

## TWENTY-THIRD INTERNATIONAL NEUROTOXICOLOGY CONFERENCE

# “Neurotoxicity in Development & Aging”

September 17-21, 2006 • DoubleTree Hotel Conference Center • Little Rock, Arkansas, USA

Sunday Afternoon 17 Sept 2006 2:00 – 5:00 PM

### Opening

#### SESSION 1: OPENING OF THE CONFERENCE

Conference Chair: **Joan Cranmer, PhD**

#### Opening, Acknowledgements & Goals of the Conference

Joan Cranmer, PhD ~ *University of Arkansas for Medical Sciences*

Welcome ~ TBA

### Symposium

#### SESSION 2: CONSEQUENCES OF CHEMICAL EXPOSURE ON COGNITION IN CHILDREN: IMPORTANCE OF EFFECT MODIFIERS

Session Chair: **Deborah Rice, PhD**  
Co-Chair: **David Bellinger, PhD**

**Theme:** This session will examine interactions between chemical exposure and endogenous and environmental factors on neuropsychological function. Factors include the socioeconomic environment of the child, the influence of individual genes, and the modification of response to environmental chemicals by the brain structure of the child.

#### Importance of Effect Modifiers for the Consequences of Chemical Exposure on Cognition in Children

Deborah Rice, PhD ~ *Maine Center for Disease Control and Prevention*

Dr. Rice will provide an overview of factors that may influence the effects of exposure to a chemical in the human population. These include the *genetic make-up* of the individual, the *expressed phenotype*, and *environmental factors* such as social milieu.

#### Impulsivity in PCB, MeHg and Pb Exposed Children Revealed Through Response Inhibition Paradigms: Current Behavioral Findings and Future Directions in Brain Imaging

Paul W. Stewart, PhD ~ *State University of New York at Oswego*

Dr. Stewart is principal investigator of a longitudinal prospective study on the effects of exposure to PCBs and other chemicals on cognitive development of the child. He will present data demonstrating an interaction between the adverse effects of PCBs and the size of various structures in the brain. For example, a smaller volume of the corpus collosum predicts a greater adverse effect of a given body burden of PCBs.

#### Using the Tools of Genetics and Neuroimaging in Assessing Developmental Vulnerability

Kim N. Dietrich, PhD ~ *University of Cincinnati College of Medicine*

Dr. Dietrich has been examining the effects of environmental chemical exposures on child development. He has served as the PI on a prospective study of lead and child development that began in 1979 and continues today. He will discuss the interactions between lead and genetic polymorphisms associated with neurotransmitter metabolism and activity. The major outcomes of interest will include cognition, behavior, adult criminality and measures of central nervous function, physiology and anatomy as assessed by fMRI, vMRI and MRS.

#### Influence of Total Social Environment on the Outcome of Chemical Exposure

David Bellinger, PhD ~ *Harvard Medical School*

Dr. Bellinger has studied the effects of a number of toxic agents on cognition in children, including lead, manganese, and arsenic. He was the PI on a major longitudinal prospective study on lead. He will discuss the important interaction between the social environment, including but not limited to the family environment, and exposure to environmental chemicals on adverse outcome.

#### Round-table Discussion and Q&A

Discussion Leaders: Deborah Rice, David Bellinger

Discussants:

Session Speakers plus:

Jean Harry ~ *NIEHS*

Joseph Jacobson (invited)

Jason Richardson ~ *UMDNJ & EOHSI*

Bernard Weiss ~ *University of Rochester*

Sunday Sept. 17<sup>th</sup>

5:00 – 7:00 PM . . .

Meet & Greet

Welcoming Reception

Sunday Evening 17 Sept 2006 6:30 – 9:30 PM

#### Informal Workshop & Think Tank

#### SESSION 3: THE EPIDEMIC OF CHILDHOOD DEVELOPMENTAL DISORDERS:

“Why are so many children sick . . . and what can be done to help them?”

Moderator: **Martha Herbert, MD, PhD**

**Theme:** Over the past several years there has been a growing body of research which documents the existence of distinct medical abnormalities in children diagnosed with neurodevelopmental disorders, specifically autism. These abnormalities include thiol deficiencies, impaired methylation, oxidative stress, inflammatory bowel disease, immune system abnormalities, mitochondrial deficiencies, decreased cerebral perfusion and increased body burdens of heavy metals with corresponding low levels of excretion.

7:00 - 7:15 PM

### Why Are so Many Children Sick?

Mark Blaxill - Vice President, SafeMinds; Research Chair

Mr. Blaxill will review the epidemiology survey literature in autism with a special focus on the question of time trends. The review will include the controversies on time trends and demonstrate the weakness in the argument that cast doubt on the increasing rates. These arguments have crucial implications for policy, funding and research.

7:15 - 8:30 PM

### What Can Be Done To Help Them?

Clinicians will discuss how to appropriately work up a child with developmental disorders and review some of the cutting edge therapies which are resulting in marked improvement in both behavior and overall general health.

**Panelists:** *The panelists are physicians whose primary specialty is the treatment of children with Autism.*

Nancy O'Hara, MD, Steve Kahler, MD, Jerry Kartzinel, MD, Elizabeth Mumper, MD

**Nancy O'Hara, MD, MPH** is a board certified pediatrician. Prior to her medical career she taught children with autism. Dr. O'Hara's practice is a consultative, integrative model that looks at the biochemical, immunologic, gastroenterologic and neurologic problems of each child. Each initial consultation integrates the information from a detailed history, physical exam, laboratory investigation, and dietary and behavioral evaluations to provide an individualized approach for each child. Dr. O'Hara is also the Assistant Medical Director for physician training for DAN! and the coordinator of the practitioner mentoring program.

**Steve Kahler, MD** received his MD degree from Duke, trained in Pediatrics at UCSD, and in clinical and biochemical genetics at UNC-Chapel Hill. His major interests include inborn metabolic errors. He worked at Duke for 14 years where he was part of the team that developed expanded newborn screening. He worked in Melbourne, Australia for five years, returned to the US (Johns Hopkins) in 2003, and moved to Arkansas in 2005. He has been interested in autism for many years, particularly the children who are responsive to diet changes, as they are similar in this way to children with defined metabolic errors. He has been part of the Defeat Autism Now! (DAN!) network since the first meeting in 1995. In Arkansas he is working closely with Jill James, PhD, on biochemical aspects of autism.

**Jerry Kartzinel, MD** is the Director of Pediatric Medicine at The Thoughtful House Center for Children. Dr. Kartzinel practiced general pediatrics in private practice for 10 years until his fourth boy was diagnosed with autism. He has since dedicated his practice of medicine to those with autism and neurodevelopmental delays. His practice is solely devoted to the research and treatment of Autism and other neurodegenerative disorders. His approach includes a comprehensive history and physical exam, and laboratory investigations that seek to find what is biologically different in a child. Once found, he implements therapeutic interventions and monitors closely how they affect restoration of health and behaviors. His current research interests include quelling chronic inflammation and the augmentation of the methylation pathway.

**Elizabeth Mumper, MD** is Medical Director for physician training for Defeat Autism Now! (DAN!). She is president and CEO for Advocates for Children in Lynchburg Virginia. She is also associate professor of Medical Specialties, Pediatrics at Virginia College of Osteopathic Medicine. Dr Mumper attended medical school at the Medical College of Virginia and completed her pediatric residency at the University of Virginia where she was invited to spend an additional year as Chief Resident. Her current research interests include: intestinal biopsies, natural killer cells and glutathione dysfunction, hyperbaric oxygen therapies, and methylation abnormalities in children with Autism. Dr Mumper serves on the DAN! Europe Board and also the MINDD Foundation Board in Australia.

8:30 - 8:40

### Video of Before and After Therapy

This session will end with a brief video of several children diagnosed with autism before and after targeted clinical interventions.

8:40 - 9:00

### QUESTION AND ANSWER SESSION

Monday Morning

18 Sept 2006

8:30 AM - 11:30

### Plenary Session

## SESSION 4. ENVIRONMENT AND NEURODEVELOPMENTAL DISORDERS: CROSS-CUTTING ISSUES & TRANSLATIONAL RESEARCH

**Session Co-Chairs:** Deborah Cory-Slechta, PhD  
Don Schmechel, MD

This session will consist of "Anchor Talks" to raise our awareness of the complexities and cross-cutting issues to be taken into account in translational research efforts to cure, conquer or alleviate childhood neurotoxic disorders, abnormal aging and neurodegenerative disorders.

8:30 - 8:40 AM

### Introduction

Deborah Cory-Slechta, PhD ~ UMDNJ and Rutgers University

8:40 - 9:10 AM

### Bionetworks of Risk Factors in Neurotoxicology: Implications for Risk Assessment and Translational Research

Deborah Cory-Slechta, PhD ~ UMDNJ and Rutgers University

It is increasingly recognized that many neurodegenerative and neurodevelopmental diseases and disorders arise not from unitary causes, but from the collective interactions of various risk factors, both risk-increasing and risk-mitigating. Contributing factors include environmental, behavioral, genetic and host-based risks, as well as intercurrent disease states inherent to human populations. It is likely that progression, severity and prognosis for any person reflects their individual collection of risk factors, and that the broad array of phenotypes observed for many nervous system diseases and disorders reflects the population variance in risk factors. Experimental studies reveal evidence of cumulative neurotoxicity from intermittent contacts with risk factors across the lifespan, as well as permanent effects in response to exposures restricted to periods of early development.

9:10 - 9:40 AM

### Of Mercury, Microbes, Mice and Men: How Translational Thinking Can Accelerate Discovery of the Role of Environmental Factors in Neuropsychiatric Disorder Pathogenesis

Mady Hornig, MD, MA ~ Columbia University

Translation is a continuous and bidirectional process: epidemiologic and clinical research findings ideally inform the design of studies in animals and in tissue culture, just as findings from animal and tissue culture experiments provide clues to strategies for risk identification, prevention, and intervention in humans. Developmental neurotoxicity poses unusual challenges for translational research. It is difficult to determine the degree to which equivalence may be established for the timing of pre- and/or postnatal exposures with respect to outcomes across species; this is even more complex for agents or doses of agents that involve gene-environment-timing interactions, or where immune or oxidative stress mediators may be important in pathogenesis. Establishing equivalence in timing for one neural cell type may lead to important differences in maturation of other cell types; equivalence for neural components may lead to deviation across species in immune system or other organ maturation that may be important in pathogenesis. Furthermore, neuropsychiatric

outcomes may not only be difficult to model in animals due to the differences in repertoire but superficially similar behaviors may rely upon different circuitry or involve different constraints or maturational timetables. Specialized strategies expedite integration of data from animal models and epidemiologic studies and the discovery of the mechanisms by which toxins or infectious agents may trigger or amplify adverse host responses and lead to disturbances of neuropsychiatric functioning.

9:40 – 10:10 AM

**Art, Creative Energy, Memory, Mood, and Inflammation: Lessons for CNS Development and Vulnerability**

Don Schmechel, MD ~ Duke University

Complex genetic and environmental interactions contribute to development, aging and neurodegenerative disorders (AD, vascular dementia, and related disorders). We will focus on the paradigm of alpha-1-antitrypsin (AAT) – an inflammatory response gene whose polymorphisms alter vulnerability to toxic exposures affecting liver and lung, but also CNS neurotoxicity. From a series of 1200+ patients presenting with mood and memory complaints, we demonstrate that AAT polymorphisms may also modulate CNS development affecting artistic vocation, creative energy, and mood. Gene-gene interactions with APOE and hemochromatosis will be discussed in AAT context. Proposed mechanisms are through effects on inflammation, lipids and metal homeostasis.

10:10 – 10:30 AM Break

10:30 – 11:00 AM

**Autism: A Brain Disorder or a Disorder that Affects the Brain?**

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

Autism has been considered a genetically determined neuropsychiatric disorder. But increases in diagnosis suggest environmental influences, while the physical symptoms commonly present (especially gastrointestinal and immune) suggest a multisystem disorder, most likely with common underlying mechanisms driving the panoply of symptoms. This perspective opens horizons for including prevention, treatment and symptom reduction in research, clinical practice and policy.

11:00 – 11:30 AM

**Toward Understanding Autism's Complexities**

Isaac Pessah, PhD ~ University of California, Davis

Autism is a neurodevelopmental disorder that presents in early childhood with deficits in social reciprocity and communication, and by unusual repetitive behaviors. Autism is a complex underlying genetic predisposition that may involve >10 defective loci, each insufficient to account for autism. Thus the etiology of autism is currently unknown. The persistent increase in prevalence of autism over the last 25 years suggests that the complex set of genetic factors may enhance the susceptibility of autistic children to the harmful effects of environmental exposure. Thus genetic and environmental factors are likely to contribute to the progression and severity of autism.

11:30 – 12:00 PM

**Discussion**

**Monday Afternoon 18 Sept 2006 1:00 – 5:00 PM**

**Symposium**

**SESSION 5-A. ENVIRONMENTAL MODULATION OF NEUROTOXICANTS IN MILITARY-RELEVANT OPERATIONAL ENVIRONMENTS**

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

**Theme:** Topics presented in this session will include current research efforts examining the role of ambient temperature, metabolic interactions, and co-exposures and susceptibility on neurotoxicant exposure and effects and describing newer methodologies to measure persistent biomarkers of neurotoxicant exposures. This session will include 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: Environmental Modulation of Neurotoxins in Military-Relevant Environments**

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

1:20 – 2:00 PM

**Role of Environmental Heat and Cold Stress on the Physiological Response to Organophosphates and Other Toxicants**

Christopher J. Gordon, PhD ~ US EPA

This presentation will provide a summary of recent research efforts concerning the role of heat and cold stress and their influence on the thermoregulatory responses to environmental neurotoxins such as organophosphate insecticides.

2:00 – 2:40 PM

**Human Metabolic Interactions of Deployment-Related and Other Environmental Chemicals**

Ernest Hodgson, PhD ~ North Carolina State University

Current laboratory research to examine metabolic interactions between different xenobiotics (such as organophosphate insecticides, permethrin, the repellent DEET, and jet fuel components) will be presented.

2:40 – 3:00 PM Break

3:00 – 3:40 PM

**The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant**

Nancy Fiedler, PhD ~ EOHHS/Robert Wood Johnson Medical School

Current research progress on a project examining the co-exposure of diesel exhaust and psychological stress in susceptible individuals will be reported.

3:40 – 4:20 PM

**Persistent Biomarkers of Exposure of Potentially Neurotoxic Compounds**

Daniel Noort, PhD ~ TNO Defense, Security & Safety

This presentation will provide a summary of newer methodologies to measure persistent biomarkers of neurotoxins.

4:20 – 5:00 PM

**Discussion, Session Summary and Research Needs**

Monday Afternoon 18 Sept 2006 1:00 – 5:00 PM

**Platform Session**

**SESSION 5-B. ADVANCING THE SCIENCE OF AUTISM SPECTRUM DISORDERS**

Session Co-Chairs: **Martha Herbert, MD, PhD**  
**Isaac Pessah, PhD**

Theme: Autism is defined behaviorally, as a syndrome of abnormalities involving language, social reciprocity and hyperfocus or reduced behavioral flexibility. It is clearly heterogeneous, and it can be accompanied by unusual talents as well as by impairments, but its underlying biological and genetic basis is unknown.

The reframing of autism from a genetically determined neuropsychiatric disorder to a set of treatable, whole-body illnesses that have environmental influences is being driven by increases in diagnosis, the common presence of physical symptoms (especially gastrointestinal and immune) and growing reports of substantial clinical improvement. Recognizing autism as a multisystem disorder, most likely with common underlying mechanisms driving the panoply of symptoms, opens horizons for including prevention and treatment in research, clinical practice and policy.

1:00 – 1:10 PM

**Advancing the Science of Autism Spectrum Disorders: Introduction**

**Martha Herbert, MD, PhD and Isaac Pessah, PhD**

1:10 - 1:40 PM

**Autism: The Clinical Picture**

**Jeff Bradstreet, MD ~ ICDRC – Florida Hospital, Celebration**

Dr Bradstreet limits his large clinical/research based practice in Florida to autism spectrum disorders. He will integrate and present the observations of oxidative stress, insufficient thiol metabolism, poor heavy metal excretion with resultant increases in total body metal burden and mitochondrial dysfunction, along with the further evidence of concurrent immunological dysregulation in both the gut and the brain. This will be presented with a perspective for selection of clinically useful biomarkers and possible interventions.

1:40 – 2:10 PM

**Evidence and Implications of Redox Imbalance in Autistic Children**

**Jill James, PhD ~ Arkansas Children's Hospital Research Institute**

Dr. James will present evidence that many children with autism exhibit a significant decrease in plasma glutathione redox ratio (GSH/GSSG) suggesting the presence of chronic oxidative stress. An impaired glutathione-dependent antioxidant and detoxification capacity would create a fragile homeostasis with reduced capacity to detoxify environmental exposures. These metabolic results suggest the provocative possibility that some autistic behaviors may be a neurologic manifestation of a genetically based environmentally sensitive metabolic derangement. A more metabolic and systemic approach to autism would encompass not only the neurologic manifestations but also the gastrointestinal and immunologic pathology associated with autism. Moreover, individualized treatment strategies directed toward correcting specific metabolic imbalance could potentially ameliorate some autistic behaviors and offer insights into the heterogeneity within the autism spectrum.

2:10 - 2:30

**Glutathione- Dependant Methionine Synthase Activity: A Sensitive Target for Neurodevelopmental Toxins and its Role in Autism Spectrum Disorders**

**Richard Deth, PhD ~ Northeastern University, Boston**

By virtue of its location at a key metabolic intersection, methionine synthase (MS) activity influences both methylation and redox buffering.

Oxidation of its cobalamin (Cob) co-factor halts the methionine cycle and diverts homocysteine (HCY) towards cysteine and glutathione (GSH) synthesis, particularly during oxidative stress. We earlier showed that a number of neurodevelopment toxins, including ethanol and the vaccine preservative thimerosal, along with inhibitors of PI3 kinase and MAP kinase signaling pathways, potently inhibit MS activity in human SH-SY5Y neuronal cells. This inhibition is due to reduced levels of GSH and MS activity can be fully restored by GSH supplementation. Methylcobalamin is required for MS activity in SH-SY5Y cells, and GSH is essential for MeCob synthesis from hydroxocobalamin. A comparison of MS activity in rat liver vs. different brain regions showed that the cerebral cortex has a particular dependence upon MeCob. Nitrous oxide, which promotes Cob oxidation, inhibits MS in both liver and cortex when assayed with hydroxocobalamin, but activity in cortex is completely restored by MeCob, whereas activity in liver is not. Thus MS activity requires MeCob in neuronal cells and cortex, and neurodevelopmental toxins impair methylation by lowering the cellular level of GSH.

2:30 – 2:45 PM Break

2:45 - 3:15

**How Genetic and Temporal Factors Constrain Outcomes after Environmental Exposures: Immune-mediated Mouse Models of Neurodevelopmental Disorders**

**Mady Hornig, MD, MA ~ Columbia University**

Dr. Hornig will present her work on genetic and maturational factors in mouse models of immune-mediated neurodevelopmental damage following exposure to low level toxicants such as thimerosal and other environmental immune disrupters. She found that low dose exposure to thimerosal during critical windows of postnatal development in a mouse strain-dependent model resulted in enlarged brains and abnormal social and learning behavior in conjunction with thimerosal-induced autoimmune disturbances. She did not find these same abnormalities in mice exposed to the same exposure but without the genetic susceptibility factors. Through microarray analyses, she is identifying key pathways associated with the alterations in developmental brain circuitry and function in the model, and laying the foundation for elucidation of the pathogenesis of autism and discovery of predictive biomarkers and novel interventional strategies.

3:15 – 3:45 PM

**Critical Mechanisms, Moving Targets: Understanding Immune System Modulation in Autism Risk**

**Isaac Pessah, PhD ~ University of California, Davis**

The complexity of autism presents unique opportunities and challenges to study interactions among multiple susceptibility genes, and how epigenetic factors and exposure to environmental modifiers may contribute to variable expression of autism, and autism-related traits. The major goals of this presentation are to familiarize attendees with (1) genetic and epigenetic mechanisms implicated in altering the ratio of excitation/inhibition within central processing circuits of the autistic brain; including nicotinic, glutamatergic, gabaergic, and calcium signaling systems; (2) early immunologic differences in humoral and cellular immunity identified in autistic children that may impact brain development and behavior; and (3) approaches that toxicologist can develop in mouse models to better understanding how specific genetic or epigenetic defects alter sensitivity to chemical exposure(s) of current concern to children's health and autism.

3:45 – 4:05 PM

**Hyperbaric Oxygen Therapy in Autistic Children Improves Symptomology, Decreases Markers of Inflammation, and Has Neutral Effects on Oxidative Stress.**

**Dan Rossignol, MD ~ University of Virginia**

Autism is a neurodevelopmental disorder currently affecting as many as 1 out of 166 children. Multiple studies have found that autism is characterized by cerebral hypoperfusion which correlates with many

core features including repetitive, self-stimulatory and stereotypical behaviors, and impairments in communication, sensory perception, and social interaction. Autistic individuals also evidence gastrointestinal and neuroinflammation, increased markers of oxidative stress, and relative mitochondrial dysfunction. Hyperbaric oxygen therapy (HBOT) has been used to treat conditions marked by diminished cerebral blood flow to overcome hypoperfusion through the increased delivery of oxygen. HBOT also demonstrates strong anti-inflammatory properties, might decrease oxidative stress, and can increase the production of mitochondria and circulating stem cells. Based upon these research findings, we hypothesized that HBOT would improve symptoms in autistic children. *Conclusions:* HBOT ameliorates some symptoms in autistic children in this prospective open label study. Further evaluation with a larger double-blind placebo-controlled study to verify these findings is indicated.

**4:05 – 4:30 PM**

**Summary of Sunday Evening Workshop**

**Martha Herbert, MD, PhD** ~ *Massachusetts General Hospital; Harvard Medical School*

Widespread volumetric, oxidative stress and inflammatory neuroanatomical changes as well as compromised brain coordination in autism are arguably consistent with an environmental etiology; they may be final common pathways resulting from mechanisms with heterogeneity of triggers, timing and vulnerabilities. Clinical interventions aimed at supporting environmentally responsive pathways have been combined in various treatment algorithms whose differential effectiveness in the autism population may indicate inter-individual differences in both vulnerability and immunotoxicological history. Since many of these treatments are GRAS ("generally recognized as safe") they may provide valuable research probes for uncovering mechanisms of disease, identifying subgroups, and optimizing and innovating treatment targets.

**4:30 – 5:00 PM**

**Roundtable Discussion:**

***"Advancing the Science of Autism Spectrum Disorders"***

Identify the evidentiary gaps in knowledge and brainstorm necessary next steps.

*Moderators:* Martha Herbert, MD, PhD and Isaac Pessah, PhD

**5:00 PM – Adjourn Monday Scientific Sessions.**

*Refresh and walk or take a trolley, taxi, bus or hotel van to the Clinton Presidential Library for camaraderie, tour and dinner. This special social evening is included in the conference registration fee.*

**Monday Evening 18 Sept 2006 5:45 – 9:45 PM**

**5:45 PM – 9:45 PM**

**Hosted Social Evening  
Tours & Dinner  
at the**

**William J. Clinton  
Presidential Library**

**Tuesday Morning 19 Sept 2006 8:30 AM – 11:50**

**Plenary Session**

**SESSION 6. NEUROTOXICITY AND THE PATH FROM EARLY BRAIN DEVELOPMENT TO AGING**

**Session Chair: Bernard Weiss, PhD**

**Theme:** In the past, we often tended to distinguish two realms of neurotoxicity based on chronological age. One centered on early development, the other on senescence. It is now profoundly clear that his distinction is arbitrary. The two realms are simply two narrow sectors from the arc of the lifespan, which itself is fundamentally a developmental journey. The arbitrary nature of this distinction becomes apparent when what are labeled as developmental disorders, such as autism, are seen to share biological mechanisms with neurodegenerative disorders such as Parkinson's disease. In parallel, early life events, whose influence is not evident at the time, may leave traces that only emerge decades later, when the patterns of vulnerability have changed. But the connection is not direct. When speaking of the aging brain we should recognize that it represents a mosaic of possibilities rather than a hapless monolith; some regions diminish, some even prosper. Finally, the legacy of earlier events is inevitably transformed by a cascade of intervening circumstances, such as stress, acting on this regrettable trek. This plenary session offers further perspectives on the principle that neurotoxicity is not simply a property of a designated chemical exposure, but is also a property dependent on the history and state of the host.

**8:30 – 8:40 AM**

**Introduction**

**Bernard Weiss, PhD** ~ *University of Rochester*

**8:40 – 9:10 AM**

**Neurotoxic Byways on the Path to Aging**

**Bernard Weiss, PhD** ~ *University of Rochester*

The brain's journey from childhood to senescence may appear continuous, but it surely is not smooth. In accompanying this journey, environmental neurotoxicants exert their influence in differing ways and with differing potencies at different times.

**9:10 – 9:40 AM**

**Inflammation and Repair in the Aging Brain: What a Difference a Decade Makes**

**Jean Harry, PhD** ~ *NIEHS*

The activation of an inflammatory response in the brain can serve as neuroprotective or neurodestructive. Quite often this distinction depends upon the ongoing events. More recently, distinctions, as a function of age, are beginning to emerge. Gaining a better understanding of these events as they impact the developing brain, the young adult, and the aging brain will significantly advance our understanding of the role and impact of inflammation as it relates to brain injury and repair.

**9:40 – 10:10 AM**

**Cumulative Impact of Lead Exposure and Stress Over the Lifespan**

**Deborah Cory-Slechta, PhD** ~ *UMDNJ and Rutgers University*

Elevated lead (Pb) exposures preferentially impact low socioeconomic status (SES) populations, the same groups thought to sustain the highest levels of environmental stress. Low SES itself is a known risk factor for various disease processes and behavioral disorders, presumably through its association with chronic stress and associated elevation of glucocorticoids. As co-occurring risk factors, therefore, Pb and stress could interact, such that combined exposures could produce greater neurotoxicity than either risk factor alone, and/or that potentiated effects could occur.

10:10 – 10:30 AM Break

10:30 – 11:00 AM

**Translational Research in Alzheimer's Disease and Parkinson's Disease**

Don Schmechel, MD ~ Duke University

W. Sue T. Griffin, PhD ~ University of Arkansas for Medical Sciences and Geriatric Research Education Clinical Center, VAMC

Translational research in Alzheimer Disease and Parkinson Disease must address the interplay of complex genetic and environmental factors and how these may result in both regional selectivity of injury and sparing. AD and PD may share some common genes affecting age of onset and cell repair as well as having unique factors specific to each illness. Both involve oxidative stress mechanisms, exaggeration of normal aging changes, and possible problems in disposal of incorrectly folded or processed peptides and oligomeric arrays. Translational research must result in tangible answers for the detection and treatment of these chronic human illnesses whose biology of onset may differ from that of progression. The challenge is great and will need involve pathology, cell system models, animal models, and recursive information from the study and treatment of humans at risk and with disease.

11:00 – 11:30 AM

**Aging and Environmental Health: EPA's Plan for Exposure-Dose-Response Research.**

Andrew M. Geller, PhD ~ NHEERL, US EPA

The rapid growth in the number of older Americans has many implications for public health, including the need to better understand the risks posed by environmental exposures to older adults. Biological capacity declines with normal aging; this may be exacerbated in individuals with pre-existing health conditions. In recognition of this issue, the U.S. EPA has developed a research program to better understand the relationships between external pollution sources → human exposures → internal dose → early biological effect → and adverse health effects for older adults. This presentation will discuss EPA's evolving strategy to understand the potential susceptibility of older adults to environmental insult and promote environmental health in older adults, and focus on issues specific to older adults in modeling exposure and the health consequences of exposure to pollutants in healthy older adults and in individuals with pre-existing health conditions.

11:30 – 11:50 AM

**Roundtable Discussion**

**"Aging and Environmental Health"**

**Moderator:** Deborah Rice, PhD

Despite our acknowledgement that development--and aging--are basically identical and continuous processes across the total lifespan, it would be deceptive to model them as smooth curves. Although they might not reveal sharp discontinuities, the road, so to speak, is bumpy and pitted (the seven ages of man--and woman?). It traverses periods of both diminished and aggravated vulnerabilities. Adolescence is one such period. Menopause is another. How many such periods can be distinguished? How can they be modeled in our usual laboratory rodents? And are calendar years a proper definition of age? Do such questions deserve more attention than we usually give them?

**Panel Discussant:** Session Speakers plus:

Sue Griffin, PhD ~ University of Arkansas for Medical Sciences & VAMC

Mady Hornig, MD, MA ~ Columbia University

Tuesday Afternoon 19 Sept 2006

1:15 – 3:15 PM

**Focus Session**

**SESSION 7-A-1: DEVELOPMENTAL NEUROTOXICITY I**

**Session Chair:** Terri Damstra, PhD

**Co-Chair:** Didima de Groot, PhD

1:15 – 1:35 PM

**Principles for Evaluating Health Risks in Children Associated with Exposure to Chemicals: The Need for a Life-Stage Approach.**

Terri Damstra, PhD ~ World Health Organization, International Programme on Chemical Safety

1:35 – 1:55 PM

**Linkages between Early Childhood Lead Exposure and Performance on End of Grade Exams.**

Marie Lynn Miranda, PhD ~ Duke University

1:55 – 2:15 PM

**Gestational Environmental Contaminant Exposure Effects on NMDA/AMPA-Dependent Plasticity Mechanisms in Adult Rat Hippocampus and Sensory Cortex.**

Darryl B. Hood, PhD ~ Meharry Medical College

2:15 – 2:35 PM

**Effects of Maternal Diet on Offspring's Vulnerability to Environmental Exposure**

Didima de Groot, PhD ~ TNO Quality of Life, Zeist, The Netherlands

2:35 – 2:50 PM

**A Proxy Measure of Prenatal Testosterone Exposure is Related to Gray Matter Volume in Human Neonates**

Rebecca C. Knickmeyer, PhD ~ University of North Carolina

2:50 – 3:05 PM Break

Tuesday Afternoon 19 Sept 2006

3:05 – 5:00 PM

**Platform Session**

**SESSION 7-A-2: ROLE OF ENVIRONMENTAL CONTAMINANTS IN THE ETIOLOGY OF ADHD-LIKE BEHAVIORS**

**Session Chair:** Richard Seegal, PhD

**Co-Chair:** Paul W. Stewart, PhD

3:05 – 3:20 PM

**An Overview: Developmental Neuroendocrine Effects of PCBs and PBDEs: Parallels with ADHD**

Richard Seegal, PhD ~ Wadsworth Center, NYSDOH

3:20 – 3:40 PM

**Perinatal PCB Exposure, Deficits in Inhibitory Control and Hypofunction of Prefrontal Dopamine: Parallels with ADHD**

Susan L. Schantz, PhD ~ University of Illinois at Urbana

3:40 – 3:55 PM

**Is Impulsive Behavior and Impaired Response Control a Final Common Path for PCB, MeHg and Pb Neurotoxicity in Children?**

Paul W. Stewart, PhD ~ State University of New York at Oswego

3:55 – 4:15 PM

**Developmental Pesticide Exposure Reproduces Features of Attention-Deficit Hyperactivity Disorder**

Jason R. Richardson, PhD ~ *University of Medicine and Dentistry-New Jersey/Robert Wood Johnson Medical School and Environmental and Occupational Health Sciences Institute*

4:15 – 4:35 PM

**Smoking During Pregnancy: Effects on Arousal and Attentional Brain Systems**

Edgar Garcia-Rill, PhD ~ *University of Arkansas for Medical Sciences*

4:35 – 5:00 PM

**Discussion**

Tuesday Afternoon 19 Sept 2006 1:15 – 5:00 PM

**Symposium**

**SESSION 7-B: NEUROPROTECTION BY ALZHEIMER'S DRUGS**

Session Chair: Toshio Narahashi, PhD  
Co-Chair: Edson X. Albuquerque, PhD

**Theme:** Alzheimer's disease is one of the most serious neurological disorders afflicting aged individuals. While many studies have been performed to determine the causes of the disease, no definitive explanations have yet been offered, and no prevention or cure of the disease has yet been developed. Thus, only symptomatic drug treatments to improve the patients' conditions are available at the present moment. In the brain of an Alzheimer's disease patient, both the cholinergic system and the glutamatergic system are down-regulated, and most drugs currently target these neuroreceptor systems. The actions of these drugs are basically "neuroprotection" via a variety of mechanisms. The present symposium will address this issue.

1:15 – 1:30 PM

**Overview: Neuroprotection by Alzheimer's Drugs**

Toshio Narahashi ~ *Northwestern University Medical School*

1:30 – 2:10 PM

**Synuclein-linked neuroimmunity and the pathogenesis of Parkinson's disease**

Howard E. Gendelman ~ *University of Nebraska, Omaha*

The pathology of Parkinson's disease (PD) includes loss of dopaminergic neurons in the substantia nigra, nitrated  $\alpha$ -synuclein ( $\alpha$ -syn) enriched inclusions or Lewy bodies and neuroinflammation. We reasoned that PD-associated oxidative protein modifications create novel antigenic epitopes capable of both microglial and peripheral adaptive T cell responses exacerbating nigrostriatal degeneration. Nitrated  $\alpha$ -syn was readily detected in cervical lymphoid tissue in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) intoxicated mice. Using a combination of genomic (gene arrays) and proteomic (SELDI-TOF, liquid chromatography-tandem mass spectrometry, Ettan DIGE, and protein array) methods, a fingerprint of  $\alpha$ -syn activated microglia was also generated. Nuclear factor- $\kappa$ B transcriptional activation and its related signaling cascades that affect cell metabolism and immune response signaled this  $\alpha$ -syn microglial response. Microglial ROS production was also induced, in a dose-dependent manner, by activation with aggregated nitrated  $\alpha$ -syn. This was inhibited by voltage-gated potassium current blockade, and to a more limited degree, by chloride current blockade. Transfer of T cells from mice immunized with oxidized  $\alpha$ -syn led to prolonged neuroinflammation and significant increases in dopaminergic cell loss. These data support the notion that nitrotyrosine modifications in  $\alpha$ -syn induce both an innate neuroinflammatory response as well as serving to break immunological tolerance to self. Both processes serve to exacerbate the pathobiology of PD.

2:10 – 2:50 PM

**Galantamine-Memantine Co-application: Beneficial Effect**

Toshio Narahashi, PhD ~ *Northwestern University Medical School*

Alzheimer's disease is associated with down-regulation of the cholinergic and NMDA systems. Whereas several drugs have been used for the symptomatic treatment of Alzheimer's disease patients, their efficacy is limited. Thus, combined use of two drugs with different mechanisms of action might improve the effectiveness. Here we present the *in vitro* basis for the beneficial action of combining galantamine, a stimulator of the ACh and NMDA systems, with memantine, a blocker of the NMDA system.

2:50 – 3:05 PM Break

3:05 – 3:45 PM

**A Novel Approach for the Treatment of Organophosphorous Compound Poisoning: Implications for Alzheimer's Disease**

Edson X. Albuquerque, PhD ~ *University of Maryland, Baltimore*

The need to identify a safe and effective means to protect against the lethal effects of organophosphorous (OP) compounds, including OP pesticides and nerve gases such as soman and sarin, has become even more pressing in view of terrorist threats. In our recent studies using guinea pigs, we have been able to identify a combination of agents that confers a degree of protection that far surpasses any currently available treatment regimens. Protection can be achieved by administration prior to OP exposure, a feature that could be very helpful in the case of first responders to an incident involving OP assault.

3:45 – 4:25 PM

**Nicotinic Treatment for Both Symptomatic Relief and Attenuation of Cognitive Decline with Aging and Alzheimer's Dementia**

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

Nicotinic receptor systems have been found to be critically important for cognitive function including attention, learning and memory. Nicotinic antagonists generally impair cognitive performance and nicotinic agonists including nicotine improve it. Nicotine skin patches have been shown to significantly improve cognitive function impaired by aging as well as Alzheimer's disease. In addition, there is preclinical evidence that nicotinic treatment can attenuate neurodegeneration and may hold promise for reducing the descent into Alzheimer's dementia.

4:25 – 5:00 PM

**Open Discussion, Session Summary and Research Needs**

Tuesday Evening 19 Sept 2006 7:00 – 9:00 PM

**Cash Bar & Snacks**

**Poster Session**

**SESSION 8: GENERAL POSTER SESSION**

Session Co-Chairs: TBA

**Poster Presentations are listed on Program pages 13 - 15**

**Pre-Doctoral Student Award Committee: TBA**

**Post-Doctoral Student Award Committee: TBA**

**NEUROTOXICOLOGY POSTER SESSION:**

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 Genera 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.

#### **STUDENT AWARD COMPETITION:**

Competing students are expected to give an overview of their work in 2-3 minutes to the judges followed by a brief set of questions and answers. Originality, significance, hypothesis, presentation material and style, as well as knowledge of the subject, will be considered in selecting the winners. All papers presented for the Student Awards must be presented from poster.

*(Posters will be on display from Sunday – Wednesday AM)*

*Judging of Pre- and Postdoctoral Student Awardees will be made from 7:00 – 8:00 PM*

#### **8:45 PM ~Presentation of Student Awards**

**Wednesday Morning 20 Sept 2006 8:30 AM – 12:00 NOON**

#### **Symposium**

#### **SESSION 9-A. HEALTH EFFECTS OF MANGANESE EXPOSURE: HUMANS & ANIMAL MODELS I**

**Session Chair: Michael Aschner, PhD**  
**Co-Chair: Anumantha Kanthasamy, 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**

#### **Health Effects of Manganese Exposure: Humans & Animal Models: Introduction**

Michael Aschner, PhD ~ *Vanderbilt University*

**8:40 – 9:15 AM**

#### **Potential Neurotoxic Responses in Rats After Pulmonary Administration of Welding Fume With Varying Concentrations of Manganese**

James Antonini, PhD ~ *NIOSH*

Questions persist regarding a possible causal association between neurological effects in welders and the presence of manganese (Mn) in welding fume. Here, our objective was to examine the potential neurotoxic effect of Mn in rats after pulmonary administration of different welding fumes.

**9:15 – 9:50 AM**

#### **Where Does Mn<sup>2+</sup> Inhibit Oxidative Phosphorylation?**

Thomas Gunter, PhD ~ *University of Rochester Medical School*

Oxidative phosphorylation produces about 92% of the ATP used by animal cells. Intramitochondrial [Ca<sup>2+</sup>], an important factor controlling ATP production, activates a series of sites in the metabolic pathways which would otherwise limit the ATP production rate. Ca<sup>2+</sup> activates NADH production at pyruvate dehydrogenase, isocitrate dehydrogenase, and  $\alpha$ -ketoglutarate dehydrogenase, and ATP production at the F<sub>1</sub>F<sub>0</sub> ATP synthase and can increase the rate of ATP production up to several fold. Both we and others have found that Mn<sup>2+</sup> inhibits oxidative phosphorylation.

**9:50 – 10:20 AM Break**

**10:20 – 10:55 AM**

#### **Manganese Upregulates Cellular Prion Proteins and Inhibits the Rate of Proteinase-K Dependent Proteolysis in Cell Culture Models of Prion Diseases.**

Anumantha Kanthasamy, PhD ~ *Iowa State University*

The accumulation of the proteinase-K resistant form of prion protein (PrP<sup>Sc</sup>) is a key pathological feature of prion diseases. However, the cellular mechanisms underlying conversion of normal cellular prion (PrP<sup>C</sup>) to PrP<sup>Sc</sup> in prion disease is not well understood. Binding of the divalent cation copper to the octapeptide repeat sequences of PrP<sup>C</sup> has been shown to be critical to the stability of the protein.

**10:55 – 11:30 AM**

#### **Changes in Dietary Iron Levels Affect Brain Manganese Accumulation and Distribution**

Michael Aschner, PhD ~ *Vanderbilt University*

Occupational exposure to manganese (Mn) has been associated with the onset of psychological and motor symptoms in some individuals, leading to a phenotype called manganism. Brain Mn accumulation has also been documented in patients with liver failure, those receiving parenteral nutrition or individuals with iron (Fe) deficiency. As it is known that Mn and Fe are transported by the same proteins, we wanted to determine whether changes in dietary Fe levels alter the brain Mn deposition patterns.

**11:30 – 12:00 PM**

#### **Discussion**

**Wednesday Morning 20 Sept 2006 8:30 – 12:00 NOON**

#### **Platform Session:**

#### **SESSION 9-B: DEVELOPMENTAL NEUROTOXICITY II**

**Session Chair: Merle G. Paule, PhD**  
**Co-Chair: Mary Ann Wilson, PhD**

**8:30 – 8:35 AM**

#### **Introduction & Overview**

Merle G. Paule, PhD ~ *National Center for Toxicological Research/FDA*

**8:35 – 9:00 AM**

#### **A Novel Rat Brain Atlas for Neurotoxicity Testing**

Didima de Groot, PhD ~ *TNO Quality of Life, Zeist, The Netherlands*

9:00 – 9:25 AM

**Low Dose Early Postnatal Diazinon Exposure Causes Impaired Working Memory on the Radial-Arm Maze in Rats During Adulthood.**

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

9:25 – 9:50 AM

**Neonatal Lead Exposure Impairs Plasticity in Developing Rat Somatosensory Cortex**

Mary Ann Wilson, PhD ~ *Kennedy Krieger Research Institute*

9:50 – 10:15 AM

**Neurobehavioral Assessment Using A Functional Observational Battery and Motor Activity in Rats Perinatally Exposed to DE-71.**

Virginia (Ginger) C Moser, PhD ~ *NHEERL/ORD, US EPA*

10:15 – 10:30 AM Break

10:30 – 10:55 AM

**NMDA-Type Glutamate Receptors and Anesthetic-Induced Neuronal Oxidative Stress During Development**

Cheng Wang, MD, PhD ~ *National Center for Toxicological Research/FDA*

10:55 – 11:20 AM

**Cross-Cultural Comparison of a Neurobehavioral Test Battery for Children.**

Diane S Rohlman, PhD ~ *Center for Research on Occupational and Environmental Toxicology, Oregon Health & Science University*

11:20 – 11:45 AM

**Neuropsychological Effects of Dental Amalgam in Children: A Randomized Trial**

David C. Bellinger, PhD, MSc ~ *Harvard Medical School*

There has been great concern (and controversy) about the possible health effects associated with the use of mercury-containing amalgam to restore dental caries. While observational studies of dental professionals have suggested adverse effects, few data are available with regard to the effects on children, a potentially sensitive subgroup. The study to be reported is one of the first two randomized trials to evaluate such effects.

11:45 – 12:00 PM

**Discussion**

**Wednesday Afternoon 20 Sept 2005 1:15 – 5:00 PM**

**Platform Session**

**SESSION 10-A: HEALTH EFFECTS OF MANGANESE EXPOSURE: HUMANS AND MODELS II**

Session Chair: Nick M. Filipov, PhD  
Co-Chair: Donna Mergler, PhD

1:15 – 1:50 PM

**Enhanced Proinflammatory Cytokine Production by Striatal Slices Exposed to Manganese and LPS *In Vitro***

Nick M Filipov, PhD ~ *Mississippi State University*

1:50 – 2:25 PM

**Manganese Exposure and Effects Over the Lifespan: Age and Gender Considerations**

Donna Mergler, PhD ~ *CINBIOSE, University of Quebec at Montreal, Quebec, Canada*

Our research group has examined manganese exposure and effects in several different groups, spanning lifetime and gender. In cohorts of pregnant women, children, workers exposed to Mn, communities of men and women whose age ranged from 20-70 years, we have assessed bioindicators of Mn in relation to exposure sources and neurotoxic effects. This presentation will examine the relation between exposure and effects at each of these stages. We will synthesize the data within a lifespan framework, with emphasis on biomarker differences with respect to age and gender differences and the implications for health and well-being.

2:25 – 3:00 PM Break

3:00 – 3:30 PM

**Neuroimaging and Neurodevelopmental Correlates of Intravenous Manganese Exposure in Parenterally-Fed Infants: A Clinical Trial in the Neonatal Intensive Care Unit (NICU)**

Judy L Aschner, MD ~ *Vanderbilt University Medical Center*

Manganese (Mn), an essential metal needed for normal growth and development, can be neurotoxic upon excessive environmental or dietary exposure. Sick infants requiring parenteral nutrition (PN) may be at increased risk of Mn neurotoxicity because neonatal PN solutions contain high concentrations of Mn and PN bypasses the normal intestinal absorptive control and biliary excretory mechanisms for Mn. Furthermore, iron (Fe) deficiency, a common problem among sick neonates, increases Mn brain uptake because Mn and Fe compete for the same carrier transport systems in the central nervous system.

3:30 – 4:00 PM

**HIGH SIGNAL INTENSITIES ON T1-WEIGHTED MRI IN THE SPECTRUM OF MANGANESE SYMPTOMATOLOGY.**

Yangho Kim, MD ~ *University of Ulsan College of Medicine, Ulsan, South Korea.*

4:00 – 4:20 PM

**Utilization of Behavioral Testing, Atomic Absorption Spectroscopy (AAS) and Isoprostane Analysis to Determine the Effects of Brain Manganese (Mn) Accumulation in Male C57BL/6J Mice.**

LA Miyatake ~ *Vanderbilt University School of Medicine*

4:20 – 5:00 PM

**Discussion**

**Wednesday Afternoon 20 Sept 2005 1:15 – 5:00 PM**

**Symposium**

**SESSION 10-B. THE SEYCHELLES CHILD DEVELOPMENT STUDY OF METHYLMERCURY EXPOSURE FROM FISH CONSUMPTION: NEW RESULTS AND CONCLUSIONS**

Session Chair: Gary J. Myers, MD

**Overview of Child Development Studies in Seychelles, Past, Present and Planned**

Conrad F Shamlaye, MD ~ *Ministry of Health Republic of Seychelles*

The Seychelles Child Development Study (SCDS) was designed to examine the relationship between exposure to prenatal MeHg from maternal fish consumption and the children's neurodevelopment. Three cohorts have been evaluated over nearly 20 years and the study is continuing to explore the relationships between MeHg exposure, fish consumption, nutrients and children's development. An overview of the study conducted to date, the studies currently ongoing and future plans will be presented. In addition, some of the underlying epidemiological principles that we have adhered to will be presented along with the reasons we feel they are important.

### Biomarkers for Methyl Mercury

Thomas W Clarkson, PhD

Elsa Cernichiari, Grazyna Zareba and Gary Myers ~ *University of Rochester, NY*

Several biological media have been used as indicators of the fetal body burden of methyl mercury and the levels in the primary target tissue, the developing brain. These media include maternal hair and blood, cord blood and placental tissue. The relative merits of each media will be considered both with regard to current knowledge of the physiology of mercury disposition in the body and also the practicality of field application with respect to sample collection, transport, storage and processing.

### Association Between Nutrients, MeHg and Child Development

J.J. Strain, PhD ~ *University of Ulster, Northern Ireland*

Fish consumption is associated with both the provision of nutrients essential in brain development and in exposure to MeHg. The interaction of nutrients and toxic agents is complex and important to understanding the toxicity. The SCDS has been investigating this relationship in a new cohort over the past five years. This presentation will focus of the nutrients that were selected for evaluation during this study and describe the reasons for their selection. They include the omega 3 long chain fatty acid, docosahexanoic acid, along with iodine, iron, and choline.

### Findings From the Seychelles Child Development and Nutrition Study

Philip W. Davidson, PhD ~ *University of Rochester, NY*

All fish contain small amounts of methylmercury and also nutrients essential for brain growth and development. Methylmercury can impair foetal neurodevelopment, but there is scientific uncertainty about the exposure level at which this effect begins. We tested the hypothesis that brain selective nutrients resulting from fish consumption during pregnancy foster neurodevelopment to a point that equals or exceeds any impairment attributable to methylmercury. We measured prenatal methylmercury exposure and maternal nutrition in 229 mother-infant pairs and evaluated the children's development through age 30 months. We found that maternal docosahexanoic acid, an omega-3 long chain fatty acid, improved psychomotor development scores at the same time as they were lowered by methylmercury. Our results confirm the importance of interactions between neurotoxins and nutrients. They also suggest that regulatory authorities should consider the overall diet when issuing advisories about fish consumption.

### Postnatal Exposure Issues

Gary Myers, MD ~ *University of Rochester, NY*

Fish consumption and exposure to MeHg begins as early as 1 year of age in Seychelles. The brain continues rapid development following birth and is still sensitive to MeHg exposure. However, the level of exposure needed to adversely affect the postnatal brain is not known. One difficulty in investigating postnatal exposure has been determining a metric to adequately measure it. In the Seychelles Child Development Study, we determined postnatal childhood exposure from hair as convenience samples at 6, 19, 66, and 107 months. We will present two different metrics and their relationship to the children's IQ measured at their 9 year evaluation using covariate-adjusted linear regression. The first metric categorized exposures as high versus low since peak exposure can be critical. We used the mean exposure of 6 ppm measured at both 19 and 66 months of age for the cohort as the cutoff. The second metric examined cumulative exposure or the area under the curve since Hg entering the brain persists and may be damaging. We used the exposure between 6 and 66 months of age to determine this. We examined these metrics in relationship to the children's IQ at the 9 year evaluation

### Methylmercury and Blood Pressure

Sally Thurston, PhD ~ *University of Rochester, NY*

Hypertension is a major global health problem. Prenatal exposure to organic methylmercury (MeHg) from fish consumption has been proposed as one cause. A study from the Faroe Islands reported a direct association between BP at age 7 years and prenatal MeHg exposure. As cord blood mercury levels increased both diastolic and systolic BP increased. We examined this relationship in the Seychelles Islands to determine if this effect was consistent across studies. *Methods:* The Seychelles Child Development Study (SCDS) main cohort includes 789 children with known prenatal MeHg exposure. The cohort has been well characterized. The children's BP was measured at ages 12 and 15 years. We analyzed the association between prenatal MeHg exposure and BP using linear regression and additive models. *Results:* BP and key covariates were available on 644 subjects at 12 years, 559 subjects at 15 years, and 524 children at both ages. At age 15 years, there was a significant overall adverse relationship between MeHg and diastolic BP in males, but no other overall associations. *Summary.* Overall associations between prenatal MeHg exposure and BP were not found except in the case of 15-year old males where a higher diastolic BP was associated with increasing prenatal MeHg exposure.

### Panel Discussion of Child Development Studies in Seychelles

*Panelists:* Session Speakers plus Representatives from governmental agencies

Michael Bolger, PhD ~ *FDA*

Christopher DeRosa, PhD ~ *ATSDR*

Annette Kirshner, PhD ~ *NIH/NIH*

TBN ~ *EPA*

Wednesday Afternoon 20 Sept 2005 1:15 – 5:00 PM

### TOURS OF NCTR

Wednesday Evening 20 Sept 2006 7:00 – 9:20 PM

### Symposium

#### SESSION 11-A: THE FETAL BRAIN ON ALCOHOL

*Session Chair:* Cynthia (Cindy) J.M. Kane

*Theme:* Prenatal ethanol exposure is the leading known cause of mental retardation in the Western World. In the U.S. the incidence of Fetal Alcohol Spectrum Disorders (FASD) is estimated at 1-10 per 1000 births and costs \$5.4 billion annually. We will discuss the most recent advances in understanding of ethanol pathogenesis in the developing brain including: inhibition of neural stem cell proliferation, the role of NMDA receptor in cortical damage, and differential genetic vulnerability to ethanol teratogenesis. In addition, emerging knowledge of the role of glia, astrocytes and microglia, as direct targets of ethanol toxicity will provide an intriguing conclusion to the discussion.

7:00 – 7:05 PM

#### The Fetal Brain On Alcohol: Introduction

Cynthia (Cindy) J.M. Kane ~ *University of Arkansas for Medical Sciences*

7:05 – 7:30 PM

#### Latent Effects of Fetal Alcohol Exposure on Neural Stem Cells: Brainstem Neurons

Michael W. Miller ~ *Upstate Medical University*

Dr. Miller's research has revealed that the targeted effect of ethanol on proliferating neural stem cells contributes to the microencephaly associated with fetal alcohol syndrome. Stereologic analysis following ethanol exposure at gastrulation has demonstrated defects in gastrulation, neuronal generation, and neural stem cell proliferation. Importantly, the impact of ethanol on neural stem cells is not fully expressed until well after the period of ethanol exposure.

7:30 – 7:55 PM

**Cortical Development, Ethanol, and NMDA-NR1 Receptors: New Mechanisms of Toxicity**

Andrea J. Elberger ~ *The University of Tennessee Health Science Center*

Dr. Elberger has investigated specific mechanisms of ethanol toxicity in mice with deletion of the NMDA-NR1 receptor gene. Investigation of the relationship between NR1 and endocannabinoids has revealed potential cause and effect relationships that may be responsible for ethanol toxicity at all ages.

7:55 – 8:20 PM

**The Influence of Genetics in Ethanol's Teratogenic Actions**

Kristin M. Hamre, PhD ~ *The University of Tennessee Health Science Center*

The severity of ethanol's teratogenic action varies with genetics in both humans and animals. Recent studies by Dr. Hamre provide a new understanding that the degree of neuronal apoptosis and the threshold of neuronal sensitivity depend on genetic differences. This research has uncovered specific, differential responses to ethanol, at the cellular and molecular level, that are mediated by the genetic profile.

8:20 – 8:45 PM

**The Cholinergic System in Astrocytes is a Target for Ethanol**

Marina Guizzetti ~ *University of Washington*

Astrocytes modulate neuronal function including axonal and dendritic outgrowth, synaptogenesis, and neuronal fate. These glial cells promptly respond to neuronal stimuli, in part through their expression of neurotransmitter receptors. Research in this laboratory has revealed that muscarinic receptor activation in astrocytes is important during brain development, and that ethanol inhibition of muscarinic receptor signaling is involved in developmental ethanol neurotoxicity.

8:45 – 9:05 PM

**Developmental Interactions Between Microglia and Neurons Are Disrupted by Ethanol**

Cynthia (Cindy) J.M. Kane ~ *University of Arkansas for Medical Sciences*

Microglia have a ying/yang relationship with neurons, influencing both neuronal survival and neuronal death. Dr. Kane has discovered that microglia are sensitive, direct targets of ethanol and that ethanol damage to the microglial population increases neuronal vulnerability to ethanol. Investigation of the molecular mechanisms of ethanol interference with neuronal-microglial interactions, in rodent models of fetal alcohol exposure, has led to the identification of pharmacologic agents that inhibit ethanol-induced cell death of neurons and microglia.

9:05 – 9:20 PM

**Discussion**

**Wednesday Evening 20 Sept 2006 7:00 – 9:00 PM**

**Platform Session**

**SESSION 11-B: NEUROTOXICITY III: OXIDATIVE STRESS, MERCURY, THERAPY**

Session Co-Chairs: **W. M. Valentine, PhD  
NVC Ralston, PhD or LJ Raymond**

7:00 – 7:05 PM

**Introduction**

7:05 – 7:25 PM

**Dithiocarbamate-Mediated Oxidative Stress in Peripheral Nerve**

William M Valentine, PhD ~ *Vanderbilt University Medical Center*

7:25 – 7:45 PM

**Exacerbation of CNS Disorders with Exposure to Neurotoxins May Be Responsive to Lipid Therapy**

Patricia Kane, MD ~ *Haverford Wellness Center*

7:45 – 8:05 PM

**Selenium's Protective Effect Against Mercury Toxicity**

Nick VC Ralston, PhD ~ *University of North Dakota*

Selenium physiology is particularly important in the brain and neuroendocrine system since selenium is essential to support activity of numerous enzymes in these tissues. Because of the extraordinarily high binding affinity between selenium and mercury the sequestration of selenium in the form of insoluble HgSe precipitates appears to be a central aspect of mercury toxicity.

8:05 – 8:25 PM

**Selenium Prevents and Reverses Methylmercury Toxicity**

Laura J Raymond, PhD ~ *University of North Dakota*

Selenium's protective effects against mercury toxicity have been studied for the past four decades and have been demonstrated in all investigated species. Dietary selenium (at a level slightly less than the average selenium content of ocean fish) has recently been shown to prevent and/or reverse the signs and symptoms of mercury toxicity.

8:25 – 8:45 PM

**Evidence of Impaired Mercury Efflux in Autism**

Dan Rossignol, MD ~ *University of Virginia*

8:45 – 9:00 PM

**Discussion**

**Thursday Morning 21 Sept 2006 8:30 – 12:00 PM**

**Plenary Session**

**SESSION 12. NEUROTOXICITY IN DEVELOPMENT AND AGING: TRANSLATIONAL RESEARCH**

Session Chair: **Evelyn Tiffany-Castiglioni, PhD**  
Co-Chair: **Richard M. LoPachin, PhD**

**Theme.** This session will address how research on mechanisms can translate into improved public health. The spectrum of biological complexity will be examined in a broad overview, followed by specific presentations on various reductionist systems and how these may have potential for screening, risk assessment and development of prophylactic or therapeutic strategies. The large gap between basic bench science, informed by epidemiologic studies that identify toxicologic hazards, and clinically useful outcomes will be addressed in a roundtable discussion by panelists whose expertise ranges from genetics mechanism, to cells, tissues, organ systems, organisms, and populations.

8:30 – 8:40 AM

**Levels of Biological Complexity in the Translational Research Scheme: Session Overview**

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

8:40 – 9:00 AM

### Translational Medicine and the NIEHS Strategic Plan

Annette Kirshner, PhD ~ NIEHS/NIH

Traditionally, environmental impacts on disease have been studied from either the perspective of the exposure or the perspective of the disease. NIEHS' goal now is to address environmental disease from a more integrated perspective enabling us to gain a greater understanding of human disease by strengthening the evidence that a given exposure is toxic, determining how specific environmental exposures affect disease etiology and progression, and using environmental exposures to identify molecular targets to determine susceptibility and intervention. This presentation will address those goals of the NIEHS Strategic Plan that relate to this integrative approach to research.

9:00 – 9:25 AM

### Are Age-Related Neurodegenerative Diseases Mediated by Thiol Adduct Formation in Nerve Terminals?

Richard M. LoPachin, PhD ~ Albert Einstein College of Medicine

This talk will present a toxicologic approach to understanding possible links between human exposures to Type-2 conjugated alkenes such as acrylamide (ACR) and neurologic disease. Humans are exposed on a daily basis to conjugated alkenes in air and food. The interaction of an alkene electrophile with a sulfhydryl group can impair the function of proteins in the nerve terminal, which could disrupt brain activity. Our research suggests that this early nerve terminal injury is caused by the endogenous production of conjugated alkenes. Based on the possible neurotoxic consequences of environmental exposure which will be discussed in this talk, Alzheimer's disease and other neurodegenerative conditions might develop when nerve cells are exposed to both internal and external (environmental) sources of Type-2 conjugated alkenes. Furthermore, ACR and other conjugated alkenes produce cumulative neurotoxicity. Therefore, low-level, lifetime exposure to these chemicals and the resulting subtle neuronal damage might be involved in the "normal" aging process.

9:25 – 9:50 AM

### Neuroinflammation and Neurodegenerative Conditions.

W. Sue T. Griffin, PhD ~ University of Arkansas for Medical Sciences and Geriatric Research Education Clinical Center, VAMC

The central hypothesis of our work is that brain-derived proinflammatory cytokines such as IL-1 and S100B promote, through a variety of mechanisms, incessant neuronal compromise and death. These, together with predisposing genetic factors, are the basis for the progressive nature of Alzheimer's disease (AD) and related disorders, as well as the neurodegenerative consequences of neural insults. A corollary of this hypothesis is that a variety of insults to the brain—direct or indirect, genetic, or simple wear and tear of time—engenders neuroinflammatory processes and promotes neurodegenerative cascades. We seek to elucidate specific mechanisms underlying these neuroinflammatory cytokine-driven neurodegenerative cascades, including specific signal transduction pathways, in human conditions, in animal models and in cell and slice cultures.

9:50 – 10:05 BREAK

10:05– 10:30 AM

### Is Polychlorinated Biphenyl Exposure a Risk Factor for Parkinson's Disease?

Lisa A. Opanashuk, PhD ~ University of Rochester, NY

A potential link between polychlorinated biphenyl (PCB) exposure and neurodegeneration was suggested in a previous study that reported elevated PCB levels in the brains of Parkinson's disease (PD) patients. Although PCB exposure has been associated with abnormal locomotor function, the molecular mechanism of neurotoxicity remains unclear. Dopaminergic (DAergic) pathways regulate motor behavior and are putative targets for PCB-mediated damage. Our studies tested the hypothesis that PCB accumulation leads to oxidative stress, which

produces DAergic neuronal injury and disrupts motor function following Aroclor 1254 (A1254) exposure.

10:30 – 10:50 AM

### Use of Ca<sup>2+</sup> Modeling as a Predictive Measure of Neurotoxicity.

Rola Barhoumi Mouneimne, PhD ~ Texas A&M University

Calcium, a second messenger, controls a wide range of cellular functions such as contraction, neurotransmitter and hormone release, metabolism, cell division and differentiation. Because calcium literally controls life and death and is involved in most aspects of cellular function, the benefits would be enormous if we could identify the individual pathways targeted during toxicant exposure, developmental neurotoxicity or even disease progression. If such individual pathways are identified, they could be used as predictive measure of toxicity as well as for development of new methods for prevention or reversal of injury. This talk will present initial work on an in vitro Ca<sup>2+</sup> model that would be suitable for early toxicity screening of potentially neurotoxic drugs (e.g., propofol) with non invasive imaging tools.

10:50 – 11:10 AM

### What Is That In Rat Days? A Web Based Approach to the Translation of Neurodevelopmental Time Across Mammalian Species

Barbara Clancy, PhD ~ University of Central Arkansas, and University of Arkansas for Medical Sciences

A central goal of translational medicine is to find a comprehensive way to equate neurodevelopmental research across a variety of experimental species and extrapolate these data to developing humans. We report that this can be done using a "bioinformatics" approach because underlying the principles that drive brain evolution is a remarkable similarity in the timing and sequence of events that occur during brain development, particularly in highly related mammalian species. This similarity of developmental schedules allows us to use regression theory applied to a highly detailed database via the Internet <http://www.translatingtime.net/>. Here a user can access detailed "translations" of the timing of neurodevelopmental events across hamsters, mice, rats, rabbits, spiny mice, guinea pigs, ferrets, cats, rhesus monkeys, and humans.

11:10 – 11:40AM

### Roundtable Discussion

#### "Translational Research in Neurotoxicology"

This Roundtable will address strategies to integrate data from in vitro models, animal models and epidemiologic studies to understand the mechanisms by which toxicants and host responses to these agents during brain maturation and aging may act as triggers or amplifying factors in the pathogenesis of some neurodevelopmental and neuropsychiatric conditions. Strategies include: 1) the use of findings from in vitro systems to identify mechanisms of cell damage and possible biomarkers, 2) use of animal models to sharpen the focus of investigations in human cohorts, creating the basis for translation into novel biomarkers and intervention strategies, and 3) rigorous testing in animal models with differing genetic susceptibilities of hypotheses generated from epidemiologic studies.

**Facilitator:** Evelyn Tiffany-Castiglioni, PhD

**Panel Discussants: Session Speakers plus:**

David C. Bellinger, Ph.D., MSc ~ Harvard Medical School

Edgar Garcia-Rill, PhD ~ University of Arkansas Medical School

Sue Griffin, PhD ~ University of Arkansas Medical School

Mady Hornig, MD ~ Columbia University

Annette Kirshner, PhD ~ NIEHS/NIH

Don Schmechel, M.D. ~ Duke University Medical School

**Questions to Invited Experts:**

- How do reductionist models, including -omics, cell culture, and animal models, relate to translational research?
- How do epidemiologic studies relate to translational research?
- How can the "disease first" approach advocated by NIEHS lead to more rapid knowledge that would benefit human health?
- How can we prospectively identify interdisciplinary opportunities in environmental health studies that will most substantially improve human health?

11:40 – 11:50 AM

**Shifting Emphasis from Exposures and Toxicants to Pathophysiologic Endpoints: a Step in the Right Direction or Not?**

Co-Chair: Richard M. LoPachin, PhD ~ Albert Einstein College of Medicine

Thursday Noon

21 Sept 2006

Noon

**NOON: CLOSING OF THE CONFERENCE**

Conference Chair: Joan M. Cranmer, PhD

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**Posters should be put up on Sunday afternoon and be taken down by Wednesday morning.**

**The poster board is 4 feet high x 6 feet wide.**

**PAPERS PRESENTED IN THE TUESDAY EVENING**

**POSTER SESSION ARE LISTED ON PAGES 13-16**

**Poster Presentations:**

Tuesday Evening

19 Sept 2006

7:00 – 9:00 PM

*Cash Bar & Snacks*

*Poster Session*

**SESSION 8: GENERAL POSTER SESSION**

*Health Effects / Imaging / Human Studies*

**QUANTITATIVE MAGNETIC RESONANCE BRAIN IMAGING OF US ARMY VETERANS WITH PRESUMPTIVE EXPOSURES TO SARIN AND CYCLOSARIN DURING THE 1991 GULF WAR.**

KJ Heaton<sup>1,2,3</sup>, CL Palumbo<sup>1,4</sup>, SP Proctor<sup>1,2,3</sup>, RJ Killiany<sup>4,5,6</sup>, DA Yurgelun-Todd<sup>6,7</sup>, RF White<sup>1,2,4</sup>. <sup>1</sup>United States Army Research Institute of Environmental Medicine, Military Performance Division, Natick, MA; <sup>2</sup>Boston Environmental Hazards Research Center, VA Boston Healthcare System, Boston, MA; <sup>3</sup>Boston University School of Public Health, Department of Environmental Health, Boston, MA; Boston University School of Medicine, Departments of <sup>4</sup>Neurology and <sup>5</sup>Anatomy & Neurobiology, Boston, MA; <sup>6</sup>Harvard Medical School, Department of Psychiatry, Boston, MA; <sup>7</sup>Neuroimaging and Neuropsychology, Brain Imaging Center, McLean Hospital, Belmont, MA

**PALLIDAL SIGNALS IN PATIENTS WITH BILE DUCT OBSTRUCTION.**

SJ Bang<sup>1</sup>, SH Choi<sup>2</sup>, Y Kim<sup>3</sup>. <sup>1</sup>Department of Internal Medicine <sup>2</sup>Department of Radiology <sup>3</sup>Department of Occupational and Environmental Medicine Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea.

**ENVIRONMENTAL EXPOSURES AND HEALTH EFFECTS IN ADOLESCENT AND ADULT AGRICULTURAL WORKERS.**

DS Rohlman<sup>1</sup>, M Lasarev<sup>1</sup>, J Muniz<sup>2</sup>, WK Anger<sup>1</sup>, L McCauley<sup>2</sup>. <sup>1</sup>Center for Research on Occupational and Environmental Toxicology, Oregon Health & Science University, Portland, OR, USA; <sup>2</sup>University of Pennsylvania, Philadelphia, PA, USA

**NEUROTOXIC EFFECTS DURING ARSENIC EXPOSURE.**

Ligia Fat<sup>1</sup>, L. Gyorffy<sup>2</sup>. <sup>1</sup>Institute of Public Health, Cluj-Napoca, Romania, <sup>2</sup>District Hospital, Baia-Mare, Romania

**A CASE OF ACUTE ORGANOTIN POISONING.**

CI Yoo<sup>1</sup>, J Kim<sup>2</sup>, Y Endo<sup>3</sup>, Y Kim<sup>1</sup>. Department of Occupational and Environmental Medicine<sup>1</sup>, Department of Neurology<sup>2</sup>, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea. Research Center for Occupational Poisoning, Tokyo Rosai Hospital, Japan<sup>3</sup>

*Post-doc Award Competition*

**CUMULATIVE LEAD DOSE IN COMMUNITY-DWELLING OLDER ADULTS AND ABNORMAL COGNITIVE AGING. IS THERE EVIDENCE OF (PSYCHOMETRICALLY DEFINED) MILD COGNITIVE IMPAIRMENT?**

RA Shih<sup>1</sup>, MC Carlson<sup>2</sup>, BS Schwartz<sup>3,4</sup>. <sup>1</sup>Division of Epidemiology, Statistics, and Prevention Research, National Institute of Child Health and Human Development, NIH, Rockville, MD, USA. <sup>2</sup>Department of Mental Health, <sup>3</sup>Department of Epidemiology, <sup>4</sup>Department of Environmental Health Sciences, Johns Hopkins School of Public Health, Baltimore, MD, USA

Mentor: Ruth Brenner, MD, MPH

*Post-doc Award Competition*

**ACUTE DELIBERATE ORGANOPHOSPHATE (COUMAPHOS) POISONING WITH INTERMEDIATE SYNDROME IN A ONE YEAR OLD CHILD**

Kiat, WK, Toxicology Unit, St. Luke's Medical Center, Quezon City, Philippines

Mentor:

*Post-doc Award Competition*

**A PROXY MEASURE OF PRENATAL TESTOSTERONE EXPOSURE IS RELATED TO GRAY MATTER VOLUME IN HUMAN NEONATES**

Rebecca C. Knickmeyer<sup>1</sup>, Y. Sampath K. Vetsa<sup>2</sup>, Bradley Moore<sup>2</sup>, Guido Gerig<sup>1,2</sup> and John Gilmore<sup>1</sup>

<sup>1</sup>Dept. of Psychiatry, University of North Carolina, Chapel Hill, NC 27599, <sup>2</sup>Dept. of Computer Science, University of North Carolina, Chapel Hill, NC 27599.

*Behavioral Assessment / Animal Studies*

**METHAMPHETAMINE EXPOSURE IN FEMALE C57BL/6 MICE: NEUROBEHAVIORAL CONSEQUENCES**

T. J. Zarcone, L. A. Opanashuk, M. Tubbs, A. Shapiro, S.A. Notter, B. Weiss; Department of Environmental Medicine and Environmental Health Sciences Center, University of Rochester School of Medicine and Dentistry, Rochester, NY.

*Post-doc Award Competition*

**VALIDATION OF THE DELAYED-NON-MATCH-TO-POSITION 8-ARM RADIAL MAZE (8ARM) TASK WITH SCOPOLAMINE, NICOTINE, AND ETHANOL.**

RI Erickson, EB Defensor, DR Middaugh, LL Rausch, JC Mirsalis, and KL Steinmetz. SRI International, Menlo Park, CA, USA.

Mentor: Karen Steinmetz, PhD, DABT

**BEHAVIORAL EFFECTS OF ACRYLAMIDE IN RATS EXPOSED TO DAILY LOW DOSES FROM GESTATION DAY 6 THROUGH 6 MONTHS OF AGE.**

J. Garey, SA Ferguson and MG Paule. Division of Neurotoxicology, National Center for Toxicological Research/FDA, Jefferson, AR, USA

**DEVELOPMENTAL NEUROTOXICITY ASSESSMENT OF LOW-LEVEL ACRYLAMIDE EXPOSURE IN FISCHER 344 RATS.**

MG Paule, SA Ferguson and J Garey. Division of Neurotoxicology, National Center for Toxicological Research/FDA, Jefferson, Arkansas, USA

*Pre-doc Award Competition*

**AGE-DEPENDENT IMPAIRMENTS OF CHRONIC ESTROGEN EXPOSURE ON DSA AND DRL OPERANT TASKS.**

VC Wang and SL Schantz. Neuroscience Program, University of Illinois, Urbana-Champaign, Urbana, IL

Mentor: Susan Schantz, PhD

*Testing / Verification / Methodologies*

**A TOOL FOR REGULATORY SAFETY TESTING: INTERVAL SCALE FOR DEVELOPMENT OF RATS AGED 0-70 DAYS**

Didima de Groot<sup>1</sup>, Gert Jacobusse<sup>2</sup>, Jan Lammers<sup>1</sup>, André Wolterbeek<sup>1</sup>, Stef van Buuren<sup>2</sup> TNO Quality of Life, Zeist<sup>1</sup> / Leiden<sup>2</sup>, The Netherlands

**EXAMINING DATABASES USED TO EVALUATE TRENDS IN NEURO DEVELOPMENT DISORDERS.**

A ter Schure and J Yager. Air Quality Health & Risk Assessment, Environment, Electric Power Research Institute (EPRI), Palo Alto, California, USA.

*Autism / LDDI / ASA / AAMR / LDAA*

**THE LEARNING AND DEVELOPMENTAL DISABILITIES INITIATIVE: PREVENTING TOXIC THREATS TO CHILD DEVELOPMENT**

Elise Miller, MEd, Executive Director

Institute for Children's Environmental Health, Freeland, Washington, USA

**THE ROLE OF THE AUTISM SOCIETY OF AMERICA**

Lee Grossman, President, Autism Society of America, Washington DC (TBA)

**TOXIC EXPOSURES IN HOMES OF CHILDREN WITH DEVELOPMENTAL DISABILITIES (DD)**

Michele (Gagnon) Wagner, Director, Environmental Health Initiative, American Association on Mental Retardation, 444 North Capitol Street, NW, Suite 846, Washington, DC 20001

**THE HEALTHY CHILDREN PROJECT OF THE LEARNING DISABILITIES ASSOCIATION OF AMERICA.**

Kathy Lawson, Healthy Children Project, Learning Disabilities Association of America, 4156 Library Road, Suite One, Pittsburgh, PA 15234-1349

**ADDRESSING NEUROINFLAMMATION IN AUTISM AND PDD WITH IV PHOSPHOLIPID AND PHENYLBUTURATE THERAPY.**

Kane PC, Braccia D, Cartaxo, A, Kane E. Haverford Wellness Center, Havertown, PA and Kinnelon, NJ USA

**GENETIC SUSCEPTIBILITY IN AUTISM.**

SE Owens<sup>1</sup>, ML Summar<sup>2</sup>, JL Haines<sup>2</sup> and M Aschner<sup>1</sup>. <sup>1</sup>Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, TN, USA. <sup>2</sup>Center for Human Genetics Research, Vanderbilt University School of Medicine, Nashville, TN, USA.

*Mechanisms / Genomics*

**EFFECTS OF LOW-LEVEL FORMALDEHYDE EXPOSURE ON APOPTOSIS-RELATED MOLECULES IN THE HIPPOCAMPUS OF MICE.**

S Tsukahara<sup>1</sup>, S Yamamoto<sup>1</sup>, Tin-Tin-Win-Shwe<sup>1</sup>, S Ahmed<sup>1</sup>, N Kunugita<sup>2</sup> and H Fujimaki<sup>1</sup>. 1: National Institute for Environmental Studies, Tsukuba, Japan; 2: University of Occupational and Environmental Health, Fukuoka, Japan

**VAST DIFFERENCE IN GENE EXPRESSION FOR NEURONAL AND HEPATIC CELLS FOLLOWING MICROMOLAR PCB EXPOSURES HIGHLIGHT THE NEED FOR ORGAN-SPECIFIC DATA IN RISK ASSESSMENT**

MS Maier, WH Hanneman, and ME Legare. ~ Colorado State University

*Post-doc Award Competition*

**ARE NONENZYMATIC FUNCTIONS OF ACETYLCHOLINESTERASE (ACHE) INVOLVED IN THE DEVELOPMENTAL NEUROTOXICITY OF ORGANOPHOSPHATES? EFFECTS OF CHLORPYRIFOS AND DIAZINON ON EXPRESSION OF ACHE SPLICE VARIANTS IN VITRO AND IN VIVO.**

RR Jameson, FJ Seidler and TA Slotkin. *Department of Pharmacology & Cancer Biology, Duke University Medical Center, Durham, NC, USA.*  
Mentor: Ted Slotkin, PhD

**EVALUATION OF HIPPOCAMPAL GENE EXPRESSION CHANGES ASSOCIATED WITH CHRONIC KETAMINE OR REMACEMIDE EXPOSURE IN RATS.** LKM Wright<sup>2,1</sup>, TA Patterson<sup>1</sup>, E Pearson<sup>3</sup>, T Hammond<sup>3</sup> and MG Paule<sup>1,2</sup>. <sup>1</sup>*Division of Neurotoxicology, National Center for Toxicological Research, Jefferson, AR, USA,* <sup>2</sup>*Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences, Little Rock, AR, USA and* <sup>3</sup>*AstraZeneca Safety Assessment, Loughborough, England (UK).*

*Division of Neurotoxicology, National Center for Toxicological Research, Jefferson, AR, USA,* <sup>2</sup>*Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences, Little Rock, AR, USA and* <sup>3</sup>*AstraZeneca Safety Assessment, Loughborough, England (UK).*

*Post-doc Award Competition*

**T CELL-MEDIATED NEUROPROTECTIVE RESPONSE IN TOXIC CHEMICAL INDUCED MEMORY-RELATED GENE EXPRESSIONS IN A MOUSE HIPPOCAMPUS**

Tin-Tin-Win-Shwe<sup>1</sup>, S. Ahmed<sup>1</sup>, S. Tsukahara<sup>2</sup>, S. Yamamoto<sup>2</sup>, M. Kakeyama<sup>1</sup>, D. Nakajima<sup>2</sup>, S. Goto<sup>2</sup>, T. Kobayashi<sup>1</sup>, H. Fujimaki<sup>2</sup>  
<sup>1</sup>*Environmental Health Sciences Division, National Institute for Environmental Studies, 16-2 Onogawa, Tsukuba, Ibaraki 305-8506, Japan* <sup>2</sup>*Center for Environmental Risk Research, National Institute for Environmental Studies, 16-2 Onogawa, Tsukuba, Ibaraki 305-8506, Japan*  
Mentor: Dr. Hidekazu Fujimaki

Mentor: Dr. Hidekazu Fujimaki

*Post-doc Award Competition*

**GASEOUS ANESTHETIC DRUG COMBINATIONS INDUCE DEVELOPMENTAL NEURO-APOPTOSIS IN THE RAT FRONTAL CORTEX**

X Zou, N Sadovova, AC Scallet, B Divine, C Hotchkiss, TA Patterson, MG Paule, W Slikker and C Wang. *Division of Neurotoxicology, NCTR/FDA, Jefferson, Arkansas, 72079*  
Mentor: Cheng Wang, MD, PhD

**THE RECOVERY OF DOPAMINERGIC INNERVATION AND THE REPAIR OF NEURODEGENERATION IS NEARLY COMPLETE IN THE BASAL GANGLIA WITHIN 6 MONTHS AFTER A SEVERE ACUTE NEUROTOXIC EXPOSURE TO AMPHETAMINE.**

John F. Bowyer. *Division of Neurotoxicology, National Center for Toxicological Research/ FDA, Jefferson, AR 72079-9502.*

*Post-doc Award Competition*

**GENE EXPRESSION PROFILING OF MPP<sup>+</sup>-TREATED MN9D CELLS: A MECHANISM OF TOXICITY STUDY.**

Jianyong Wang, Zengjun Xu, Hong Fang, Helen M. Duhart, Tucker A. Patterson, and Syed F. Ali. *Neurochemistry Laboratory, Division of Neurotoxicology, National Center for Toxicological Research, Jefferson, Arkansas, USA*  
Mentor: Syed F. Ali, PhD

*Pre-Doc Award Competition*

**AGING ACCELERATES THE PROGRESSION AND MANIFESTATION OF SEIZURES IN POST-TRAUMATIC MODEL OF EPILEPSY**

Amar Jyoti, Pallavi Sethi and Deepak Sharma. *Neurobiology Laboratory, School of Life Sciences, Jawaharlal Nehru University, New Delhi-67, India.*

Mentor: Dr. Deepak Sharma

*Pre-Doc Award Competition*

**UTILIZATION OF BEHAVIORAL TESTING, ATOMIC ABSORPTION SPECTROSCOPY (AAS) AND ISOPROSTANE ANALYSIS TO DETERMINE THE EFFECTS OF BRAIN MANGANESE (MN) ACCUMULATION IN MALE C57BL/6J MICE.**

LA Miyatake<sup>1</sup>, V Fitsanakis<sup>1</sup>, D Milatovic<sup>1</sup>, J Anderson<sup>2</sup>, KM Erikson<sup>2</sup>, M McDonald<sup>3</sup>, and M Aschner<sup>1, 4, 5</sup>. <sup>1</sup>*Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, TN.* <sup>2</sup>*Department of Nutrition, University of North Carolina – Greensboro, Greensboro North Carolina.* <sup>3</sup>*Department of Pharmacology, Vanderbilt University, Nashville, TN.* <sup>4</sup>*Department of Pharmacology and the* <sup>5</sup>*Kennedy Center, Vanderbilt University Medical Center, Nashville, TN.*  
Mentor: Dr. Vanessa Fitsanakis

*Pre-Doc Award Competition*

**EQUATING NEURODEVELOPMENT ACROSS MAMMALIAN SPECIES USING NEUROINFORMATICS.**

Brandon M. Kersh, James R. Hyde, Barbara Clancy. *University of Central Arkansas, Conway AR /INBRE, University of Arkansas for Medical Sciences, Little Rock, AR*  
Mentor: Barbara Clancy, PhD

*Redox State / Oxidative Stress*

**COMPARING THE RELATIVE IMPORTANCE OF GLUTATHIONE V. ASCORBATE IN PROTECTING THE DEVELOPING BRAIN.**

CP Curran, Y Chen, EH Johansson, DW Nebert, TP Dalton. *Department of Environmental Health, University of Cincinnati Medical Center, Cincinnati, Ohio, USA*

**IMPAIRMENT IN OXIDATIVE BIOTRANSFORMATION OF A REACTIVE INTERMEDIATE OF DOPAMINE METABOLISM.**

JA Doom, VR Florang, JN Rees, DG Anderson, and NK Brogden. *Division of Medicinal and Natural Products Chemistry, College of Pharmacy, The University of Iowa, Iowa City, Iowa, USA.*

**KETAMINE PRODUCES OXIDATIVE DNA DAMAGE AND LOSS OF MONKEY FRONTAL CORTICAL NEURONS IN CULTURE**

C Wang, N. Sadovova, X. Zou, A.C. Scallet, C. Hotchkiss, T.A. Patterson, J. Hanig, M.G. Paule and W. Slikker. *Division of Neurotoxicology, NCTR, FDA, Jefferson, Arkansas, 72079*

*Pre-Doc Award Competition*

**1-METHYL-4-PHENYLPYRIDINIUM-INDUCED ALTERATIONS OF GLUTATHIONE AND REDOX ENVIRONMENT IN IMMORTALIZED RAT DOPAMINERGIC NEURONS.**

DA Drechsel, LP Liang, and M Patel. *Department of Pharmaceutical Sciences, University of Colorado at Denver and Health Sciences Center, Denver, CO, USA.*

**INCREASED INTRACELLULAR FREE RADICAL PRODUCTION AND DECREASED GLUTATHIONE REDOX RATIO IN LYMPHOBLASTOID CELL LINES FROM AUTISTIC CHILDREN.**

Stepan Melnyk, Stefanie Jernigan, Alena Savenka, and S. Jill James. *Arkansas Children's Hospital Research Institute, University of Arkansas for Medical Sciences, Little Rock, AR*

**METHYLMERCURY CAUSES GLIAL OXIDATIVE STRESS AND IL-6 SECRETION.**

JY Chang *Department of Neurobiology and Developmental Sciences, University of Arkansas for Medical Sciences, Little Rock, Arkansas.*

**EFFECTS OF ETHANOL ON OXIDATIVE STRESS IN THE NEONATAL RAT CEREBELLUM.**

Cynthia J.M. Kane, Jason Y. Chang, Tarun K. Garg, and Lihong Han. *Dept. of Neurobiology & Developmental Sciences, University of Arkansas for Medical Sciences, Little Rock, AR 72205*

**AUGUST 29, 2006 - PRELIMINARY PROGRAM: Subject to Change See [www.neurotoxicology.com](http://www.neurotoxicology.com) for Program updates**

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Contact: Dr. Joan Cranmer, Conference Chair, Department of Pediatrics, UAMS College of Medicine, Little Rock, AR email: [CranmerJoanM@uams.edu](mailto:CranmerJoanM@uams.edu) Tel: 501-364-2986

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**POSTER ABSTRACTS WILL BE ADDED  
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