses the impact of environmental exposures on neurological development in children.

Autism, Genes and the Environment

Dr. Martha Herbert, MD, PhD ~ Massachusetts General Hospital, Harvard Medical School

Martha Herbert is a pediatric neurologist and brain development researcher at the Massachusetts General Hospital and Harvard Medical School, specializing in neurodevelopmental disabilities, particularly autism. Her work explores the mechanisms and significance of widespread abnormalities, such as the tendency in autism toward large brains and increased white matter volume, the relationship between systemic abnormalities (such as gastrointestinal and immune disturbances) and the biological mechanisms that may underlie abnormal structural and functional brain connectivity, and the role environmental factors may play in contributing to these problems.

Specific Policies Related to Regulating and Reducing Neurotoxicants

Lynn R. Goldman, MD, MPH ~ Johns Hopkins University

Lynn Goldman, a pediatrician and epidemiologist, is a Professor in the Department of Environmental Health Sciences at the JHU's Bloomberg School of Public Health, where her areas of focus are children's environmental health, public health practice, and chemical and pesticide regulatory policy. As Assistant Administrator for Toxic Substances at the U.S. EPA, she directed the Office of Prevention, Pesticides and Toxic Substances (OPPTS) from 1993 through 1998.

Panel Discussants

Overview of the Learning and Developmental Disabilities Initiative

Elise Miller, MEd ~ Institute for Children's Environmental Health

Elise Miller is founder and executive director of the national Institute for Children's Environmental Health (ICEH) based in the Seattle, Washington area. The primary mission of ICEH is to foster collaborative initiatives among diverse sectors to reduce and ultimately eliminate environmental exposures that can undermine children's healthy development. One of ICEH's major national programs is the Learning and Developmental Disabilities Initiative, a working group of the Collaborative on Health and the Environment.

Autism Society of America's efforts in this regard

Lee Grossman, Autism Society of America www.autism-society.org

Lee Grossman is the President & CEO of the Autism Society of America (ASA) which is the largest Autism organization in the United States. The ASA has identified environmental health and

neurotoxicology issues as among its highest priorities for solving the puzzle of Autism and in addressing the "epidemic" increase in Autism Spectrum Disorders. Mr. Grossman will discuss the efforts of the ASA in dealing with these and other issues in helping individuals with Autism throughout the lifespan and their families.

Learning Disabilities Association of America's efforts in this regard

Kathy Lawson, *Healthy Children's Project, LDA*

Kathy Lawson is coordinator of the Learning Disabilities Association of America's (LDA) Healthy Children Project (HCP). Based in Pittsburgh, she helped launch the HCP in August of 2002. HCP translates scientific knowledge about the impact of environmental toxins on fetal and child brain development into accessible information for consumers seeking to protect themselves and their families.

American Association on Mental Retardation's efforts in this regard

Michele Gagnon, *Environmental Health Initiative, AAMR*

Michele Gagnon is the Director of the Environmental Health Project with the American Association on Mental Retardation based in Washington, DC. The goals of the project are to prevent neurotoxic exposures to the fetus, infant, and child that manifest as developmental disabilities and to prevent further toxic exposure to those who have developmental disabilities.

Monday Morning 12 Sept 2005 8:30 – 11:40 AM

Symposium

SESSION III-A. PBPK/PD MODELS FOR DEVELOPMENTAL NEUROTOXICOLOGY: RISK ASSESSMENT STRATEGIES AND RESEARCH RECOMMENDATIONS

Session Chairs: William Slikker, Jr., PhD
Donald R. Mattison, MD

Theme: Over the past decade regulatory agencies in developed countries have recognized that infants, children, and adolescents handle chemicals differently than adults (indeed, adults are not pharmacologically homogeneous). While recognizing those pharmacological differences has led to increased attention to preclinical and clinical data gaps, the information needed to fill those gaps can not be simply addressed by testing chemicals in pediatric populations. The concepts of efficacy and safety must be reformulated in the context of development, and new approaches for preclinical and clinical testing (including clinical trial designs) developed and validated in immature animals and humans. These testing methods, especially for the nervous system, must be grounded on an understanding of healthy developmental trajectories as well as the impact of disease and treatment on healthy development. Clearly this constraint suggests that there is little of relevance from adult pharmacology and it is necessary to develop preclinical and clinical testing for pediatric pharmacology and developmental neurotoxicology.

8:30 – 8:45 AM

PBPK/PD Models for Developmental Neurotoxicology: Introduction and Overview of Session

Chair: William Slikker, Jr., PhD ~ FDA - NCTR

8:45 – 9:10 AM

Computational Tools for Comparisons across Stages of Neurodevelopment

Julia M. Gohlke, PhD ~ NIH-NIEHS

- Prenatal vs. postnatal models
- Why children aren't small adults for drug therapy!
- When do infants/children start becoming small adults for PBPK considerations?

9:10 – 9:35 AM

Inclusion of "omics" Data in Model Development for the Nervous System

Rory Conolly, PhD ~ EPA-NCCT

- Is this more than understanding mechanisms?
- How to incorporate omics into PBPK/PD models

9:35 – 10:00 AM

PB/PB Modeling of Early Life Stages in Rodents

Hugh Barton, EPA-NCCT

10:00 – 10:25 AM

Which PBTK Model Outputs Should be Considered as Inputs for Pharmacodynamic Modeling of Neurodevelopmental Effects?

Dale Hattis, PhD ~ Clark University, Worcester, MA

10:25 – 10:45 AM Break

10:45 – 11:15 AM

Panel Discussion of Kinetic Modeling

Panel Discussants: Above speakers plus:

- R. Woodrow Setzer, Jr., PhD ~ EPA-NCCT
Linda Sheldon, PhD ~ EPA/NHEERL

Questions to Invited Experts:

- How do you integrate exposure assessment into mathematical models of effect?
- How do pharmacokinetic parameters change as a function of life stage and other modifiers?
- How do you estimate cumulative risk using pk models?
- Relevant questions of dosimetry?
- Actual examples of the progression of models to address these questions with regards to developmental toxicity and neurotoxicity and how they might play into the risk assessment process.

11:15 – 11:30 AM

The Next Generation of Models: Vision of the Future

Donald R. Mattison, MD ~ NIH/NICHD

11:30 – 11:40 AM

Session Summary and Research Recommendations *

Co-Chairs: William Slikker, Jr., PhD and Donald R. Mattison, MD

* **Note:** Session Summaries and Research Recommendations will be published in the *NeuroToxicology* issue following the Conference along with the Meeting Report and Abstracts.

11:40 AM – 1:00 PM Break for Lunch (on your own)

Monday Morning 12 Sept 2005 9:00 – 11:30 AM

Workshop

SESSION III-B. DEVELOPMENTAL EFFECTS ON THE IMMUNE SYSTEM: IMPLICATIONS FOR AUTISM AND NEURODEVELOPMENTAL DISORDERS

Session Chairs: G. Jean Harry, PhD and Monica Carson, PhD

Theme: In recent years, evidence for the role of infectious and inflammatory processes as mediators of brain injury has been growing. The immune response within the brain as well as linkages between the immune and nervous system are becoming well documented. With regards to development, clinical correlations between fetal plasma cytokines and neurological outcomes in the premature infant have been established. Recent work suggests that maternal infection and

inflammatory responses in the offspring are associated with increased risk for diseases such as schizophrenia and autism. Several studies have reported systemic immunologic aberrations in autism spectrum disorders (ASD) that are associated with both autoimmunity and with dysfunctional immunity such as abnormalities or deficits of function in immune cell subsets. The following sessions will focus on work underlying these hypotheses in both the human clinical setting as well as the establishment of experimental animal models. The translation of adverse effects as the result of an innate immune response in the brain following exposure to environmental agents and the contribution of the immunological competence as a factor determining susceptibility will be discussed. Such interactions may contribute to the phenotypic differences of diseases seen in the human population.

9:00 – 9:15 AM

Introduction: Immune-Mediated Responses During Development
Jean Harry, PhD ~ Laboratory of Neurobiology, NIEHS

9:15 – 9:45 AM

Microglia: A Heterogeneous Population of CNS-Specific Macrophages

Monica Carson, PhD ~ University of California – Riverside

The innate immune system in the brain is highly regulated and serves many functions. Microglia serve in brain monitoring and maintenance however, many of the cell surface markers expressed by microglia are also expressed by infiltrating cells of the immune system that require down regulation. Distinguishing the resident microglia of the brain requires an identification of the cells as nervous system specific or as “self” to allow for functional activity in the absence of an “immune rejection” response.

9:45– 10:15 AM

Prenatal Exposure to Maternal Infection and Cortex Development

John H. Gilmore, MD ~ UNC Schizophrenia Research Center, University of North Carolina – Chapel Hill

Prenatal exposure to infection increases risk for schizophrenia, data generated from this group has led to the hypothesis that inflammatory cytokines, generated in response to maternal infection, alter neuron development and increase risk for schizophrenia. Examination of structural components of cortical neuron development suggests that pro-inflammatory cytokines can significantly reduce dendrite development and complexity of developing neurons consistent with the neuropathology of schizophrenia.

10:15 – 10:30 AM Break

10:30-11:00 AM

Autism and the Immune System: An Overview

Kimberly A. Stigler, Indiana School of Medicine, Indianapolis, IN

11:00 – 11:30 AM

Neuroinflammatory and neuroglial CNS responses in autism

Carlos Pardo-Villamizar, Johns Hopkins University School of Medicine

Evidence exists supporting a role for genetic, environmental, and immunological factors in the pathogenesis of autism. Work will be presented regarding the investigation as to the involvement of immune-mediated mechanisms in the pathogenesis of autism. Immunocytochemistry, cytokine protein arrays, and enzyme-linked immunosorbent assays were used to study brain tissues and cerebrospinal fluid (CSF) from autistic patients. Discussions on this data will focus on the magnitude of neuroglial and inflammatory reactions and their cytokine expression profiles.

11:30 AM – 12:30 PM Break for Lunch (on your own)

Monday Afternoon 12 Sept 2005 12:30 PM – 2:30 PM

Workshop - continued

SESSION III-B. ENVIRONMENTAL PERTURBATIONS OF THE IMMUNE SYSTEM: IMPLICATIONS FOR AUTISM AND OTHER NEURODEVELOPMENTAL DISORDERS

Session Co-Chairs: Cindy Lawler, PhD
Judy van de Water, PhD

Theme: Several studies have reported systemic immunologic aberrations in autism spectrum disorders (ASD) that are associated with both autoimmunity and with dysfunctional immunity such as abnormalities or deficits of function in immune cell subsets. The relationship between these abnormalities and the development of neuropathologic changes is not yet known. There has been speculation, however, that aberrant immune system activation occurring during critical periods of nervous system development and maturation may significantly contribute to the susceptibility of the organism to environmental exposure. Such interactions may contribute to the phenotypic differences of diseases seen in the human population.

Invited experts will present **clinical and epidemiological evidence** of an involvement of immune status and immune mediated responses during development and relationship to long term neurobehavioral changes.

12:30 – 12:45 PM

Introduction: Environmental Perturbations of the Immune System: Implications for Autism and other Neurodevelopmental Disorders

Cindy Lawler, PhD ~ NIEHS

12:45 – 1:15 PM

A case-control study of antibodies to central nervous system proteins and measles virus in children with autism.

William McMahon, MD ~ University of Utah

Recent data shows an increased frequency of the C4B null allele (C4BQ0) in subjects with autism. The suggestion that the human leukocyte antigen class III C4BQ0 increases the risk for autism supports the hypothesis of possible susceptible populations as a function of immune background. This data and the potential impact of environmental factors will be discussed.

1:15 – 1:45 PM

Suboptimal IgG response to bacterial vaccine antigens in patients with autism spectrum disorder (ASD)

Judy van de Water, PhD ~ UC-Davis

To better define the immune status of children with ASD, we examined the cytokine profiles of patients and age matched typically developing controls following mitogen and recall antigen stimulation. PBMC were isolated and cultured for 48 hours in the presence of media alone, PHA, LPS, and vaccine antigens from tetanus and MMR. Following stimulation, cytokine responses in ASD children were significantly altered compared with age-matched controls. The implication of these findings for hypotheses regarding immune in ASD will be discussed.

1:45 – 2:15 PM

Maternal Immune Status During Pregnancy and Childhood Autism

Lisa Croen, PhD, Kaiser Permanente Division of Research

Given the need to address the more broad spectrum of neurodevelopmental disorders, what is currently speculated as potential risk factors associated with autistic disorders may be applied to other diagnosed neurobehavioral disorders. How might the available data from epidemiology studies on autism may offer insights into future study design and evaluation of the interactions between the immune system and the developing nervous system and the contribution to disorders that manifest throughout the life-span.

2:15 – 2:30 PM Discussion
Roundtable Discussion of Session

Monday Afternoon 12 Sept 2005 2:45 – 5:05 PM

Platform Session

SESSION IV-A. CHILDREN'S ENVIRONMENTAL HEALTH

Co-Chairs: Cynthia Bearer, MD, PhD
William Suk, PhD, MPH

2:45 – 3:05 PM

Environmental Accumulation and Synergy of Multiple Neurotoxicants and Children's Learning Achievement in New Orleans, Louisiana, USA.

Howard W. Mielke, PhD ~ *Xavier University of Louisiana*

3:05 – 3:25 PM

Clearance of Neurotoxins by Phospholipid Emulsion in Autism and PDD.

Patricia Kane, PhD ~ *Haverford Wellness Center*

3:25 – 3:45 PM

Sensitivity Analysis in Studies of Continuous Outcome Measures: The Example of Methylmercury Exposure and Neuropsychological Testing in Children.

Michael Goodman, PhD, MPH ~ *Emory University School of Public Health*

3:45 – 4:05 PM

Effect of Solvents on L1 Distribution in Lipid Rafts.

Cynthia F. Bearer, MD, PhD ~ *Case Western Reserve University*

4:05 – 4:25 PM

Seychelles Child Development Study: Analysis of Postnatal MeHg Exposure.

Gary Myers, MD ~ *University of Rochester Medical Center*

4:25 – 4:45 PM

Sensitive Brains-Lasting Harm: Environmental Neurotoxins and Learning and Developmental Disabilities in Children.

Kathleen Schuler, MPH ~ *Institute for Agriculture and Trade Policy*

4:45 – 5:05 PM

Preventing Neurodevelopment Disorders: The CDC Should Lower the Blood Lead Action Level From 10 to 2 mcg/dL.

Steven G. Gilbert, PhD ~ *Institute of Neurotoxicity & Neurological Disorders*

Monday Afternoon 12 Sept 2005 1:00 – 5:00 PM

Symposium

SESSION IV-B. NEUROTOXICANT EXPOSURES IN MILITARY DEPLOYMENTS AND PUTATIVE ASSOCIATIONS WITH NEURODEGENERATIVE DISEASES

Session Co-Chairs: Susan P. Proctor, DSc
COL Karl E. Friedl, PhD

Theme: Topics presented in this session will include epidemiologically focused research on neurotoxicant exposures and putative associations with neurodegenerative diseases. This session will feature presentations of on-going projects sponsored by the US Army Military Research and Materiel Command, Military Operational Medicine Research Program and the US Army Research Institute of Environmental Medicine. This session is sponsored by the US Army Research Institute of Environmental Medicine (USARIEM) and the Neurotoxin Treatment Research Program of the US Army Medical Research and Materiel Command (USAMRMC).

1:00 – 1:20 PM

Overview: Neurotoxicant Exposures in Military Deployments and Putative Associations with Neurodegenerative Diseases.

Susan P. Proctor, DSc and COL Karl E. Friedl, PhD ~ *U.S. Army Research Institute of Environmental Medicine*

1:20 – 2:00 PM

Prospective Study of Military Service and Risk of Amyotrophic Lateral Sclerosis and Parkinson's Disease.

Marc Weisskopf, PhD ~ *Harvard School of Public Health*

This presentation will cover recent work by the presenters on their prospective assessment of the relationship between military service and ALS and PD mortality among participants in the Cancer Prevention Study II cohort of the American Cancer Society.

2:00 – 2:40 PM

Polychlorinated Biphenyls, Organochlorines, and Parkinson's Disease (PD) Risk: A Case Control Study in Alaskan Natives

Carolyn M. Tanner, MD, PhD ~ *The Parkinson's Institute, Sunnyvale, CA*

Current progress regarding a case-control study of PD among Alaskan natives exposed to PCBs and Persistent Organic Pollutants (POPs) will be reported.

2:40 – 3:00 PM Break

3:00 – 3:40 PM

Polychlorinated Biphenyls Alter Dopamine Function in Older Capacitor Workers.

Richard F. Seegal, PhD ~ *New York State, Dept of Health, Albany, NY*

A current epidemiological research project is underway to investigate the hypothesis that occupational exposure to PCBs leads to reduction in central dopamine nerve terminal integrity in humans. An update on current progress will be presented.

3:40 – 4:20 PM

SHOAMP: The Study of Health Outcomes in Aircraft Maintenance Personnel.

Catherine D'Este, PhD ~ *Royal Newcastle Hospital, Newcastle, NSW, on behalf of the SHOAMP Team*

This presentation will provide a summary of current epidemiologic research efforts in Australia concerning adverse health effects of jet fuel solvent exposures during fuel tank repair and maintenance activities.

4:20 – 5:00 PM

Discussion, Session Summary and Research Needs

5:00 PM – 7:00 PM Break for Dinner (on your own)

Monday Evening 12 Sept 2005 7:00 – 9:00 PM

Symposium

EVENING SESSION A. AQUATIC AND INVERTEBRATE MODELS OF DEVELOPMENTAL NEUROTOXICITY FOR MECHANISTIC AND HIGH THROUGHPUT STUDIES

Co-Chairs: Edward D. Levin, PhD and Jonathan Freedman, PhD

Theme: Fish and invertebrates offer useful models complementary to the classic mammalian and in vitro models of neurotoxicity. These simple but functionally intact systems provide visual access during the process of development that is unavailable in mammals. The aquatic and invertebrate models provide the anatomic and temporal integrity of the whole animal unavailable with in vitro preparations. Elegant genetic methods are available for sophisticated studies of the molecular bases of developmental neurotoxicity. Rapid assessment techniques using *C. elegans* and zebrafish embryos are being developed for high throughput screening studies. Reliable behavioral assays are being constructed to determine the functional consequences of neurodevelopmental insults. These newer complementary models can provide important information for initial triage of the multitude of chemicals to be tested in the necessary but more expensive and time consuming mammalian studies as well as identifying important molecular targets for the toxicodynamic effects of toxicants on neurodevelopment.

7:00 – 7:10 PM

Overview

Edward D. Levin, PhD ~ *Duke University Medical Center*

7:10 – 7:30 PM

Development of Medium-Throughput Toxicity Screens Using *C. Elegans*.

Jonathan Freedman, PhD ~ *Nicholas School of Environmental and Earth Sciences*

7:30 – 7:50 PM

***C. Elegans* Model for Determining Metal-induced Dopamine Neurodegeneration and Alternations in Neurodevelopment**

Richard Nass, PhD ~ *Vanderbilt University*

7:50 – 8:10 PM

Strategies Towards Using Zebrafish as a Complementary Neurotoxicological Model

Elwood Linney, PhD ~ *Duke University*

8:10 – 8:30 PM

Neurobehavioral Consequences of Neurodevelopmental Toxicity Zebrafish

Edward D. Levin, PhD ~ *Duke University Medical Center*

8:30 – 9:00 PM

Discussion, Session Summary and Research Needs

Monday Evening 12 Sept 2005 7:00 – 9:00 PM

Symposium

EVENING SESSION B. ENDOCRINE ACTIVE COMPOUNDS AND THEIR EFFECTS ON BRAIN DEVELOPMENT: INTEGRATION OF METHODS AND APPROACHES

Session Co-Chairs: Eva Polston, PhD and Robert Handa, PhD

Theme: *Throughout an animal's lifetime, steroid hormones have profound effects on brain function. Because the brain is sensitive to low concentrations of steroids and steroid-like compounds, there is growing concern that low levels of endocrine-active compounds (EACs) in the environment may exert toxicological effects in the brain. In contrast to necrosis-inducing neurotoxins that cause histopathological damage, the effects of EACs are likely to result in subtle and specific alterations of neuronal function. This workshop will present a multifaceted approach through which changes in the developing and adult brain can be assessed. Talks will focus on cellular/molecular, neuroanatomical, and functional approaches for detecting perturbations in hormone-sensitive neuronal systems.*

7:00 – 7:10 PM

Endocrine Active Compounds and their Effects on Brain Development

David C. Dorman, DVM, PhD ~ *CIIT Centers for Health Research*

7:10 – 7:30 PM

Prenatal Exposure to Fenitrothion: Are Changes in the SDN-POA a Concern?

Melanie Struve, PhD ~ *CIIT Centers for Health Research*

Fenitrothion is an organophosphate insecticide that also has antiandrogenic properties. This presentation will discuss whether perinatal exposure to fenitrothion is associated with altered SDN-POA development in rodents. Data describing the effects of in utero fenitrothion exposure and esterase activity in the rat dam and fetus will also be presented.

7:30 – 7:50 PM

Estrogen Receptor Signaling in Sexual Differentiation of the Brain: Can We Teach an Old Dogma New Tricks?

Robert Handa, PhD ~ *Colorado State University*

During rodent hypothalamic development, the intracellular aromatization of testosterone to estrogen, and subsequent binding to estrogen receptor has been a well documented phenomenon underlying the differentiation of the brain in a male direction. A critical component to this hypothesis is that the early presence of plasma proteins that bind

circulating estrogen and prevent circulating estrogens from affecting brain organization. As a result, it is thought that intracellular aromatization is a necessary mechanism to bypass sequestration of circulating estrogen. Dr. Handa will discuss his recent studies demonstrating that relatively low amounts of estrogen given during early development can have an effect on brain function. He will also present microarray results identifying some of the estrogen responsive genes that may underlie sexual differentiation of the brain.

7:50 – 8:10 PM

Sex and the Brain: Evaluating Sex Differences in Neuroendocrine and Behavioral Circuits

Eva Polston, PhD ~ *CIIT Centers for Health Research*

Early exposure to sex steroids causes sexual differentiation of the brain circuits that control reproduction. This talk will describe some of the important forebrain areas that are involved in regulating neuroendocrine and behavioral functions. Available tools for measuring sexually dimorphic neuroanatomical features, such as brain nuclear volumes, cell numbers, axonal projection densities, and synapse formations, will also be discussed.

8:10 – 8:30 PM

Beyond the Brain: How EAC's Affect Neuroendocrine Systems and Complex Behaviors

Heather Patisaul, PhD ~ *CIIT Centers for Health Research or TBA*

As neuroscientists, we tend to focus on the structure and function of neural circuits when evaluating the potential toxicity of substances. But we must also look beyond these physical changes and evaluate whether or not an observed change in gene expression or protein synthesis ultimately affects how the animal functions in its environment. This presentation will discuss how impaired reproductive behavior, abnormal responses to stress, or altered maternal behavior may decrease the fertility and survivability of an individual.

8:30 – 8:50 PM

Does Sex Matter? Male Brains, Female Brains, and Environmental Exposures

Bernard Weiss, PhD ~ *Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry*

8:50 – 9:00 PM

Discussion, Session Summary and Research Needs

Tuesday Morning 13 Sept 2005 8:30 AM – 11:30 AM

Symposium

**SESSION V. MOLECULES TO (WO)MAN: A. ANIMALS
*Dissecting the Dysfunction to Look at the Whole Picture***

Session Co-Chairs: Isaac N. Pessah, PhD
Richard F. Seegal, PhD

Theme: *Invited Speakers in this Symposium will present an integrated overview of the multidisciplinary approaches needed to understand risk factors contributing to developmental disorders and aging. Goal: To provide mechanistic data that will aid in the interpretation of epidemiological data and in understanding the role that environmental agents play in inducing central nervous system dysfunctions. Identifying the principal molecular targets that are responsible for producing toxicosis has been a cornerstone of risk assessment. Prominent examples include the activity of dioxins at the AhR, anticholinesterase activity of organophosphates and carbamates, and the interaction of pyrethroids with sodium channels. Understanding the relationship among low level exposure to environmentally persistent chemicals, their critical molecular targets, ensuing cellular dysfunction, and defining often subtle consequences on animal and human neurodevelopment is perhaps one the most challenging goals of modern toxicology.*

8:30 – 8:35 AM

Overview and Goals of Molecule to (Wo)Man Session – Part A: Animals

Co-Chairs: Isaac N. Pessah, PhD and Richard F. Seegal, PhD

8:35 – 9:00 AM

Genetic and Epigenetic Mechanisms Conferring Susceptibility to Environmental Agents

Isaac N. Pessah, PhD ~ UC Davis

This talk will address sources of genetic vulnerability to environmental chemicals.

Main themes:

- chromosome abnormalities
- Gene polymorphisms (e.g., SNP, splice variants, truncations, deletions)
- altered expression (epigenetic mechanisms of transmission)

Goal: Specific examples of heritable dysfunctions that may be influenced by environmental triggers will be presented.

9:00 – 9:30 AM

PCBs, Methylmercury and Dopamine: From Tissue Culture to Humans

Richard F. Seegal, PhD ~ Wadsworth Center, NYSDOH

Linking molecular mechanisms to cellular dysfunction to human disorders

9:30 – 10:00 AM

Defining Mouse Behaviors Related to Autism

Jacqueline N. Crawley, Ph.D., National Institute of Mental Health IRP and University of North Carolina

This talk will describe mouse behavioral tasks relevant to the symptoms of autism.

Main themes:

- social approach and reciprocal social interactions
- social communication using olfactory and auditory modalities
- perseverance tests for stereotypies, ritualistic behaviors, and restricted interests

Goal: Specific examples of inbred strains of mice and knockout mouse models will be presented.

10:00 – 10:20 AM Break

10:20 – 10:50 AM

Mouse Models of Social Behavior: Gene Toxicant Interactions

Robert F. Berman, PhD ~ University of California School of Medicine, Davis

This talk will describe the development and use of a battery of behavioral tests to characterize the effects of neonatal exposure to environmental toxins (e.g., ethylmercury, PCBs) on brain development and expression of social behaviors and social interactions. The strengths and weaknesses of using genetically engineered mice to examine behavioral and cognitive functions will also be discussed, along with strategies for examining gene-environment interactions.

10:50 – 11:20 AM

Cholinergic Involvement in Neurocognitive Function: From Zebra Fish to Humans

Edward D. Levin, PhD ~ Duke University Medical Center

Translation among complementary model systems requires the determination of common mechanisms of effect. Cholinergic systems have been widely shown to be critical for cognitive function in human and rodent models. This talk will extend the involvement of cholinergic systems in cognition with the toxicological and pharmacological manipulations of cholinergic systems in a new complementary model system zebrafish.

11:20 – 11:30 AM

Discussion

11:30 AM – 12:45 PM Break for Lunch (on your own)

Tuesday Afternoon 13 Sept 2005

12:45 – 3:45 PM

Symposium

SESSION V: MOLECULES TO (WO)MAN – B. HUMANS

Dissecting the Dysfunction to Look at the Whole Picture

Session Co-Chairs: Susan L. Schantz, PhD
S. Jill James, PhD

12:45 – 12:50 PM

Overview and Goals of Molecule to (Wo)Man Session – Part B: Humans

Susan L. Schantz, PhD ~ University of Illinois

12:50 – 1:15 PM

Applying Data from Animal Models in Epidemiological Research

Susan L. Schantz, PhD ~ University of Illinois

This talk will cover a transition from animal to human studies, which will continue after the lunch break.

1:15 – 1:40 PM

Oxidative Stress in Children with Autism: Metabolic Biomarkers and Genetic Polymorphisms

S. Jill James, PhD ~ University of Arkansas for Medical Sciences, and Arkansas Children's Hospital Research Institute

Dr. James and coworkers reported results from a recent study that revealed, relative to the control children, children with autism had significantly lower baseline plasma concentrations of methionine, SAM, homocysteine, cystathionine, cysteine, and total glutathione and significantly higher concentrations of SAH, adenosine, and oxidized glutathione. Therefore an increased vulnerability to oxidative stress and a decreased capacity for methylation may contribute to the development and clinical manifestation of autism. More importantly, children with autism may possess heightened susceptibility to xenobiotics that mediate their toxicity *via* oxidative stress.

1:40 – 2:05 PM

Defining the Autism and Broad Autism Phenotypes

Joseph Piven, MD ~ Director, Autism Center, Univ of North Carolina

This talk will focus on identifying Autism endophenotypes based on genes, behavior and environment. Examination of familial aggregation of behavioral characteristics in non-autistic family members and relating brain phenotypes (defined by MRI) and their potential relationship to selected candidate genes. Specific examples will be used to suggest that individual components of autism may be inherited in families segregating for autism and these intermediate phenotypes provide a complementary approach to conceptualizing genetic studies of autism

2:05 – 2:20 PM Break

2:20 – 2:45 PM

From Antiquity to the 21st Century: The Past, Present and Future of Lead Toxicity

Herbert L. Needleman, MD ~ Dept of Psychiatry, Univ of Pittsburg School of Medicine

An epidemiological design to examine the association between prenatal lead exposure and Alzheimers' disease will be presented.

2:45 – 3:15 PM

Update on the National Children's Study

Carole A. Kimmel, Ph.D. ~ Consultant, National Children's Study Program Office, National Institute of Child Health and Human Development, NIH, DHHS, Bethesda, Maryland, USA

3:15 – 3:45 PM

Q&A, Open Discussion, Session Summary and Research Needs*

Speakers from both morning and afternoon sessions will provide questions related to the above topics (how best to incorporate lab

science results into clinical and epidemiological studies; how to facilitate bi-directional information transfer) to stimulate audience discussion.

* **Note:** Session Summaries and Research Recommendations will be published in the *NeuroToxicology* issue following the Conference along with the Meeting Report and Abstracts.

END AT 3:45 FOR GENERAL POSTER SESSION

Tuesday Afternoon 13 Sept 2005 3:45 – 5:45 PM

Cash Bar & Snacks

Poster Session

SESSION VII: GENERAL POSTER SESSION

Session Chairs: Ken Reuhl, Ginger Moser, Toshio Narahashi

Pre-Doctoral Student Award Committee:
TBA after abstracts are received

Post-Doctoral Student Award Committee: TBA

The poster session is a highlight of this conference series and provides an ideal opportunity for one-on-one personal exchange of research information and ideas in an informal setting with a unique consortium of participants expert in various aspects of the theme and neurotoxicology in general. The General Poster Session has proven to be a wonderful venue for informal, in-depth discussion, collaboration building, and mentoring of young scientists. It is an important networking opportunity for students. Judging and selection of Pre – and Post-Doctoral Student Awardees will be made during the session. All papers on neuroscience plus toxicology are invited. Posters do not need to address the theme; they can be on any aspect of toxicology.

Tuesday Evening 13 Sept 2005 5:30 – 10:00 PM

SESSION VIII

Conference Social Evening

5:30 – 6:30 PM

Poolside Cocktails

6:30 – 10:00 PM

North Carolina Pig Pickin'

Presentation of Student Awards

Wednesday Morning 14 Sept 2005 8:30 AM – 11:30

Symposium

SESSION IX-A. CONTEMPORARY HEALTH ISSUES ASSOCIATED WITH OVER EXPOSURE TO MANGANESE

Session Co-Chairs: Michael Aschner, PhD
Thomas Gunter, PhD

Theme: This multidisciplinary session will address contemporary research issues associated with the health effects of manganese (Mn) both in humans and animal models. Speakers will discuss recent findings on the specific cellular, molecular, and physiologic mechanisms by which manganese mediates its adverse effects. Speakers will also note factors, such as age, pre-existing disease, and genetics, as conditions that might predispose individuals to enhanced susceptibility to manganese toxicity. The session will span studies in various tissue culture models to non-human primates, incorporating diversity of techniques, from molecular biology to imaging.

Timely Topics to be Addressed:

- Consideration of the relevant health issues associated with over exposure to manganese.
- Characterization of exposures
- Development of appropriate biomarkers of exposure.
- Quantifying the relationships between exposure and ill health, including pharmacokinetics.
- Understanding the mechanisms of transport, damage and repair
- Understanding and utilizing invertebrate models such as the *C. elegans* to probe for mechanisms of Mn neurotoxicity

8:30 – 8:40 AM

Introduction

Co-Chairs: Michael Aschner, PhD and Thomas Gunter, PhD

8:40 – 9:10 AM

Factors that Influence the Pharmacokinetics of Inhaled Manganese

David Dorman, DVM, PhD ~ CIIT

This presentation will discuss manganese inhalation exposure conditions that result in manganese accumulation within the brain of adult nonhuman primates as well as in fetal, juvenile, adult, and aged rodents. Dr. Dorman will discuss the pharmacokinetics of inhaled manganese and the effect of particle solubility on this process.

9:10 – 9:40 AM

Dietary Iron Modulates Manganese Neurotoxicity

Michael Aschner, PhD ~ Vanderbilt University

Manganese and iron are essential metals for normal growth and development. Both metals compete for and share the same cellular transporters. Thus, during periods of low dietary Fe intake, the transport and deposition of Mn in the brain are increased. This presentation will address magnetic resonance (MR) studies monitoring the accumulation of brain Mn when dietary Fe levels are modulated.

9:40 – 10:10 AM

Characterization of Welding Fumes and their Neurotoxic Effects

James Antonini, PhD ~ NIOSH

Dr. Antonini will report on recent characterization of welding fume metal composition and particle size. He will also address the pulmonary and neurotoxic effects of animals exposed to welding fumes by inhalation.

10:10 – 10:30 AM Break

10:30 – 11:00 AM

Discovery of Biomarkers of Manganese Exposure in Humans

Wei Zheng, PhD ~ Purdue University

This presentation will discuss the possibility of using blood levels of manganese, iron, or iron metabolism-associated proteins as biomarkers for manganese toxicity based on human studies of welders with occupational exposure to manganese in welding fume. The outcomes of clinical intervention with chelating agents will also be discussed.

11:00 – 11:30 AM

Neurochemical Changes in the Living Non-human Primate Brain following Chronic Mn Exposure

Tomás Guilarte, PhD ~ Johns Hopkins University

This presentation will deal with the effects of low level chronic manganese exposure on imaging and neuropathological endpoints in the non-human primate brain. The speaker will detail the distribution of manganese accumulation in the basal ganglia and the effect of manganese exposure on other metals such as iron, copper and zinc. The presentation will also describe early onset changes in dopaminergic system function and other biochemical endpoints.

11:30 AM – 1:30 PM Break for Lunch (on your own)

Wednesday 14 Sept 2005 8:30 AM – 4:00 PM

NOTE:

Attendance at the Developmental Toxicology Technical Workshop is limited to 50 registrants in addition to the 20 invited experts on the panel. Pre-registration is required and attendance will be on a "first-come" basis.

Wednesday 14 Sept 2005 8:30 AM – 4:00 PM

Developmental Toxicology Technical Workshop
SESSION IX-B. OPTIMIZING THE DESIGN AND INTERPRETATION OF EPIDEMIOLOGICAL STUDIES FOR ASSESSING NEURODEVELOPMENTAL EFFECTS FROM IN UTERO CHEMICAL EXPOSURE

Session Chair: Roger Ladda, Hershey Medical Center

Session Theme and Description: *While many epidemiologic studies of children's environmental health have been completed, and more are being planned, a comprehensive critical examination of the methodologies commonly used in past studies has not been conducted. In fact, in some of the completed studies (e.g., those related to pharmaceuticals and environmental chemicals such as lead, methylmercury, and PCBs), the authors have acknowledged the limitations of existing methods. Currently, there is a great deal of interest in conducting additional epidemiologic investigations into environmental chemicals and children's health. For example, the proposed National Children's Study (NCS) is likely to investigate environmental and other factors influencing the health and development of children in utero, through birth, childhood, and into young adulthood.*

Therefore, as new studies are being planned, this is an appropriate time to determine whether existing methods as they have been practiced will serve future studies, especially those designed to assess the potential impacts at current exposures. In short, such an examination serves to identify the key methodological factors that ultimately determine the value and strength of future research. Thus, investigators designing new studies will benefit from this thoughtful examination as they develop future study designs and analyze resulting study data. The outcome of this session will provide valuable input not only to the design of future investigations, but also metrics whereby scientists and others can judge the adequacy of reported studies. However, the scope of the session will focus only on scientific methodological issues (i.e., the development of 'best practices' for future study design, conduct, reporting and interpretation); that is, specifically, it will not include an evaluation of conclusions or findings from previous epidemiological studies of environmental health.

The Expert Panel assembled for this session will address a series of topics with related questions prior to, and during, the session. These topics and questions include:

Study Design:

- ? What is the best experimental design and methodology to assess the likelihood that *in utero* exposure to an environmental chemical can result in adverse neurodevelopmental effects in newborns that continue into childhood?
- ? What are the statistical issues that must be addressed to conclude with adequate confidence that an *in utero* exposure to a specific environmental chemical can result in adverse neurodevelopmental effects?

Measurement Tool:

- ? What specific measurement tools/tests are best suited and validated for assessing the variety of potential neurodevelopmental and behavioral deficits? What is the known sensitivity, specificity and

predictive value of each endpoint being measured? How reproducible is/are the measurement(s)?

- ? Are there particular sampling strategies or data collection methods that are especially relevant to detecting potential neurodevelopmental effects from *in utero* exposure? What sampling and analysis strategies can be employed to avoid Type II (failure to detect a real effect) errors?
- ? What is the relationship between the estimated window of exposure and the *nature* of a potential effect, and how might this affect the selection of tests?
- ? How might data and methods from the field of molecular epidemiology be used to enhance traditional epidemiologic approaches?

Exposure Assessment:

- ? Which specific measurement tools and biomarkers are best suited and validated for assessing the nature, extent, and patterns of *in utero* exposure to a particular environmental chemical? How might these differ from tools and biomarkers used to assess post-natal exposure?
- ? To avoid exposure misclassification or misleading estimates when assessing potential exposure, how frequently should exposure be estimated (i.e., what temporal units should be used for serial exposure measurements)? If appropriate temporal units are chemical- or tissue-specific, what data or criteria should be used to determine the optimal units? How should critical timeframes – critical windows of vulnerability in neurodevelopment - be taken into account when designing an exposure assessment approach?
- ? How should potential aggregate exposure from multiple routes (inhalation, ingestion, dermal) be addressed? How should potential cumulative exposure to multiple chemicals be addressed? How can trends in exposure and trends in neurodevelopmental outcomes be assessed?

- ? How long should the subject be followed with appropriate studies (e.g., school age, puberty, reproductive ages)?

Participant Selection:

- ? What is the most appropriate and valid way to select and follow exposed and control groups for studies attempting to demonstrate an association between *in utero* exposure to a specific environmental chemical and adverse neurodevelopmental effects?

Confounders:

- ? What guidance can be offered with respect to selecting and measuring potential confounders? What criteria should be applied when selecting control variables for inclusion in a multivariate analysis? How should potential mediating factors be identified and analyzed?
- ? Are there cultural aspects to neurodevelopmental tests that should be considered before use?

Reporting:

- ? How is clinical significance versus population significance defined and reported?
- ? How do researchers address the issue of labeling of children based on study results and how should the study results be reported to parents?

Research Needs and Recommendation:

- ? What are the key needs for future research? What are the primary uncertainties and gaps in our knowledge that should be addressed with future research?

Expert Panel of Participants

Robert W. Amler, MD, FAAP, FACPM
Dean and Professor, New York Medical College

Stanley Barone, Jr., Ph.D.
Research Biologist, Effects Identification & Characterization Workgroup
NCEA/ORD, Neurotoxicology Division, US EPA

Aysenil Belger, Ph.D.
Associate Professor, Department of Psychiatry, UNC at Chapel Hill

Cheston M. Berlin, Jr., MD (Steering Committee)
University Professor of Pediatrics, Professor of Pharmacology
Department of Pediatrics, Children's Hospital
Milton S. Hershey Medical Center

Christopher Cox, Ph.D.
Professor of Epidemiology, Department of Epidemiology
Johns Hopkins University

Harry Frank, Ph.D.
Professor Emeritus of Psychology, The University of Michigan

Michael Goodman, MD, MPH
Assistant Professor, Department of Epidemiology
Emory University School of Public Health

Jean Harry, Ph.D.
Head, Neurotoxicology Group, Laboratory of Neurobiology
National Institute of Environmental Health Sciences

Stephen R. Hooper, Ph.D.
Professor of Psychiatry, Research Professor of Psychology, Clinical
Professor of Education
Associate Director of the Center for Development and Learning
Director, Child and Adolescent Neuropsychology Consultation Program
Clinical Center for the Study of Development and Learning
University of North Carolina School of Medicine

Roger Ladda, MD, Workshop Chair
David S. and Amy S. Goldberg Professor of Genetics and Pediatrics
Chief, Division of Human Genetics, Growth and Development
Milton S. Hershey Medical Center
Pennsylvania State University College of Medicine

Judy S. LaKind, Ph.D. (Steering Committee)
LaKind Associates, LLC
Hershey Medical Center, Penn State College of Medicine
University of Maryland School of Medicine

Paul H. Lipkin, M.D.
Assistant Professor of Pediatrics
The Johns Hopkins University School of Medicine

Lewis P. Lipsitt, Ph.D.
Professor Emeritus of Psychology, Medical Science, & Human
Development
Research Professor of Psychology
Department of Psychology, Brown University

Matthew N. Lorber
National Center for Environmental Assessment, US EPA

Ann M. Mason (Steering Committee)
Managing Director
Research Foundation for Health and
Environmental Effects

Gary Myers, MD
Professor of Neurology and Pediatrics, Division of Pediatric Neurology
University of Rochester Medical Center

Larry L. Needham, Ph.D.
Chief, National Center of Environmental Health
Division of Environmental Health Laboratory Sciences
Centers for Disease Control and Prevention

Theodore D. Wachs, Ph.D.
Professor, Dept of Psychological Sciences, Purdue University

Janice W. Yager, Ph.D., MPH (Steering Committee)
Research Program Manager

Environment Division
Electric Power Research Institute

Wednesday Morning 14 Sept 2005 8:30 AM – 11:30 AM

Platform Session

**SESSION IX-C: NEUROTOXICITY OF MIXTURES,
SOLVENTS, AND METALS IN VIVO AND IN VITRO**

**Session Co-Chairs: Evelyn Tiffany-Castiglioni, PhD
Virginia Moser, PhD**

Theme: Session IX-B will present an overview of the neurotoxicity of mixtures and multiple agents, including insecticides, metals, and solvents. Topics will include both *in vivo* and *in vitro* approaches for understanding the mechanisms and toxicologic interactions of organophosphate (OP) compounds *in vivo* and *in vitro*. The influence of age (young vs. adult) as well as dose sequence on the outcome of OP pesticide mixtures will be described. State-of-the-art physiologically based pharmacokinetic and pharmacodynamic (PBPK/PD) modeling approaches will be illustrated for OP compounds. Talks will also focus on *in vitro* models for screening and investigating interactions of complex mixtures and multiple sequential agents, as well as neurotoxicity of solvents and copper. The focus of *in vitro* studies will be mechanisms and relevance to neurologic disease.

8:30 – 8:35 AM

Overview

Virginia Moser, PhD ~ USEPA

8:35 – 8:55 AM

**Comparison of the Non-Additive Interactions of an
Organophosphorus Pesticide Mixture in Adult and Prewaning
Rats.**

Virginia Moser, PhD ~ NTD/NHEERL/ORD, US EPA, RTP, NC USA

8:55 – 9:15 AM

**Exposure Sequence Influences Cholinergic Toxicity in Neonatal
Rats Exposed To Two Organophosphorus Insecticides.**

Carey N. Pope, PhD ~ Oklahoma State University, OK, USA

9:15 – 9:35 AM

**Effects of Binary or Ternary Mixtures of Organophosphates on
Esterases *In Vitro*.**

Janice E Chambers, PhD ~ Mississippi State University, MS, USA

9:35 – 9:55 AM

***In Vitro* Models for Assessing Neurotoxicity of Mixtures.**

Evelyn Tiffany-Castiglioni, PhD ~ Texas A&M University, TX, USA

9:55 – 10:15 AM Break

10:15 – 10:35 AM

**Dietary Copper Supplementation Enhances the Peripheral
Myelinopathy Produced by Dithiocarbamates in Rats.**

William M. Valentine, PhD, DVM ~ Vanderbilt University Medical
Center, TN, USA

10:35 – 10:55 AM

Copper-Regulated APP Expression in Human Astrocytoma Cells.

Yongchang Qian, PhD ~ Texas A&M University, TX, USA

10:55 – 11:30 AM

Discussion, Session Summary and Research Needs

11:30 AM – 1:30 PM Break for Lunch (on your own)

Wednesday Afternoon 14 Sept 2005 1:00 – 3:45 PM

Symposium – continued

**SESSION IX-A. CONTEMPORARY HEALTH ISSUES
ASSOCIATED WITH OVER EXPOSURE TO MANGANESE**

Session Co-Chairs: Tomás Guilarte, PhD
Anumantha Kanthasamy, PhD

1:00 – 1:30 PM

Mitochondrial Effects of Manganese

Thomas Gunter, PhD ~ *University of Rochester*

Mn²⁺ is known to be readily sequestered by mitochondria including neuronal cells. Furthermore, Mn²⁺ is also known to bind to almost every Ca²⁺ binding site, usually more strongly than Ca²⁺ itself. Dr. Gunter will discuss mechanisms by which Mn²⁺ may cause cell damage by interfering with Ca²⁺ activation of ATP production and inhibition of mitochondrial enzymes.

1:30 – 2:00 PM

The Role of Prion Protein in Manganese Neurotoxicity

Anumantha Kanthasamy, PhD ~ *Iowa State University*

Altered Mn is known sequelae of prion disease, but little is known about the role of Mn in this disease. Dr. Kanthasamy will address the binding of Mn to cellular prion protein and the potential role it plays in the pathogenesis of sporadic prion disease.

2:00 – 2:30 PM

Manganese-induced Dopaminergic Neuron Degeneration in *C. elegans*: A Pharmacogenetic Analysis

Richard Nass, PhD ~ *Vanderbilt University*

Manganese (Mn²⁺) neurotoxicity resembles a number of aspects of the dopamine (DA) neuron degenerating disorder Parkinson's disease (PD). Expression of the pre-synaptic protein α -synuclein and the oxidative stress-induced protein parkin has been proposed to contribute to the pathogenesis of both disorders. Dr. Nass will discuss a novel pharmacogenetic model using the genetically tractable nematode *C. elegans* to dissect and characterize the molecular components involved in DA neuron degeneration and its utility in characterizing Mn-induced neurotoxicity

2:30 – 2:50 PM **??Break or Continue without a Break???**

2:50 – 3:20 PM

A Study of the Nervous System in Welders

Dag Ellingsen, MD, PhD ~ *National Institute of Occupational Health, Oslo, Norway*

The speaker will address investigations of neurological effects in manganese-exposed workers in Russia: 1) a cross-sectional study of 96 welders and age-matched referents, and 2) a clinical study of 27 manganese patients. The results of these will detail associations between degradation of neurobehavioral endpoints (e.g., digit span, finger tapping test scores) and level of manganese exposure (as measured in blood and urine) in welders.

3:20 – 3:45 PM

Discussion, Session Summary and Research Needs

Wednesday Afternoon 14 Sept 2005 1:00 – 4:00 PM

Platform Session

SESSION X: ENVIRONMENTAL TOXICANTS AND DISEASES

Co-Chairs: Toshio Narahashi, PhD
TBA

Theme: Environmental agents not only could cause direct toxic effects on humans but also are suspected to be related to various diseases. These direct and indirect effects are in most cases the result of interactions with specific target receptors or molecules. This session deals with a few examples of such studies ranging from pesticides/heavy metals to Alzheimer's disease/peripheral myelinopathy.

1:00 – 1:05 PM

Overview

Toshio Narahashi, PhD ~ *Northwestern University Medical School*

1:05 – 1:25 PM

Studies of Autoimmune and Neurological Diseases in Communities Concerned About Environmental Exposures.

Dee Williamson, PhD ~ *Agency for Toxic Substances and Disease Registry*

1:25 – 1:45 PM

Role of Neuroreceptors in Selective Toxicity of Insecticides In Insects and Mammals.

Toshio Narahashi, PhD ~ *Northwestern University Medical School*

1:45 – 2:05 PM

Developmental Pesticide Exposure Alters the Dopaminergic System and Increases MPTP Toxicity

Jason R. Richardson, PhD ~ *Environmental and Occupational Health Sciences Institute*

2:05 – 2:20 PM Break

2:20 – 2:40 PM

Effects of Peripheral Inflammation on the Dopaminergic Toxicity of the Fungicide Maneb in Two Strains of Mice.

Nick M. Filipov, PhD ~ *College of Veterinary Medicine Mississippi State*

2:40 – 3:00 PM

Gamma-Interferon (IFN γ) Causes Dendritic Retraction in Sympathetic Neurons *In Vivo*

Pamela J. Lein, PhD ~ *Oregon Health & Science University*

3:00 – 3:20 PM

Alzheimer's Drug Modulation of Nicotinic Receptors and NMDA Receptors: Basis for Therapeutic Effects

Toshio Narahashi, PhD ~ *Northwestern University Medical School*

3:20 – 4:00 PM

Discussion

Thursday Morning & Afternoon - 15 Sept 2005 9 AM – 3:30 PM

9:00 AM - 3:30 PM

Post-Conference Tours of CIIT Centers for Health Research and the US Environmental Protection Agency Laboratories

9:00 AM

Buses to EPA

Tour EPA Laboratories ~ Organized by Ginger Moser

Lunch in EPA Cafeteria

12:30 NOON

Buses to CIIT

CIIT Demonstrations and Tours ~ Organized by David Dorman