NATIONAL CAPITAL AREA CHAPTER
SOCIETY OF TOXICOLOGY NEWSLETTER
Electronic Edition

June 2006 Issue 21

Renew Your SOT and NCAC Membership at
http://www.toxicology.org/script/loginredirect2.asp?page=dues

The National Capital Area Chapter of the Society of Toxicology (NCAC-SOT) was established to provide a regional focus for scientists of all disciplines interested in toxicology. The Chapter acts to:

- Sponsor and co-sponsor symposia on current issues in toxicology.
- Provide an annual award to an outstanding student in toxicology to assist in attending the annual meeting of the SOT.
- Maintain communication with the National SOT regarding current toxicology and regulatory concerns.
- Sponsor regional Chapter events at the annual meeting of the SOT.

MESSAGE FROM THE PRESIDENT

First I would like to say how honored I am to be the President of the NCAC-SOT Chapter for the upcoming year. I look forward to another productive and interesting year for our chapter. I would like to welcome our new officers. Dr. Gary Burin is the new Vice President/President Elect. He will be organizing our fall and spring symposiums. Hopefully we will see all of you there. We have a new secretary, Dr. Deborah Burgin, from the EPA. And we have a new councilor, Dr. Michael Orr from the FDA. Michael will be taking over the responsibility of being the editor of our chapter's newsletter. If you have any articles/items you would like to share with other chapter members, please let Michael know. We also have a new student representative, Christopher Sheth, from Johns Hopkins University.

I would like to thank Dr. Harry Milman for his excellent leadership as President of the chapter last year. Through his diligence and hard work, our chapter had several major accomplishments. In fact when Dr. Milman and I attended the regional chapter officers' meeting at the SOT convention in San Diego, NCAC was singled out and complimented for many of the programs that we have offered in the past year. I would also like to thank Dr. Pam Chamberlain for her hard work as chapter secretary for the last few years and Dr. David Jacobson-Kram for his council as Past President this past year.

Our Spring Symposium "Public Health Concerns in Disaster Preparedness" was a resounding success. Every speaker gave an excellent talk. The abstracts from this symposium can be found on our website. We had about 50 students from the Science and Mathematics Academy at Aberdeen High School that attended the symposium as our guests. The students listened to the presentations and also were given the opportunity to have lunch with the speakers. The students really enjoyed the experience and sent us very positive critiques of their field trip.

As we plan our activities for the upcoming year, the executive committee would welcome ideas from all of the members. We are looking for topics for our symposiums that would be of interest to our members. We also would like to strengthen our student activities and would welcome new creative ideas from our members.

I look forward to seeing all of you at chapter activities and I encourage you to contact me or any of the other officers with your suggestions for future NCAC-SOT events.

Suzanne Fitzpatrick
301-827-4591

MESSAGE FROM THE NEWSLETTER EDITOR

I look forward to an exciting term as your Newsletter Editor. I want to start off by thanking Dr. Gary Burin for his guidance during my transition into my new role. In addition, I look forward to working with the other NCAC-SOT executive committee members in the upcoming years.

During my tenure, I would like to identify and highlight as many local toxicology related events as possible from diverse groups such as the ILSI Health and Environmental Sciences Institute (http://www.hesiglobal.org/Events/) and Association of Government Toxicologists (http://www.agovtox.org/). Please feel free to contact me with seminars or upcoming not-for-profit events in Virginia, Maryland and the District of Columbia that may be of interest to toxicologists. The NCAC newsletter is used to disseminate information of interest to Toxicologists and members of related professions in the National Capital Area. Please send these announcements to my attention (Michael.Orr@fda.hhs.gov), as we are very willing to publicize upcoming events.

This issue of the NCAC newsletter contains, in addition to the usual features such as the reports of our President and Treasurer, the student abstracts from our Spring Symposium on the topic of “Public Health Concerns in Disaster Preparedness”. An application for membership can also be found at the end of the newsletter. Feel free to distribute this edition of the newsletter to colleagues who may be interested in joining our local chapter. The cost is nominal ($20 for full membership, $10 for student membership) and membership in the local chapter is an excellent introduction to local activities in the toxicology field. Additional information on our local chapter can be found at our website (http://www.toxicology.org/isot/rc/ncac/default.htm).

Mike Orr
301-796-1604

MESSAGE FROM THE STUDENT REPRESENTATIVE

Welcome to what will prove to be a very exciting year for graduate students in the National Capital Area Chapter! As NCAC's Student Representative for SOT's Student Advisory Committee, I'd like to express my gratitude to Mashael Al-Namaeh (Howard University), the outgoing Student Representative, for her hard work and dedication this past year. Mashael put together a very successful and informative Student Day 2005, and we will greatly miss her input this year. On that same note, I'd also like to welcome Christopher Sheth (Virginia Commonwealth University) to the NCAC executive board as the Vice-Student Representative. I look forward to working with you, Chris!

This year we're going to change things up a bit. Instead of having our annual student symposium the day following the Fall Symposium (tentatively scheduled for December), it will be held in November at one of the campuses in our region. The topic this year will entail career options following graduate school. We all have to graduate at some point, whether we want to or not, so I expect everyone to attend! Within the next couple weeks, we will also send out a survey. It will be relatively painless, so I would appreciate if we can get everyone's input on what they would like to see the NCAC do for them. Please keep an eye out for more details regarding the survey and the symposium.

Chris and I look forward to meeting each of you at this year's symposia. If you have any comments, questions or suggestions, please feel free to contact us at dgrah001@umaryland.edu or shethcm@vcu.edu.

Devon Graham and Christopher Sheth

ILSI UPDATE

The ILSI Health and Environmental Sciences Institute (HESI) Risk Assessment Methodologies Technical Committee will hold a workshop on "Approaches to Weight of the Evidence Evaluation in Risk Assessment" December 7th and 8th in Baltimore, MD. This international, multi-sector workshop will provide a public forum for the exchange of information on approaches to weight of evidence analysis within the context of risk assessment. Goals of the meeting include identification and characterization of the current uses of weight of evidence analysis in human health risk assessment associated with Federal policy or regulatory decision making, and exploration of commonalities and differences in the application or understanding of weight of evidence analysis.

Meeting panelists and speakers include scientists, regulators, and representatives from various national and international sectors, including government agencies, (USEPA, Cal EPA, USDA, USFDA, NIH, IARC, Health Canada, and Environment Canada), the pharmaceutical and chemical industries, academia, and several NGOs. The workshop introductory lecture will be delivered by Dr. Douglas Weed, of the National Cancer Institute, whose 2005 paper, "Weight of Evidence: A Review of Concept and Methods[1]" is a foundation for the technical committee's work. Dr. Paul Gilman, director of the Oak Ridge Center for Advanced Studies at Oak Ridge National Laboratory, and the former science advisor for the USEPA, will serve as the plenary speaker and panel moderator.

Through providing this platform for informational exchange among a diverse group of risk assessors from different technical fields and regulatory objectives, HESI hopes to develop a workshop "white paper" on the current state of the practice, identify opportunities for synergy, and establish an active dialogue among interested parties.

If you are interested in participating in this workshop or learning more about this and other HESI activites, please contact Dr. Michelle Rau Embry, HESI Scientific Program Manager, at membry@hesiglobal.org.

[1]Weed, D.L. (2005). Weight of Evidence: A Review of Concept and Methods. *Risk Analysis*. **25(6)**: 1545-1557.

EXECUTIVE COMMITTEE MEMBERS

National Capital Area Chapter – Society of Toxicology

President:	Suzanne Fitzpatrick (’06-’07) US FDA 301-827-4591 sfitzpat@oc.fda.gov
Vice-President/ President-Elect	Gary Burin (’06-’07) Technology Sciences Group Inc. 202-828-8980 gburin@tsgusa.com
Immediate Past President	Harry Milman ('05-'06) ToxNetwork.com 301-871-6714 hmillman@verizon.net
Secretary:	Deborah Burgin (’06-’09) US Environmental Protection Agency 202-566-0269 burgin.deborah@epa.gov
Treasurer:	Jennifer Weeks Sekowski ('05-‘08) US Army CHPPM 410-436-8774 jennifer.sekowski@us.army.mil
Councilors:	Michael Orr ('06-'09) US Food and Drug Administration 301-796-1604 michael.orr@fda.hhs.gov Lynn Flowers (‘04-‘07) US EPA 202-564-1537 Flowers.lynn@epa.gov Thomas Flynn (‘05-‘08) US Food and Drug Administration 301-827-8382 thomas.flynn@fda.hhs.gov
Student Representative	Devon Graham (’06-’07) University of Maryland 410-550-1532 dgrah001@umaryland.edu
Student Vice- Representative	Christopher Sheth (’06-’07) Virginia Commonwealth University shethcm@vcu.edu

ABSTRACTS FROM MAY, 2006 NCAC-SOT SYMPOSIUM

Meeting the Challenges in Public Health Emergencies

David Rutstein, MD
HHS Chief Medical Officer
Department of Health and Human Services

Public health emergencies occur in the context of larger disasters and catastrophic events. The Federal government has established policies for responding to these emergencies articulated in the National Response Plan (NRP) and an annex, Emergency Support Function # 8 (ESF-8). However, neither the NRP nor ESF-8 has proven to be adequate for catastrophic events. A careful and dispassionate review of recent national experiences with public health emergencies, both domestically and abroad, provides us with ample insight into possible policy revisions in the manner in which: Federal agencies are organized and responses are led; the allocation of appropriate resources at all levels of government is made; the preparedness of the Nation is fostered, and; the collection, distribution and communication of public health information and medical data is facilitated. Current efforts to modify Federal policies in these areas, and commitments to translate them into operational capabilities, offer the hope reducing the National vulnerability to all manner of catastrophic events and improving the collective ability to respond to public health emergencies.

Clean up: Occupational Health Risks in Disaster Situations: Hurricane Katrina and Lessons Learned

Bruce Bernard, MD, MPH
Chief, Medical Section,
Hazard Evaluation & Technical Assistance Branch
NIOSH

The National Institute for Occupational Safety and Health (NIOSH) is responsible for coordinating CDC's occupational safety and health activities associated with emergency preparedness and response. This presentation will cover NIOSH activities following Hurricane Katrina, and cover assessment of occupational health and exposure risks of concern, including flood waters and sediment, debris, mold, work stress, infectious disease, risks of handling human and animal remains, etc. Overall results of the evaluation of illness, injury, and stress in New Orleans Police Department and New Orleans Firefighters will be presented. NIOSH field responders provided guidance on controlling exposures to protect workers, including engineering controls, administrative controls, and use of appropriate personal protective equipment.

Ethical Issues In Human Subject Research Related To Disasters

BA Schwetz, DVM, PhD
Office for Human Research Protections

Research conducted on human subjects in the wake of a disaster can raise numerous regulatory and ethical issues. Regulatory jurisdiction depends on funding sources, location of the study, and other considerations. Ethical issues may include failure to obtain protocol approval from an Institutional Review Board, failure to properly obtain informed consent from

subjects, and use of coercive techniques to recruit subjects or taking advantage of people in a vulnerable state. Unethical research could jeopardize the conduct of research in future disaster situations that would be very important for the health of the public.

Food Defense

Dave Acheson, MD
Director, Office of Food Safety, Defense, and Outreach
Center for Food Safety and Applied Nutrition
Food and Drug Administration

Food safety and food security are both integrated and high priority goals for the Food and Drug Administration. Since 9/11 the Center for Food Safety and Applied Nutrition has devoted significant resources to food defense. The development of a food defense strategy has involved a variety of approaches one of the most important of which was to determine vulnerabilities using an operational risk management approach. By examining a variety of agents, food commodities and various scenarios between the farm and the table it was possible to determine the "higher" risk combinations and thus focus resources based on a determination of risk. This approach has driven a number of activities including the development of guidance documents, research activities and emergency response planning. This preventative strategy has been augmented by new research for the development of rapid and sensitive methods, as well as the development of a clear emergency response plan should a deliberate food contamination event occur. Current activities are further focused on CARVER assessments of the higher risk foods and close interaction with stakeholders to further ensure preparedness. The 2002 Bioterrorism Act has further extended the protection of the U.S. food supply through the development of a number of rules. Overall, while there has been a significant increase in focus on food defense this has been integrated as far as possible into food safety activities which remain an ongoing and high priority for FDA.

Pandemic Influenza- Planning and preparation

Boris Lushniak, MD, MPH
Assistant Commissioner, Counterterrorism
Office of the Commissioner
Food and Drug Administration

This presentation will provide a overview of the current state of affairs in pandemic influenza planning with an emphasis on activities at the FDA. These activities include issues surrounding antiviral therapies, vaccines, diagnostics and personal protective equipment, emergency preparedness, food and feed safety, and enforcement.

***In Vivo* Attenuation of the Parkinsonian Phenotype by Induction of the Keap1-Nrf2 Pathway.**

NC Burton, TW Kensler, TR Guilarte. Dept. of Env. Hlth Sci., Johns Hopkins University Bloomberg School of Public Health, Baltimore MD.

Parkinson's Disease (PD) is a progressive neurodegenerative disorder characterized by the loss of nigrostriatal dopaminergic neurons. It is hypothesized that damage from endogenous reactive oxygen species is involved in the disease process. Administration of 1-methyl-4-

phenyl-1,2,3,6-tetrahydropyridine (MPTP) produces a parkinsonian phenotype in mice. We hypothesized that *in vivo* activation of Nrf2, a transcription factor that regulates the expression of Phase 1, Phase 2, and antioxidative enzymes, is protective in the MPTP-model of PD. We compared the effect of MPTP administration on dopamine transporter (DAT) levels in the striatum of wildtype (+/+) and Nrf2 knockout (-/-) mice seven days after exposure. Striatal DAT level was used as a marker of dopaminergic neuronal terminal integrity. A 20 mg/kg MPTP dose had no significant effect on DAT levels in (+/+) mice, while DAT levels decreased by 20% in (-/-) mice. This suggests that Nrf2 (-/-) mice are more susceptible to MPTP toxicity. We then characterized a dose-response curve following administration of increasing MPTP dose (20, 30, 40 and 60 mg/kg) in (+/+) and Nrf2 (-/-) mice. Analysis of variance indicates a significant genotype effect ($F_{1,47}$= 7.9; p= 0.007) on striatal DAT levels with (-/-) mice having a greater striatal DAT percent loss than (+/+).
To examine a potential role of *in vivo* Nrf2 induction on MPTP neurotoxicity, we examined the effect of the Nrf2 inducer 1,2-dithiol-3-thione (D3T) on MPTP-induced striatal DAT loss in (+/+) mice. D3T was administered orally (0.5mmol/kg) 1, 3 and 5 days prior to MPTP treatment. Striatal DAT levels seven days post-MPTP showed that D3T confers a rostrocaudal gradient of protection from MPTP neurotoxicity, with approximately 30% protection in the rostral striatum and nearly 100% protection in the caudal aspects. This was present in the absence of an effect of D3T on MPTP metabolism. These findings suggest that the Nrf2 pathway is an important determinant of the parkinsonian phenotype in the MPTP mouse model.

Androgen Levels May Not Mediate the Association Between Current Alcohol Use and Hot Flashes in Midlife Women

C. Schilling, L. Gallicchio, S. Miller, L.M. Lewis, H. Zacur, and J.A. Flaws
(University of Maryland Department of Epidemiology and Preventive Medicine, Baltimore, MD 21201, Johns Hopkins University, Departments of Epidemiology and Gynecology and Obstetrics, Baltimore, MD 21287)

Little is known about the etiology of hot flashes, though millions of women experience hot flashes each year during their transition to menopause. We have previously shown that current alcohol use reduces the risk of frequent and severe hot flashes in midlife women and that this association is not mediated by estrogen levels. The purpose of this study was to examine the relation between current alcohol use, androgen levels, and hot flashes in midlife women using a case-control study design. Cases were midlife women who reported ever experiencing hot flashes (n=362). Controls were midlife women who reported never experiencing hot flashes (n=264). Each participant completed a questionnaire and provided a blood sample that was used to measure androgen levels (androstenedione and testosterone) by enzyme-linked immunosorbent assay. The results indicate that current alcohol users had lower odds than non-users of experiencing any hot flashes (odds ratio (OR): 0.66, 95% confidence interval (CI): 0.45, 0.96), independent of age, race, obesity, and smoking habits. When androstenedione or testosterone levels were added to the model, the odds of experiencing any hot flashes were unchanged (OR: 0.66, 95% CI: 0.45, 0.97). In addition, current alcohol users had similar levels of androstenedione (geometric mean: users 2.04±0.10 ng/ml, non-users 2.01±0.19 ng/ml; $p<0.7$) and testosterone (geometric mean: users 0.47±0.03 ng/ml, non-users 0.51±0.11 ng/ml; $p<0.5$) compared to non-users of alcohol. These data suggest that current alcohol use is associated with a reduced risk of hot flashes in midlife women by a mechanism that may not include changes in androgen levels. Supported by NIH Grant AG18400 and a grant from the Women's Health Research Group at the University of Maryland.

Evaluation of Public Knowledge Regarding Environmental-Mercury-Related Fish Advisories in the Greater Washington, DC Area

Monica del C Pourrat, MD[1,2], Alene Kennedy[2], Jerome Paulson, MD[1,2] and Benjamin Gitterman, MD[1,2]. [1]General and Community Pediatrics, Children's National Medical Center, Washington, DC, United States and [2]George Washington University School of Public Health and Health Sciences, Washington, DC, United States.

Background: Methyl-mercury is a neurotoxicant present in high concentrations in predatory fish. Fish-advisories have been issued regarding consumption of locally caught fish. Sport fishermen studies have shown compliance with recommendations, but differences in knowledge exist among Caucasian, Latino and African-American fishermen. EPA/FDA developed fish-consumption recommendations for pregnant, childbearing-age, breastfeeding women, and young children. However, a previous study of urban, low−income African-Americans and Latino has shown limited knowledge about EPA/FDA fish-advisories. **Objective:** Determine levels of and differences in knowledge regarding fish consumption and potential mercury toxicity among different ethnic and SES groups in the Washington, D.C area. **Design/Methods:** Cross−sectional study of knowledge about mercury−related fish consumption recommendations. Interviews administered to diverse SES population in pediatric and WIC clinics in Washington, D.C. Descriptive and analytical statistics used. **Results:** 283 people were surveyed. 45% were African-American, 24% Caucasian, and 23% Latinos. Interviewees were 85% childbearing-age women. 69.44% of Latinos had incomplete high-school, vs. 27.8% of African-Americans. College-graduate education rates were: Caucasians, 86.6%; African-Americans, 24.4%; Latinos, 14.3%. Caucasian knew the target-population of the fish-advisories better than African-American and Latinos ($p<.0001$). Results were similar controlling for education: Caucasian-African-American, (p.0007), Caucasian-Latinos, (p.014). Graduate-level-educated African-American knew the target-population of the fish-advisories better than incomplete high-school African-American (p.030). 27.7% of subjects didn't know about fish-advisories; of them, 65% were Latinos with less than high-school. **Conclusions:** Knowledge about mercury contamination of fish and related risks is associated with educational levels, ethnicity and SES. Future educational efforts should take these differences into account and be more specifically directed at target-populations.

Comparison of Gene Expression Changes in the Striatum, Cortex and Hippocampus of Rats Treated with an Escalating Dose-Binge Methamphetamine (METH) Regimen.

D.L. Graham[1,2], P.-A.H. Noailles[1], O. Asanbe[1], K.G. Becker[3], W.H. Wood III[3], V. Prabhu[3], and J.L. Cadet[1] [1]Molecular Neuropsychiatry Branch, DHHS/NIH/NIDA/IRP, [2]Program in Toxicology, University of Maryland School of Medicine, [3]Gene Expression and Genomics Unit, DHHS/NIH/NIA/GRC, Baltimore, MD

Methamphetamine (METH) is a known neurotoxicant which causes monoamine depletion, nerve terminal degeneration, and apoptosis. In addition, use of the drug is associated with significant cognitive disturbances. In spite of the deleterious effects of the drug, METH abuse has reached epidemic proportions throughout the United States. Because chronic intake of METH causes tolerance to its euphoric effects, the user must increase both the dose and frequency of drug intake to sustain the “high”. In order to measure possible toxic effects of repeated METH injections, we have developed a chronic model in an attempt to mimic human drug abuse

patterns. Male Sprague Dawley rats were given an escalating dose (ED) of METH or a saline equivalent for two weeks before receiving a challenge dose of METH (3 x 10 mg/kg, every 2 hrs) or saline. Animals were sacrificed at 2 and 24 hrs following the final challenge dose. Brain regions were dissected, and microarray analysis was performed on the striatum, frontal cortex, and hippocampus. Among the genes that were significant were members of the syntaxin and ubiquitin families. Because of their integral roles in apoptosis, exocytosis and protein degradation, it is possible that expression of these genes following an ED-binge regimen might correlate with functional adaptation. Additionally, genes related to the apoptotic cascade, including caspase 9, were found to be expressed differentially between treatment groups and different regions of the brain.

Birth Defect Reduction and Differential Placental Protein Expression due to Non-specific Immune Stimulation with IFN-gamma in C57Bl/6N and CD-1 Methylnitrosourea-Exposed Mice

Chelsea Lee Laudermilch[1], Steven David Holladay[1], Dan Phillip Sponenberg[1], Geoffrey Kirk Saunders[1], Daniel Lee Ward[1], and Mary Renee Prater [1,2]*
[1]Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Department of Biomedical Sciences and Pathobiology, Blacksburg, Virginia
[2]Edward Via Virginia College of Osteopathic Medicine, Department of Biomedical Sciences, Blacksburg, Virginia

Nonspecific maternal immune stimulation is known to ameliorate methylnitrosourea (MNU)-induced fetal distal limb and digital defects in outbred CD-1 mice and to a lesser extent in immunologically sensitive inbred strain of mice, C57Bl/6N. The aim of this study was to determine the effects of maternal immunostimulation via mid-gestational administration of the cytokine interferon-gamma (IFN-γ). Fetal digital and distal limb development as well as placental protein expression and integrity were examined to determine if the immune stimulant reduced defects. Dams were given an intraperitoneal injection of IFN-γ on gestation day 7 (GD7) to stimulate the maternal immune system, and then the teratogenic dose of MNU was administered intraperitoneally on GD9. Fetal limb lengths, digital deformities, protein expression and placental histopathology from control and treatment groups were evaluated on GD14. IFN-γ protection against MNU-induced fetal digital deformities was demonstrated as the incidence of syndactyly, polydactyly, and webbing was reduced by 47%, 100%, and 63% respectively in C57Bl/6N mice. CD-1 mice, in comparison, exhibited reduced effects by 39, 71, and 20%, respectively. Administration of IFN-γ also significantly diminished MNU-induced endothelial and trophoblast placental damage in both strains of mice. Vascular endothelial growth factor (VEGF) is an angiogenic protein that causes endothelial dysfunction when placental concentrations increase. VEGF levels in the placentas of CD-1 IFN-γ and MNU treatment groups were significantly higher than control. MNU also caused a significant increase in monocyte chemoattractant protein-1 (MCP-1) levels in CD-1 placentas. MCP-1 is an inflammatory chemokine that has been associated with vascular changes in pre-eclampsia. MCP-1 and VEGF levels in the C57Bl/6N mice showed no significant changes. These findings support a possible link between maternal immunity, placental integrity, and fetal distal limb development. Further, these results suggest that IFN-γ might act through placental improvement to indirectly protect against MNU-induced fetal limb malformations.

In Ovo Incubation Temperature Alters Post-Natal Immune Development In Broiler Chickens

R. P. Kerr[1], David Caldwell[2], Keith Ameiss[2], Michael Hulet[3], Audrey McElroy[4], Robert M. Gogal Jr.[1,5,*]
[1]Center for Molecular Medicine and Infectious Disease, Virginia Maryland Regional College of Veterinary Medicine, Virginia Tech, [2]Department of Poultry Science, Texas A&M University, [3]Poultry Science Department, Penn State University, [4]Department of Animal and Poultry Science, Virginia Tech, [5]Department of Biomedical Sciences, Virginia College of Osteopathic Medicine

Research regarding *in ovo* incubation parameters has shown that incubation temperature positively affects broiler performance post hatch. Despite this growing body of work, there is a paucity of data relating temperature to immune status in domestic broiler flocks. Currently, vaccinations are performed *in ovo* requiring a more developed embryonic immune system. The emphasis on bird performance coupled with the increased stress from vaccination impacts bird immunocompetency increasing producer loss from mortality and morbidity. The optimization of incubation parameters to increase bird health would thus be beneficial. In this study, eggs were incubated at ether 100°F or 105°F. On the day of hatch, birds were randomly assigned to non-treated, vehicle treated, vehicle and bovine serum albumin (BSA) treated, or *Eimeria*-vaccinated groups and maintained in commercial growing batteries. Birds were treated on the day of hatch and administered a booster 21 days post hatch. Immune status was assessed at several time points. Splenic CD8+CD4- expression was significantly increased in non-treated, vehicle-treated, and vehicle-BSA 100°F bird groups compared to the respective 105°F groups during week 2. Lymphocyte transformation assays did not support a functional difference in T and B cell populations between respective temperature groups. In a concurrent Eimeria challenge study comprising non-treated and vaccinated birds housed in floor pens, lesions were evaluated 6 days post *Eimeria* challenge. Body Weight data suggested that 100°F groups performed better during grow out that 105°F birds. Lesion scores indicated that the vaccinated 105°F group had less GI lesions than the respective 100°F group and thus were better protected. The results of these studies would appear to show that changes *in ovo* incubation affect bird health.
This work was supported by a grant from the Virginia Agriculture Council.

Mice Deficient in Cyclooxygenase-2 Are More Susceptible Than Wild-Types to Kainic Acid Excitotoxicity

Christopher D. Toscano and Francesca Bosetti
Brain Physiology and Metabolism Section, National Institute on Aging, Bethesda, MD National Institutes of Health

Excitotoxicity (ET), neuronal damage evoked by excessive excitatory neurotransmission, is thought to contribute to the progression of certain neurodegenerative diseases. Investigations into the mechanism of ET have suggested a role for cyclooxygenase (COX), the primary enzyme that metabolizes arachidonic acid (AA) to eicosanoids. These previous studies have demonstrated that COX both potentiates and protects against ET; conflicting observations most likely due to the reliance on various COX inhibitors to perform these studies. Employing a novel approach that allowed us to avoid pharmacologic inhibition of COX, we attempted to clarify the role of COX in ET by exposing mice with a genetic deletion in COX-1 or COX-2 to the prototypic excitotoxin, kainic acid (KA). Median KA-induced seizure intensity, measured using the Racine seizure scale, was significantly elevated in KA-exposed COX-$2^{-/-}$ mice compared to wild type and COX-1-/- mice. In addition, only COX-2-/- mice exposed to KA exhibited hippocampal, thalamic and amygdalar neurons positive for Fluoro-Jade B, a histochemical stain that detects

damaged neurons. Since COX-2, but not COX-1, can inactivate endocannabinoids (EC), AA metabolites that increase neuronal excitability by suppressing GABAergic inhibitory tone, we hypothesized that COX-2-/- mouse susceptibility to ET is a result of increased EC signaling. Pretreatment of COX-2-/- mice with the EC receptor antagonist AM-251, however, augmented KA-induced seizure intensity and neuronal damage in both COX-2-/- and wild type mice, suggesting that this mechanism was not involved. Also, the increased susceptibility of COX-2 -/- mice to ET was not associated with an alteration in KA binding in the brain as assessed by ex vivo [^{3}H]-kainate receptor autoradiography. However, microarray analysis of gene expression revealed alterations in the GABAergic system of COX-2-/- mouse brain. Additionally, $PGE_{2,}$ levels, a product of COX-2 shown to be protective in other seizure models, are decreased in the brains of COX-2-/- , but not COX-$1^{-/-}$, mice. In summary, our study is the first to demonstrate that COX-2 -/- , but not COX-1 -/-, mice exhibit an increased sensitivity to ET. While the exact mechanisms still remain unclear, these results suggest both a protective role for COX-2 in ET and that selective abrogation of COX-2 activity, a clinical approach used to treat chronic inflammation in humans, may increase susceptibility to ET.

NATIONAL CAPITAL AREA SOT, FALL 2006 SYMPOSIUM

Mark your calendar-

Topic: "**Computational Toxicology**"

Location: Lister Hill Auditorium, Bethesda, Maryland

Date: December 11, 2006

TREASURERS REPORT

June 27, 2006

I. Official checking account balance (5/30/06 statement): $16,315.08

Spring Symposium Poster Awards (May 22, 2006)
1) Christopher Toscano- $350.00
2) Neal Burton- $250.00
3) Chrissy Schilling- $150.00

II. Not yet recorded by SOT Headquarters (as of 6/26/06)

A. Profits not yet reflected in official balance: total= $2,985.00

1) Registrations from Spring Symposium- $1,905.00
2) Long Range Planning Initiative Award- $990.00
3) New memberships (since May, 2006): $90.00
student (1): $10
full (4) :$80

B. Costs not yet reflected in official balance: total= $1,669.91

1) Metropolitan Board Installers- $295.00
2) Rockledge Café- $1023.82
3) Bus transportation for SMA- $351.09

III. Unofficial Balance as of 6/27/06: $17,630.17

Respectfully Submitted,
Jennifer Sekowski
27 June, 2006

National Capital Area

MEMBERSHIP APPLICATION

Name: _____

Affiliation: _____

Address _____

_____

City: _____

State: _____ Zip Code: _____

Area Code: _____ Phone: _____FAX:_____

E-mail: _____

Membership Type _____ Full Member ($20) _____ Student ($10)

Please check the most appropriate responses:

SOT Member

_____ Yes

_____ No

Highest Degree Attained

_____ A.S.
_____ B.A.
_____ B.S.
_____ D.V.M.
_____ D.V.M./Ph.D.
_____ M.D.
_____ M.D./Ph.D.
_____ M.P.H.
_____ M.S.
_____ M.A.
_____ Ph.D.
_____ Sc.D.
_____ V.M.D.
_____ V.M.D./Ph.D.

Type of Affiliation

_____ Academia
_____ Consulting
_____ Contract Lab
_____ Government
_____ Industry-Chemical/Petroleum
_____ Industry- Pharmaceutical
_____ Industry- Other
_____ Other- _____

Please complete the information above and send with a check, money order or credit card (payable to [specific RC], no POs) to the address below. The chapter to which you are applying will review your application and you will be notified within 30 days. Those not accepted will receive a full refund. *Current RC members: please do not use this form since your renewal dues are billed annually through SOT.*

Payment Type: Money Order_____ Check _____ Credit Card _____
Credit Card # _____ Exp date _____
Name on Card _____

Send to:

Jennifer Weeks Sekowski, Treasurer
US Army
CHPPM ATTN MCHBS TS THE, 5158 Blackhawk Road
Aberdeen Proving Ground, MD 21010