

Center Line

Bowles Center for Alcohol Studies
School of Medicine, University of North Carolina at Chapel Hill

Our mission is to conduct, coordinate, and promote basic and clinical research on the causes, prevention, and treatment of alcoholism and alcoholic disease.

Volume 13, Number 3, 2002

UNC Scientist Leads Bowles Center Efforts to Prevent Fetal Alcohol Syndrome

In its May 24, 2002, issue of the *Morbidity and Mortality Weekly Report*, the US Centers for Disease Control (CDC) designates maternal alcohol use during pregnancy as a major public health concern in the United States. Alcohol use during pregnancy can cause a spectrum of detrimental effects in the developing baby that result in lifelong physical and mental impairment. The best known of these sequelae is fetal alcohol syndrome, which is characterized by specific facial abnormalities, growth deficiency, and brain dysfunction. Fetal alcohol syndrome is the leading cause of mental retardation in the United States. Besides fetal alcohol syndrome, maternal alcohol use has lesser known, but more common, consequences including *alcohol-related neurodevelopmental disorder* (i.e., mental impairment without the characteristic fetal alcohol syndrome-associated craniofacial defects) and *alcohol-related birth defects* (i.e., skeletal and organ defects other than the characteristic craniofacial defects). Full-blown fetal alcohol syndrome occurs in up to 1.5 in 1,000 births as reported in the CDC's 1995-1997 five-state study, the most recent to be published. Alcohol-related neurodevelopmental disorders and alcohol-related birth defects affect an estimated three times more children than does fetal alcohol syndrome.

Only during the past two decades has alcohol consumption during pregnancy been definitively established as a cause of these sequelae—thanks in part to research conducted by Bowles Center for Alcohol Studies researcher Dr. Kathy Sulik and her laboratory. In the early 1980s, Dr. Sulik and her laboratory conducted research that



The FAS Research & Prevention Team. L to R: Corey Johnson, Bill Dunty, Debbie Dehart, Jan Smith, Dr. Marianne Meeker, Heather Baudet, Dr. Kathy Sulik, and Dr. Shao-yu Chen.

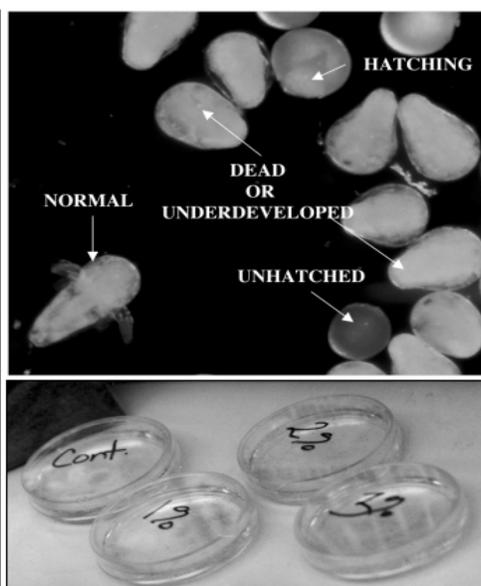
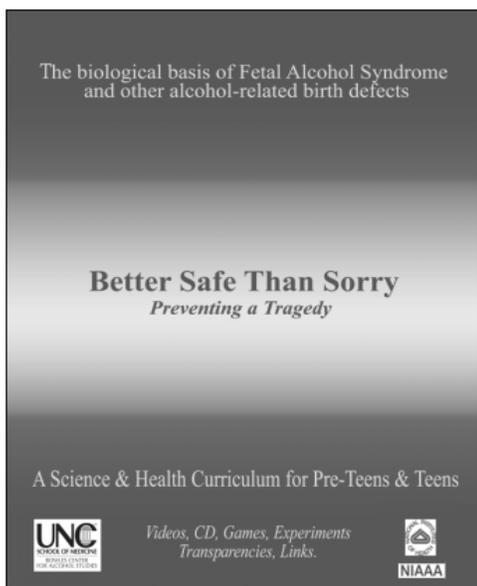
helped to establish alcohol as the causative factor in fetal alcohol syndrome. They discovered that, under controlled genetic and nutritional conditions, alcohol administered to mice during a particular time in gestation (the equivalent of heavy binge drinking during the third week of human pregnancy) resulted in craniofacial and other birth defects comparable to those occurring in babies of women drinking alcohol during pregnancy. These discoveries aided in the U.S. Government's decision to pass the Alcoholic Beverage Labeling Act of 1988 which requires alcoholic beverage manufacturers to place health warning labels on all alcoholic beverage containers.

Since 1980, Dr. Sulik has continued her research on alcohol's teratogenic effects, identifying the events in embryonic development that are adversely impacted by maternal alcohol use. During the past few years, she has extended her work by

taking her science to the community, where she has engaged in targeted educational initiatives and developed creative programs to inform the public about the dangers of prenatal exposure to alcohol.

Dr. Sulik, in collaboration with Dr. Marianne Meeker of the Department of Cell and Molecular Physiology at the University of North Carolina and with the support of a grant from the National Institute of Alcohol Abuse and Alcoholism, has developed a modular science curriculum called *Better Safe Than Sorry: Preventing a Tragedy*. Targeted for pre-teens and teens, the curriculum is designed for science and health teachers to use in teaching about alcohol and its effects on the developing fetus. Middle and high school teachers can select from the curriculum the materials and activities appropriate for the amount of time they can

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The "Better Safe Than Sorry" curriculum's hands-on experiment illustrates that brine shrimp hatching and development are adversely affected by exposure to alcohol. Students place eggs in sea water with 1%, 2%, or 3% alcohol, or with no alcohol (control). Hatching, viability, and full development are alcohol concentration dependent. (supported by NIAAA)

devote to the topic and to the age and interests of their students. For example, the curriculum includes an interactive quiz game that can be played on computer or on paper, an educational video, transparencies to be used in classroom instruction, suggestions for classroom activities, and lists of web links and print materials containing information on fetal alcohol syndrome.

The curriculum includes a hands-on experiment with developing brine shrimp, a favorite in the school lab. The experiment involves exposing the tiny brine shrimp, each about the size of a pepper grain, to varying concentrations of alcohol and observing alcohol's effects. The brine shrimp come to the students in a small plastic packet of powder that resembles dust—the brine shrimp eggs. By dipping a moist toothpick into the packet, students withdraw a quantity of brine shrimp eggs and then place them in a series of salt water-filled Petri dishes. When the students add the brine shrimp eggs to salt water, the brine shrimp babies come to life, and the water swarms with tiny, wriggling brine shrimp. The effect is strikingly different when the students add the brine shrimp eggs to water containing varying concentrations of alcohol. While the Petri dish containing no alcohol teems with life, the dish con-

taining 1% alcohol contains about half as many wriggling brine shrimp, and the dish containing 2% alcohol about half as many again. In the dish containing 3% alcohol, almost no brine shrimp are alive. The toxic effects of alcohol on the developing brine shrimp are particularly marked when viewed under a hand magnifying lens or laboratory microscope but are also visible to the naked eye. "The brine shrimp experiment is a way to bring home the effects of alcohol in a way that is memorable for the student," says Dr. Sulik. "The experiment provides an opportunity for stu-

dents to be actively involved in learning a very important lesson: alcohol is toxic to developing organisms. If this lesson prevents just one of the female students or the males' partners, when they have grown older and become prospective parents, from drinking alcoholic beverages during pregnancy, our work is a success. Of course, our ultimate goal is to prevent alcohol consumption among all pregnant women."

Dr. Sulik's curriculum has been field tested in North Carolina in the Caswell County and Alamance County school systems and will be tested in a third system before being finalized by the end of 2002. She hopes that the program will eventually become a model useful to school systems across the nation. In addition to these initiatives, Dr. Sulik has developed an

Internet slide show, available on the Bowles Center for Alcohol Studies web site, that takes the viewer step-by-step through the causes, signs, symptoms, and results of fetal alcohol exposure. The show, partially funded by The Medical Foundation of North Carolina, is appropriate for both children and adults.

Dr. Sulik is currently involved in raising awareness of fetal alcohol syndrome and the need for prevention at the state and national level. Because of the efforts of Dr. Sulik, Alcohol/Drug Council of NC, Arc Durham & Wake County, Healthy Mothers/Healthy Babies, March of Dimes, Wake Forest University and many other organizations throughout the state, North Carolina for the first time will officially observe International Fetal Alcohol Syndrome Awareness Day on September 9, when

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Kathleen K. Sulik, PhD

Professor, Department of Cell and Developmental Biology, UNC-Chapel Hill

PhD in Anatomy, University of Tennessee Center for Health, 1976; BS in Biology, Education and Art, Drake University, 1970.

Recent Publications

Chen S-Y, Wilkmeyer MF, Sulik KK, and Charness ME (2001) Octanol antagonism of ethanol teratogenesis. *FASEB* 15: 1649-51

Dunty, WC, Chen S-Y, Zucker RM, Dehart DB, and Sulik KK (2001) Selective vulnerability of embryonic cell populations to ethanol-induced apoptosis: implications for alcohol related birth defects and neurodevelopmental disorder. *Alcohol Clin Exp Res* 25:1523-35

Fitzky BU, Moebius FF, Asaoka H, Waage-Baudet H, Xu L, Xu G, Maeda N, Kluckman K, Hiller S, Yu H, Batta AK, Shefer S, Chen T, Salen G, Sulik K, Simoni RD, Ness GC, Glossman H, Patel SB, and Tint GS (2001) 7-Dehydrocholesterol Accelerates Proteolysis of 3-hydroxy-3-Methylglutaryl CoA Reductase in Mice with a Targeted Disruption of Dhcr7. *J Clin Invest.* 108:905-15

Web page

<http://www.med.unc.edu/alcohol/faculty/SulikKK/Sulik.htm>

Research funded by NIAAA.





The Director's Column

Fulton T. Crews, Ph.D.
Director,
Bowles Center for Alcohol Studies

Although many have focused on rehabilitation of children with Fetal Alcohol Syndrome, we at UNC agree that prevention is the best approach to reducing what is the largest known cause of mental retardation. It is a joy and pleasure to work with Kathy Sulik and her discovery-education team's efforts to translate her research on the fetal toxicity of alcohol to prevention education. For higher-level prevention education, she has obtained unique human embryo images that show the human embryo is almost identical to the mouse embryo at early stages of development. This provides a foundation for her mouse images of ethanol teratogenicity (nonheritable birth defects caused by ethanol consumption) that show the increased programmed cell death of neural crest and others cells that lead to the facial and cranial (physical) abnormalities associated with FAS. The images are impressive and must impact medical and science students. All people, but particularly health professionals, need to know the devastating effects of alcohol on fetal development.

My favorite prevention education activity is the simple brine shrimp experiment

developed for middle school students and designed to be done with the simplest of equipment in any school. I smile thinking of how the students will become excited by the wonder of life that they will see as the tiny black brine shrimp eggs come to life in a petri dish of salt water. I think this will draw some of them into the biological sciences because they are eager to gain a greater understanding of the mystery of life. Although we know a lot about how a small black dot becomes an active, swimming organism, I think it is still a bit of a miracle. Observing the impact of alcohol on this miracle as the brine shrimp eggs fail to hatch or the newly emerging creatures fail to fully develop likely fascinates these young individuals while burning the message of the effects of alcohol into their memories. We hope the students will share this message with their parents, peers and others throughout their life. Changing behavior is hard, but it starts with education and peer support. Dr. Sulik's prevention education plan is one way to stimulate interest in science while driving home the message that alcohol can be a curse on the miracle of life.

Post-Doctoral Fellowships Available

The Bowles Center for Alcohol Studies is offering post-doctoral fellowships in a multidisciplinary training program funded by NIAAA. Research is focused on molecular and cellular studies on alcohol actions. Applicants must have an M.D. or Ph.D., U.S. citizenship, and an interest in alcohol research. Send applications to a faculty mentor of interest. For more information about the post-doctoral fellowships, please visit <http://www.med.unc.edu/alcohol/postdoc>.

George R. Breese, Ph.D.

Action of ethanol on ligand-gated ion channel receptors defined with patch-clamp electrophysiology and single-cell RT-PCR; Basis of ethanol withdrawal anxiety.

David A. Brenner, M.D.

Molecular mechanisms of alcohol-induced hepatic fibrosis

Fulton T. Crews, Ph.D.

Neurodegeneration and neurogenesis

Clyde W. Hodge, Ph.D.

Neurobiological and molecular mechanisms of alcohol self-administration

John J. Lemasters, M.D., Ph.D.

Confocal microscopy of liver cell injury

A. Leslie Morrow, Ph.D.

Molecular mechanisms of GABA_A receptor regulation: Relationship to ethanol dependence

David H. Overstreet, Ph.D.

Serotonergic mechanisms underlying strain differences in ethanol self-administration

Kathleen K. Sulik, Ph.D.

Pathogenesis and mechanisms underlying alcohol-related birth defects

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they will kick off a fetal alcohol syndrome prevention initiative. As part of this initiative, posters and stickers developed to raise awareness of the importance of remaining alcohol-free during pregnancy, will be distributed in public places, including college campuses.

Dr. Sulik also participates on the Fetal Alcohol Syndrome Center for Excellence Steering Committee, which was recently organized by the federal government. The Steering Committee is devoted to identifying, developing, and implementing means of preventing fetal alcohol syndrome.

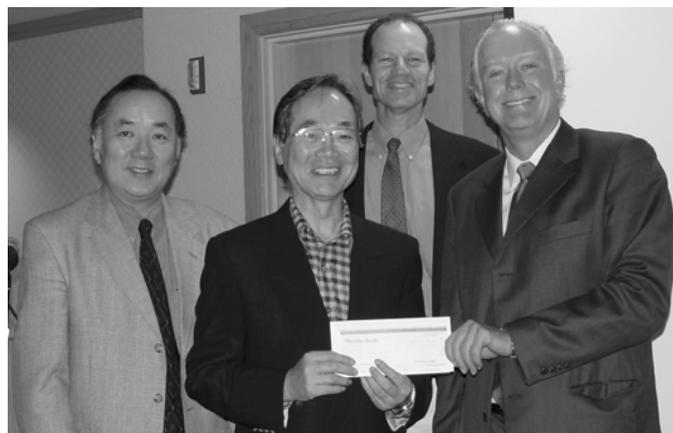
"It's fun—and rewarding," says Dr.

Sulik, when asked how she finds the energy to engage tirelessly in these educational activities as well as to keep up with her laboratory research and a rigorous university teaching schedule that includes medical school classes in gross anatomy and embryology. "As a scientist, I am lucky in being able to see our work go from the benchtop to practice. Fetal alcohol syndrome and related deficits, unlike many other birth defects, should be 100% preventable. The goal of prevention is achievable if pregnant women can be taught to abstain from drinking. We hope to aid in achieving that goal by teaching people about what the science shows."

Thurman Memorial Symposia Draws Liver Pathology Experts to RSA/ISBRA 2002

Ronald G. Thurman was an exceptional investigator in the fields of hepatic metabolism, alcoholic liver injury and toxicology. With his death on July 14, 2001, his large family of colleagues and friends lost a productive and creative researcher and teacher. Dr. Fulton T. Crews, Director of the Bowles Center for Alcohol Studies, organized a satellite symposium of the 2002 RSA/ISBRA Scientific Meeting entitled "*Alcohol and the Liver: A Memorial for Ron Thurman*" to honor the late Dr. Ronald Thurman's accomplishments in alcohol and liver research. Researchers from around the world traveled to San Francisco on June 28, 2002 to attend the symposium that brought together the world's best liver pathology experts and drew an outstanding response from the alcohol toxicology research community. Drs. Nobuhiro Sato, David Brenner, Hidekazu Tsukamoto and Fulton Crews served as moderators and discussants.

The symposium highlighted the latest advances in alcohol and liver research as well as discussions about the scientific contributions of Dr. Thurman. Dr. Tsukamoto, Director of the Research Center for Alcoholic Liver and Pancreatic Diseases at the Univ. of Southern California, gave a lecture called "*Ron Thurman and the Tsukamoto-French Model of Alcohol Liver Inquiry*." Dr. Ronald Mason of the NIH discussed the mechanism of in vivo ethanol free radical metabolite formation. Other speakers include Amin A. Nanji,



Symposia moderators stand together as Dr. Sato presents a \$10,000 contribution to the Thurman Lectureship Award. L to R: Drs. Tsukamoto, Sato, Brenner, and Crews

Univ. of Hong Kong; Samuel W. French, UCLA; Yoshiyuki Takei and Kenichi Ikejima, Juntendo University; Chantal Rivera, Baylor; and Peter Schemmer, Univ. of Heidelberg. UNC speakers were Blair Bradford, John Lemasters, Michael Wheeler, and Gavin Arteele.

One of the many highlights of the symposium was Dr. Sato's \$10,000 contribution to the Center for Alcohol Studies to support the Thurman Lectureship Award. The Center hopes to endow a lectureship in Ron Thurman's name to recognize scientific contributions to our understanding of alcoholic liver disease. In addition, Dr. Tsukamoto announced that his Center would match all contributions to the Award after giving a heartwarming account of Dr. Thurman's contributions to alcohol and liver research.

To make a contribution to the Lectureship Award Endowment, contact Elizabeth Amend.

Triangle Voices of Recovery Celebration

The Healing Place of Wake County
1251 Goode St., Raleigh, NC
Saturday, Sept. 28, 2002 11-3 pm



The Bowles Center for Alcohol Studies

Tel. (919) 966-5678
Fax. (919) 966-5679

To become involved in our mission, call Elizabeth Amend at (919) 843-6204 or email amend@unc.edu.

For treatment information call UNC Health Care's Alcohol and Substance Abuse Program at (919) 402-1644.

www.med.unc.edu/alcohol

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A. Leslie Morrow, Editor-in-Chief; Angela D. Fariior, Managing Editor; Jane Saiers, Science Writer

UNC Bowles Center for Alcohol Studies
CB# 7178, Thurston-Bowles Building
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina 27599-7178

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