



ONE WORLD,

ONE MEDICINE,

ONE HEALTH

One Health Intellectual Exchange

Weekly Discussions / Course: Philosophy to Practical Integration of Human, Animal and Environmental Health

A weekly discussion series, sponsored by the **North Carolina One Health Collaborative** within the NCBC IEG Program to enhance collaborations between physicians, veterinarians, researchers and other local/global/environmental health professionals by increasing public awareness of the interconnectedness of people, animals and the environment.

(Available each spring for credit if desired)

13th 2013 Weekly Session - Tuesday, April 9

5:30 – 7:30 p.m.

**Alternative Models for Comparative Vertebrate Research:
Applications to Regulatory Science**

William S. Stokes, DVM ,DACLAM, DACAW, BCES, FATS
and

**Innovative Approaches to Invertebrate Health Research:
Applications to Environmental Health Science**

Michael K. Stoskopf, D.V.M., Ph.D., D.A.C.Z.M.

Meets Tuesdays, 5:30 – 7:30 p.m. at the North Carolina Biotechnology Center
15 T.W. Alexander Drive Research Triangle Park, NC 27709

Directions: www.ncbiotech.org/directions

Suggestions? Ideas? Contact Cheryl Stroud, Steering Comm. Chair cms7earth@gmail.com

Add yourself to the listserv with Listserv Manager Liz Selisker, liz_selisker@ncsu.edu

For Speaker Bio's, Suggested Readings, Cancellation notices and additional background

<http://nconehealthcollaborative.weebly.com/index.htm>

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For more information on the course option contact: Course TA Anne Stine anne.stine@duke.edu

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William S. Stokes



Michael K. Stoskopf

William S. Stokes, DVM ,DACLAM, DACAW, BCES, FATS

Dr. William S. Stokes is the former Director of the U.S. National Toxicology Program's Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) at the National Institute of Environmental Health Sciences, and former Executive Director for the U.S. Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). NIEHS is one of the 27 Institutes and Centers of the National Institutes of Health, the nation's biomedical research agency. The mission of NIEHS is to discover how the environment affects people in order to promote healthier lives. NICEATM and its interagency committee serve a critical role in translating advances in science and technology into approved safety assessment methods necessary to prevent disease and injuries and to protect public health, animal health, and the environment. Dr. Stokes also served as Chief of the Comparative Medicine Branch and Animal Program Director at NIEHS. He is currently an adjunct Professor in the Department of Comparative Biomedical Sciences in the College of Veterinary Medicine at North Carolina State University.

Dr. Stokes recently completed his uniformed services career as an officer in the U. S. Public Health Service Commissioned Corps, where he attained the rank of Rear Admiral and Assistant Surgeon General and served as the 8th Chief Veterinary Officer. The USPHS Commissioned Corps is a multidisciplinary "One Health" organization with a diverse range of professionals, including veterinarians, physicians, scientists, and engineers. Dr. Stokes also served on the American Veterinary Medical Association's One Health Initiative Task Force and contributed to the establishment of the national One Health Commission. For the past three years, he has participated as a member of the North Carolina One Health Collaborative.

Dr. Stokes received his B.S. with a major in biomedical engineering from the University of Louisville and his D.V.M. from The Ohio State University. He is a board certified Diplomate of the American College of Laboratory Animal Medicine and the American College of Animal Welfare. He is also a Board Certified Environmental Scientist, Fellow of the Academy of Toxicological Sciences, and a former Council member of the Institute of Laboratory Animal Research at the National Academy of Sciences. He has received numerous awards, including the HHS Secretary's Award for Distinguished Service, the Surgeon General's Exemplary Service Medal, the NIH Director's Award, and the K.F. Meyer-James H. Steele Gold Headed Cane Award from the American Veterinary Epidemiological Society.

Alternative Models for Comparative Vertebrate Research: Applications to Regulatory Science

Vertebrate species serve as important animal models for biomedical research and testing. Their use has supported tremendous progress in the understanding of the pathogenesis of debilitating diseases and the development of safe and effective treatments and prevention strategies. In the last two decades there has been significant advances in the use of cells and tissues as part of the toolbox for an integrated approach to chemical and drug safety assessments in the context of regulatory science. These simpler systems allow for investigation into the molecular perturbations associated with diseases and exposures that lead to adverse health effects from chemicals, drugs, and other substances in our environment. Such models are now used in an iterative approach with animal models and human studies and experience to more efficiently and effectively address research, efficacy, and safety questions. Examples of several alternative models and how they have been incorporated into safety assessment decision-making will be discussed.

Learning Objectives

1. Explain advantages and disadvantages of cells and tissue models compared to in vivo models for biomedical research and testing.
2. Describe three cell or tissue models that have been adopted for safety assessments for new drugs or products that can substitute for the use of vertebrate animal models.
3. Describe the concept of “adverse outcome pathways”, and how cell and tissue models based on an understanding of AOPs can be incorporated into safety assessment strategies.

Suggested Readings:

1. Birnbaum L and Stokes WS, 2010: Safety Testing: Moving Towards Alternative Methods. *Environmental Health Perspectives* 118(1): A12-13. Available: http://iccvam.niehs.nih.gov/docs/about_docs/EHP-BirnbaumStokes-Jan10.pdf
2. Stokes WS et al. 2012. Validation of the 21st Century Toxicology Toolbox: Challenges, Opportunities, and the Way Forward. *ALTEX Proceedings* 1/12: 323-328. Available: http://www.altex.ch/resources/323328_Stokes22.pdf
3. ICCVAM, 2012. Biennial Progress Report of the Interagency Coordinating Committee on the Validation of Alternative Methods (2010-11). NIH Publication No. 12-7873. Research Triangle Park, NC: National Institute of Environmental Health Sciences. Available: <http://iccvam.niehs.nih.gov/docs/annrpt/Biennial2012-508.pdf>
4. NIEHS, 2012. The NICEATM-ICCVAM Five-Year Plan (2013-2017): A plan to advance innovative test methods of high scientific quality to protect and improve the health of people, animals, and the environment (Draft: May 14, 2012, 68pp). National Institute of Environmental Health Sciences, Research Triangle Park, NC. Available: <http://iccvam.niehs.nih.gov/docs/5yrPlan/2013-5YP-14May2012v2-draft.pdf>

Michael K. Stoskopf, D.V.M., Ph.D., D.A.C.Z.M.

Dr. Michael K. Stoskopf is a professor of Wildlife and Aquatic Health and the Director of the Environmental Medicine Consortium at the College of Veterinary Medicine, North Carolina State University. He also holds faculty appointments in the College of Natural Resources (Forestry and Natural Resources Management), Agriculture and Life Sciences (Environmental and Molecular Toxicology), and Engineering (Biomedical Engineering). He serves on the Fisheries, Wildlife and Conservation Biology Faculty as Director of Graduate Programs for veterinary graduate students in that program and is a former chair of the Marine Sciences Council and a current member of the Marine and Coastal Sciences Faculty. He Co-Directs the Marine Magnetic Resonance Imaging and Spectroscopy facility at NCSU's Center for Marine Sciences and Technology where his Marine Ecological Metabolomics Laboratory focuses on assessment of environmental impacts on the metabolism of wild animals and mechanisms of adaptation to global change. He is a Co-PI and active participant of the Southeastern Climate Science Center and actively involved in the Center for Comparative Medicine and Translational Research's Conservation Genomics Working Group. He has long served as the Chair of the Red Wolf Recovery Implementation Team assisting U.S. Fish and Wildlife Service efforts to reestablish red wolves and is a member of the Wyoming Toad Recovery Implementation Team.

The former and founding Chief of Medicine at the National Aquarium in Baltimore, Dr. Stoskopf is considered a pioneer in fish medicine, pioneering many clinical approaches in a wide range of aquatic and marine species. His book, "Fish Medicine" is considered a landmark publication in the discipline. Widely published in the scientific literature Dr. Stoskopf has contributed important new insights into questions ranging from the physiology of dinosaurs to the lipid metabolism of cockroaches. He has had active editorial responsibilities for 10 major scientific journals and is currently on the editorial boards of Marine Pharmaceuticals and International Veterinary Medicine. He is a former president of the American College of Zoological Medicine and of the International Association of Aquatic Animal Medicine, and takes pride in the success of the numerous graduate students and residents he has mentored in the clinical, and scientific arts, including 16 students receiving masters degrees in Art as Applied to Medicine.

Dr. Stoskopf received his B.S. In Veterinary Sciences and his D.V.M. from Colorado State University and a PhD in Environmental and Biochemical Toxicology from Johns Hopkins University. He is a board certified Diplomate of the American College of Zoological Medicine and a former Council member of the Institute of Laboratory Animal Research at the National Academy of Sciences. He has been a nominee for the Indianapolis Prize for Contributions to Conservation and has received numerous awards, including the Jalanka Medal for distinguished research on health and welfare of wild animals from the University of Helsinki, the Dolensek Award from the Wildlife Conservation Society and American Zoo Veterinary Association for Clinical Contributions in zoo and wildlife medicine, and the International Association of Aquatic Animal Medicine N.O. Christiansen Award for Excellence in Fish Health.

Innovative Approaches to Invertebrate Health Research: Applications to Environmental Health Science

Application of advanced technologies to broadly comparative studies of invertebrates provide powerful tools for obtaining data useful in the assessment of impacts of environmental stressors on health at individual, population and ecosystem scales. Advances of techniques to permit high quality

sampling in field conditions broadens the ability to address questions at the ecosystem, landscape and other large scales as well as the potential for clinical applications for wildlife health assessment. Survival sampling under controlled environmental conditions using these techniques supports powerful longitudinal study designs that control key variables, reduce data variability and reduce consumptive use of study animals. Combined with “low tech” simple study approaches such as the “Rolling Study” consumptive use of research animals can be minimized and metabolomic techniques may be suitable for early assessment monitoring. The discussion will introduce the potential for advanced NMR metabolomic assessments of invertebrates to inform our understanding of the physiologic responses of key species to a wide range of environmental perturbations. Examples of advances in and the importance of this understanding to environmental health decision making will be considered, and as a tantalizing tidbit, the importance of serendipity and observation in advancing one science in general and one health questions in particular will be introduced.

Learning Objectives

1. Explain advantages of survival techniques compared to more traditional lethal sampling for environmental health research.
2. Describe the “Rolling Study Design” approach that can be used to minimize animal use when species response to a perturbation or chemical exposure is unknown.
3. Explain the concept of Ecological Metabolomics, and how assessment of invertebrate metabolomes can help guide environmental health decisions.
4. Describe the concept of serendipity and consider its role in advances in science.

Suggested Readings

1. Stoskopf MK. (2005) Observation and cogitation: how serendipity provides the building blocks of scientific discovery. *ILAR journal / National Research Council, Institute of Laboratory Animal Resources* 46(4): 332-337. <http://ilarjournal.oxfordjournals.org/content/46/4/332.full>
2. Gustafson, L., Showers, W., Kwak, T., Levine, J., Stoskopf, M. (2007) Temporal and spatial variability in stable isotope compositions of a freshwater mussel: implications for biomonitoring and ecological studies. *Oecologia* 152:140-150. http://www4.ncsu.edu/~tkwak/Gustafson_et_al_2007.pdf
3. Tikunov, Andrey P., Christopher B. Johnson, Haakil Lee, Michael K. Stoskopf, and Jeffrey M. Macdonald (2010) Metabolomic Investigations of American Oysters Using ¹H-NMR Spectroscopy. *Marine Drugs*. 8(10):2578-2596; doi:10.3390/md8102578 <http://www.mdpi.com/1660-3397/8/10/2578/pdf>
4. Henson-Ramsey, Heather, Ashley Schneider, Michael Stoskopf (2011) A Comparison of Multiple Esterases as Biomarkers of Organophosphate Exposure and Effect in Two Earthworm Species. *Bulletin of Environmental Contamination and Toxicology* 86(4):373-378. DOI 10.1007/s00128-011-0236-9 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3208328/>

Additional Readings for this session:

1. NRC, 2007. Toxicity testing in the 21st Century: a vision and a strategy. Washington, DC: National Academies Press. Available: http://www.nap.edu/catalog.php?record_id=11970

2. Huh D, Leslie DC, Matthews BD, Fraser JP, Jurek S, Hamilton GA, Thorneloe KS, McAlexander MA, Ingber DE (2012). A human disease model of drug toxicity-induced pulmonary edema in a lung-on-a-chip microdevice. *Science Translational Medicine* 4 (159): 159ra147

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