YOUR HEALTH & THE ENVIRONMENT

NEWS FROM THE UNIVERSITY OF ROCHESTER
ENVIRONMENTAL HEALTH SCIENCES CENTER • WINTER ISSUE 2004

Does Sex Matter?

Male Brains, Female Brains, and Environmental Exposures

By Bernard Weiss, Ph.D.

Charles Darwin created the term,sexual dimorphism, to describe fundamental differences between the males and females of a species. To those of us who ask questions about the coupling of health and our chemical environment, sex differences can offer critical clues about the origins of certain kinds of disorders. Although science and medicine have long been aware of sex differences in disease susceptibility, it wasn't until 1993 that Congress mandated the inclusion of both sexes in research funded by National Institutes of Health. The Food and Drug Administration also began in 1993 to require an examination of sex differences in clinical trials of new drugs.

One area of biomedical research that needs to be exquisitely sensitive to sex differences is in understanding the ways in which our health is influenced by chemicals in the environment. Unlike research with drugs, which are administered deliberately in doses designed to alter the body's responses,scientists at our Environmental Health Sciences Center study chemicals such as lead and pesticides to which we are exposed mainly as a by-product of environmental contamination. Only rarely, as in accidents, do such exposures occur at a level great enough to engender flagrant disease. More typically, because we usually deal with much lower exposures, they are also more likely to produce relatively elusive signs of disease and dysfunction or contribute to the risks of recognized diseases rather than inducing them unequivocally. But we have to recognize that such exposures are not accompanied, as with drugs, by medical monitoring, and that they can include

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The University of Rochester Environmental Health Sciences Center is housed in the Department of Environmental Medicine, and is one of 25 such centers sponsored by the National Institute of Environmental Health Sciences, a component of the National Institutes of Health. Its research programs are designed to expand our knowledge about those environmental factors that influence our health. Some of the work undertaken and reported on in this publication is supported by NIEHS Center Grant ES01247. For more information go to: www2.envmed.rochester.edu/envmed/

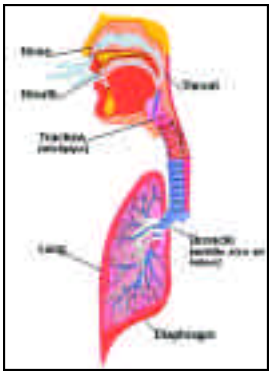
Childhood Asthma

Asthma is the leading cause of serious chronic illness in children and is the number one chronic cause of children's lost school days.

Asthma is a disease where the bronchial airways of the respiratory system are inflamed causing them to become over-reactive and produce increased mucus, swelling and muscle contraction. Asthma is the leading cause of serious chronic illness in children and is the number one chronic cause of children's lost school days. Most children have mild problems with asthma that can be controlled by treatment at home or in a doctor's office. However, for some children the illness becomes a serious medical condition, causing visits to the hospital emergency room. Asthma episodes are caused by "triggers", conditions which activate the over-reactive respiratory system. These triggers include respiratory infections, reactions to allergens, cooling and drying of the airways and cigarette smoke. Asthma cannot be cured, but it can be controlled by avoiding trigger factors. Asthmatic children usually exhibit symptoms of the disease before the age of five. Children can inherit the tendency to have asthma from their parents.

The respiratory system is made up of your nose and mouth, your windpipe, lungs and air tubes that connect to your nose and your mouth with your lungs.

A diagnosis of asthma by a medical doctor will include a physical examination of the child and a discussion with the child and parents about symptoms that they are experiencing. Asthma signs and symptoms include wheezing, frequent coughing or respiratory infections (pneumonia or bronchitis), chest tightness and shortness of breath. During the physical exam the doctor will listen to the chest using a stethoscope and measure the function of the child's lungs with a spirometer or peak flow meter (a device that measures the maximum speed at which the child can blow air out). Medications that are available for asthmatics include bronchodilators (drugs that relax the muscles of the airways and treat the inflammatory component).



Children with early –onset asthma sometimes outgrow it during adolescence. For some, symptoms return in adulthood.

Parents should notify the school if their child has asthma. Some schools allow asthmatic children to carry inhalers, with their parents' permission, if they are trained to use them. In some schools, medications are kept in a school nurse's office and are administered there when needed. Parents should also plan to meet with the child's teacher and make him/her aware of the problem.

Some Outdoor Asthma Triggers:

- Pollen
- Cold/dry weather
- Smoke
- Air pollution (ozone, particles, sulfur dioxide)

Some Indoor Asthma Triggers:

- House dust mites
- Pet fur and dander
- Cigarette smoke
- Cockroaches
- Household cleaning products
- Wood stove smoke

Some Helpful Reading About Asthma for Parents:

Children with Asthma: A Manual for Parents – by Thomas F. Plaut. This book has sections devoted to infants, children and teens and is referred to as "the asthma bible". 1996. ISBN: 0-914625-21-7

The Asthma Sourcebook: Everything You Need to Know by Francis Adams, M.D. 1995 Paperback. Little, Brown and Company ISBN: 1-56565-471-4.

Asthma Magazine – 1-800-654-2452 – A publication for people with asthma who are interested in learning more about their condition and how to manage it. The magazine is published 6 times a year. It provides the latest news, research, tips and strategies to help to take the mystery out of asthma management. This publication has been endorsed by the American Lung Association.

Some Helpful Reading About Asthma for Children:

Winning Over Asthma – by Eileen Dolan Savage. This is a fictional story about of a five-year old who is just learning to deal with asthma. This book explains the facts about asthma through the experiences of a five-year old and it describes what happens during an asthma attack. 1997 Pedipress ISBN 0-914625-26-8

I'm Tougher Than Asthma! – Siri M. Carter and Alden Carter. Eight year-old Siri tells her own story of her life with asthma. Paperback, 1996. ISBN: 0807534757

The ABC's of Asthma: An Asthma Alphabet Book for Kids of All Ages – Gosselin, Ravanelli and Mitchell. In this book, each letter of the alphabet matches to a word that explains asthma, things that trigger asthma episodes, and items used in the treatment of asthma. Publisher JayJo Books, LLC (Special books for special kids). ISBN: 1891383043

Asthma Web Sites

http://www.lungusa.org/asthma
Asthma information from the American Lung Association

http://asthma.nationaljewish.org/ - All about asthma: symptoms, daily living, treatments and medications

http://www.lungusa.org/asthma/ascpedfac99.html
Asthma
in children fact sheet on controlling your child's asthma

http://www.njc.org/intro2.html - The Asthma Wizard teaches kids all about asthma

Recent Research into Causes of Asthma

By William S. Beckett, M.D., M.P.H.

An increase in asthma, mainly in children, occurring in the US and many other countries between the 1970s and 1990s spurred intensified research that has now answered many questions about the causes of this most common chronic serious medical condition of children. Perhaps 5% of Americans have asthma at some point in their lives. The causes are both genetic — inherited from one or both parents - and environmental — requiring exposure to certain factors at key times during growth and development. In many cases, both the presence of specific inherited parental genes and the environmental factors must combine to result in asthma.

Overall, genes are slightly more important, accounting for perhaps 60% of the total risk for asthma, while environmental factors may account for about 40% of that risk. The genetic part of this disease is quite complex. There is no one "asthma gene" but rather more than a dozen gene variants which may contribute to the possibility of an individual developing clinical asthma. A number of laboratories are focusing in on some of these genes, and are beginning to identify how their protein products play a role in the symptoms of asthma.

The environmental component of asthma causation is similarly complex. Here, environment includes in utero conditions, early life respiratory infections, exposure to environmental tobacco smoke, home and outdoor allergens, nutritional factors, and workplace exposures. Timing seems key — a particular kind of common viral infection striking at a certain age may lead to the onset of asthma then or later in life. Sequences of events may also be important — for example, a viral infection in the first two years of life, followed by an inhalant allergen in the home, and perhaps the modifying effects of obesity due to excess caloric intake and insufficient exercise.

Asthma is an episodic condition, with mild asthmatics having as few as one attack per year, and severe asthmatics relying on daily medication to maintain their function. For some, "triggers "— factors likely to initiate an asthma attack — can be identified and then be avoided as part of an overall asthma treatment program (see related article on "Childhood Asthma, " above). Research on prevention of asthma has focused on the indoor home environment, the outdoors, schools, and workplaces. Controlling outdoor air pollution and asthma-causing workplace exposures are effective in reducing the severity or frequency of asthma. Although many efforts to improve the home environment of asthma sufferers have been tried, we are still not certain which are effective. For children with frequent, severe asthma attacks, sub-standard housing with mice, rats and

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Meet Kim LaCelle, the Newest Member of our Life Sciences Learning Center Staff

My background in research and teaching has provided me with much preparation for my position as a Science Educator at the Life Sciences Learning Center (LSLC). I received a B.S. in Biology from Bates College in Lewiston, Maine where the small college atmosphere allowed me to do research with one of the psychology professors. I then worked as a research assistant at Biogen in Cambridge, Massachusetts studying cancer, before moving to Albany, NY to work in research on protein transport, and testing for nutritional deficiencies. I obtained my Master's degree in Education at SUNY Albany, and taught at a special school for students with disabilities and behavioral problems. My husband's post-doctoral research position brought us to Case Western Reserve University in Cleveland where I continued to work in the lab in Molecular Biology and Immunology. Upon moving to Rochester, I worked as a middle and high school science teacher where I taught life science, physical science, earth science and biology at Our Lady of Mercy High School and Marion Central School. While at Marion Central School, two other teachers and I formed a team that was one of five schools chosen to participate with Dr. Dina Markowitz on her grant linking Social Studies, Health, and Biology to address Environmental Health issues. I have also worked with Dina for several years as an instructor for the Middle School Science Explorations Camp and, before that, I spent a summer as an instructor for the High School Summer Science Academy.

I joined the LSLC full time in September 2003 because I wanted the challenge of working with many different groups of students and to get the chance to work side by side with many talented and dedicated classroom teachers. My background has both teaching and research aspects,and this job allows me to combine both interests. I have taught at the summer science programs for about six years so I was familiar with the goals of the program.

Working at the LSLC has been a wonderful opportunity to teach in many different situations. We run teacher workshops, advanced placement biology classes, middle and high school science classes, summer science camps, and Saturday morning science classes. Another program offered by the LSLC is the Lab Skills Development program where we go into city classes and teach hands-on material with the classroom teacher. The teachers we get to work with have a wide range of experience and often bring new perspective to our teaching methods.

As LSLC science educators, we try to get the students familiar with using high quality instruments to do inquiry based science and get a real feel for what it is like to work in a lab. All students wear lab coats during their visit and that alone, their teachers tell us, is very exciting! Many schools do not have the resources to provide this kind of unique opportunity to their students and welcome a chance to visit this kind of environment. Teachers also tell us that coming here and having us reinforce what they have been talking about in the classroom validates the use of science for their students.

For more information on the Life Sciences Learning Center, visit http://lifesciences.envmed.rochester.edu

Asthma Research Continued from page 3

cockroaches present can contribute to poor asthma control, and a multifactorial approach to controlling allergens appears to be helpful.

One of several ongoing studies of asthma risk in children, supported by the National Institute for Environmental Health Sciences (NIEHS), is beginning to shed light on the role of the home environment in asthma development in children. By enrolling children at birth who have an older sibling with physician-diagnosed asthma, and then following the children while studying their home environment, we hope to discover factors that could be tested for effectiveness in research intervention trials. One of the first findings of this study was a confirmation of the very high rate of asthma among Puerto Rican families living in the Northeast, roughly three times that of the general population. Gas and kerosene space heaters and wood stoves were associated with more frequent respiratory symptoms in infants too young to have developed asthma. For infants in the first year of life whose mothers had a diagnosis of asthma, both cockroach allergen and the presence of persistent mold in the home were both associated with an increase over the usual frequency of respiratory symptoms. Persistent mold was also associated with an excess of symptoms in children whose mothers did not have asthma. Careful measurement of allergens in the homes of these children showed that potentially significant levels of dog and cat allergens may be present even in homes where there is no dog or cat to be found. But a complex picture is emerging from many studies of dog and cat allergens in the home, suggesting that in some situations exposure to the animal may in some way be protective, at least at certain stages in life, as well as causing or triggering asthma symptoms.

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a research referred to is supported by Grant numbers ES07456 and ES05410 from the National Institute of Environmental Health Sciences

We're Getting the Lead Out

Katrina Smith Korfmacher, Ph.D.
Outreach Coordinator

GLO is the first community-based primary prevention of lead poisoning project in Rochester.

The Get the Lead Out project ("GLO"), a partnership of the Jay and Orchard Street Neighborhood Association (JOSANA), the Monroe County Health Department, a VISTA volunteer, and the University of Rochester, has made significant progress in its first year. GLO is the first community-based primary prevention of lead poisoning project in Rochester. Pilot Project funding from our NIEHS Center grant allowed Dr. Katrina Korfmacher to hire five students last summer who administered surveys, conducted educational visits, and followed up with families and property owners to address lead hazards in their homes. To date, around fifty homes have been visited. These properties have been referred to Rochester City and Monroe County programs to fund lead hazard reduction work. The City of Rochester recently awarded GLO a $100,000 contract under a grant it received from the US Department of Housing and Urban Development (HUD). This contract insures the future and expansion of GLO over the next two years and will be implemented in partnership with the JOSANA community group and Action for a Better Community. In a press conference on December 10, 2003, Rochester Mayor Bill Johnson attributed the city's success in getting the largest amount of funding from HUD of any US city in this grant cycle to the strong partnerships with groups like GLO in the community. The EHSC role will include continuing to foster such partnerships, evaluating the progress of GLO, and sharing lessons learned from other communities striving to prevent lead poisoning of their children.

Does Sex Matter?

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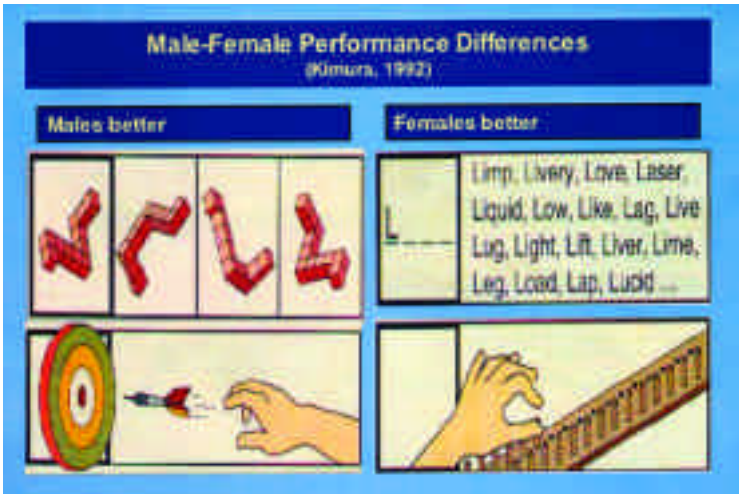
sensitive groups such as pregnant women,the very young, and the elderly. Because of such subtleties, and the challenges they present to researchers, we have to be keenly attuned to the contours of these effects. By studying how they may enhance or reduce sex differences, or how they may take different forms in the two sexes, we might discover a health risk that would be overlooked without such explicit comparisons.



Sex differences are recognized in several aspects of environmental health research. One example is the standard method for assessing whether or not a particular chemical poses a cancer risk. In such an experiment, two species, typically rats and mice, may be fed the chemical in their diet for as long as two years, but the guidelines issued by federal entities such as the Environmental Protection Agency also stipulate equal numbers of both sexes. The guidelines recognize that a particular chemical might, for example, induce tumors in male rat kidneys but in female rat livers.

Chemicals whose toxic targets include the brain haven't received an equivalent emphasis on sexually dimorphic responses. Sexually dimorphic behavioral responses to environmental exposures present unique challenges. Unlike more obvious outcomes such as, say, the incidence of abnormal development of the reproductive organs, differences between males and females in behavior can only be described by averages. Behavior and biology are linked by how the brain is organized, and brain anatomy is sexually dimorphic in humans. To begin at the beginning, the undifferentiated fetal brain is basically female, but the testosterone secreted by fetal males, which is converted for this purpose to the female hormone estradiol, molds the sex differences in brain structure. Male brains are more asymmetrical than female brains, with one side larger or thicker than the other. Certain nuclei, or groups of nerve cells, are larger in male brains while others are larger in female brains. Male brains, corrected for height, are 2-3% larger than female brains. Female brains have a larger percentage of gray matter (nerve cells) than male brains.

These subtle differences in brain anatomy and behavior have become more important in evaluating the risks of environmental exposures because they ultimately arise from differences in hormonal balance. We now appreciate that many chemicals in our environment may mimic or obstruct hormonal function. Some may act as estrogens. Others may act as anti-androgens. Several affect the thyroid gland. Such chemicals are labeled as endocrine disruptors, may exert their influence at remarkably low doses, and have generated extensive efforts to identify them and to assess their health effects.

Some of the research conducted in our Center on endocrine disruption targeted dioxin, the exceedingly potent contaminant found in Agent Orange, the herbicide sprayed over vast swaths of Vietnam. We became interested in a possible connection between dioxin and sex differences in behavior from experiments conducted at the University of Wisconsin. These investigators discovered that small amounts of dioxin given to pregnant rats impaired sexual performance in the male offspring.

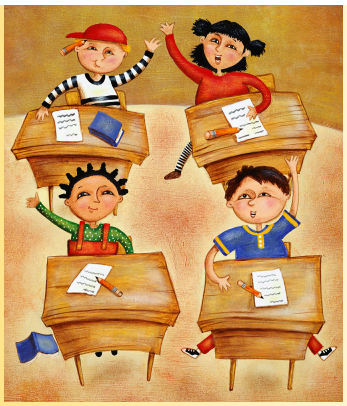
We began with the premise that male rat sexual behavior depends on proper sexual differentiation of the brain, a process that begins early in brain development. If sexual behavior is modified by dioxin, could sex-linked behaviors not directly coupled to reproduction, such as cognitive function, also be affected? In one of our experiments, we administered dioxin to pregnant rats and then tested cognitive performance in the offspring. To do so we used a specially-designed test chamber in which they had to press a lever to earn small food pellets. In such a situation, males typically press the lever at higher rates than females. Offspring from rat mothers that had not been given dioxin showed the usual pattern of sex differences.

Offspring from exposed mothers reversed the typical difference. Males reduced their response rates while females increased their rates. When we looked at brain structure, we found that male rat brains became more symmetrical, the female norm, while female brains showed a slight tendency to become less symmetrical, the male norm.

We can draw a wider lesson from our research results than just the conclusion that dioxin produces different effects in male and female offspring. Investigators from the Netherlands began a study more than 10 years ago to assess the effects on child development of exposure to PCBs and dioxins, which tend to occur together in foods. They enrolled over 200 pregnant women and have followed the children since birth. None of the women had been poisoned; the investigators were simply interested in the relationships between the amount of PCBs and dioxins carried in the mother's body and their children's development, because these chemicals are transmitted to the fetus during pregnancy and to the infant during breast feeding. During the course
of this continuing study, they have assayed both mental and physical development, and, like others, found that the higher the mother's burden of PCBs/dioxins, the lower the mental development test scores in the child.

But last year, this group published what may be the most intriguing and provocative of their findings. Their goal was to evaluate how exposure to PCBs/dioxins influenced the children's play behavior—choices of toys (guns or dolls), activities (playing house or engaging in sports), and preferences (pretty things or rough and tumble play.) They used a behavioral activity inventory that assesses masculine or feminine play behavior. In boys, higher PCB levels were associated with less masculine play; in girls, they were associated with more masculine play. In both sexes, higher dioxin levels were associated with more feminized play. The investigators suggested that exposure to these chemical compounds disturbs the hormonal balance required for normal sexual differentiation of the brain. Many other persistent environmental pollutants, including DDT and other pesticides, have the potential to act in the same way

What we should carry away from such findings is how subtly and insidiously some environmental chemicals can affect who and what we are. Because so many of the chemicals found in our common environment exert sexually dimorphic toxic effects, the government, as it did for drugs and medical research, should insist that explicit investigation of sex differences be a standard part of any protocols to assess the risk of adverse health effects. Sex does matter!

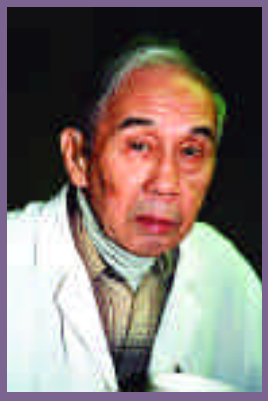


A New Center for Science Education and Outreach

Dina Markowitz, Ph.D., the Director of our EHSC Community Outreach and Education Program has been named Director of the newly created Center for Science Education and Outreach at the University of Rochester. The Center's mission will be to centralize, expand, and advance many of the science education and community outreach initiatives that exist within the University.

The Center for Science Education and Outreach will utilize the unique resources of University of Rochester's scientists and facilities to develop and operate innovative programs that serve educators, pre-college students, and the general public. These programs provide hands-on science curricula during the school year as well as through summer science camps, teacher professional development, and support to enhance scientific literacy in the community. The Center includes educational research projects to study the effects of its science outreach programs on students and on teachers' classroom practices. The Center's activities will also facilitate interactions between University of Rochester scientists and the general public. Creation of the Center will enable the University to effectively utilize the expertise of Markowitz and her collaborators who have become a leading resource for the development of national models of successful science education and community outreach initiatives.

The Center's programs are supported by over $3 million in funding from the National Institutes of Health, the Howard Hughes Medical Institute, the Toyota USA Foundation, private foundations, industry and local philanthropists. The Center, which will be housed within the Department of Environmental Medicine, will include the two dedicated teaching laboratories of the Life Sciences Learning Center and will incorporate the talents of faculty members, graduate students and staff from a number of departments within the University of Rochester as well as collaborating institutions.



Remembering Taft

On December 29, 2003, Dr. Taft Toribara passed away while under hospice care. Dr. Toribara was born and raised in Seattle, WA. He attended the University of Washington where he graduated summa cum laude in chemical engineering. He received his Ph.D. in analytical chemistry from the University of Michigan in 1941. In 1948, Dr. Toribara accepted a position at the University of Rochester to work on the Atomic Energy Project. In 1982, Dr. Toribara retired, but returned as Professor Emeritis and became the head of the analytical core of the Environmental Health Sciences Center. Dr. Toribara is the author of a paper entitled "Microdetermination of Phosphorus" (Anal. Chem. 28: 1280, 1953), that is one of the most frequently cited papers in the field of analytical chemistry.

Taft was well-known around the University campus for his competitiveness at playing squash and he gained national recognition as a squash champion.

A memorial service was held on Saturday January 10, 2004 at the Interfaith Chapel on the River Campus at the University of Rochester.

Taft is survived by his wife, daughter Lynne, son Neil and two granddaughters.

For more information about our Toxicology Training Program, go to: *www2.envmed.rochester.edu/envmed/tox*. or call Joyce Morgan at (585) 275-6702.

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