

s e n t i n e l

the center for environmental health and susceptibility
at the university of north carolina, chapel hill

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the
sentinel

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INTERNATIONAL
COLLABORATION
TO EXPLORE
GENES,
ENVIRONMENT
AND MELANOMA

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OUTREACH AND
EDUCATION
NEWS:
ASTHMA
AND SKIN
CANCER

Understanding the Environment's Effect on Asthma

When it comes to the link between asthma and the environment, researchers ask two basic questions: How does the environment contribute to a person becoming asthmatic?

And, once someone has asthma, what aspects of the environment make the disease worse?

At the UNC Center for Environmental Medicine, Asthma and Lung Biology (CEMALB), Director David Peden MD, PhD and his research team are working to answer these questions. CEMALB is one of the leading centers in the world for translational research aimed at understanding the relationships between

the environment and health and translating that knowledge into measures that improve public health and help physicians identify and treat susceptible individuals.

CEMALB works closely with the U.S. Environmental Protection Agency, which provides substantial funding for the Center and built the Human Studies Research Laboratory in the heart of the UNC campus.



The facility features human exposure chambers that can mimic atmospheres found in polluted areas or study a particular pollutant such as ozone, diesel exhaust or particulate matter.

“Our *tour de force* is that the only species we study in this building are humans, and we have developed expertise in safely and ethically studying the effects of controlled exposure to low levels of various pollutants in diseased as well as healthy volunteers,” says Peden, who is a member of the UNC Center for Environmental Health and Susceptibility.

“For asthma,” he continues, “we expose healthy volunteers and those with asthma to low-level pollutants so we can observe changes in the lung cells and other symptoms in order to understand the mechanisms by which people’s asthma worsens. We use that information to find potential targets for intervention and to study what people with asthma can do for themselves, aside from just hiding inside, to prevent these exacerbations.”

In addition to Peden, an asthma expert who specializes in pediatrics allergy and immunology and clinical

[continued on back panel >>](#)

The Center for Environmental Health and Susceptibility (CEHS) at the UNC-Chapel Hill School of Public Health is funded by the National Institute of Environmental Health Sciences to:

- improve our understanding of the environmental and genetic determinants of disease in different populations;
- enhance interdisciplinary research in order to further our knowledge about how toxic chemicals affect humans; and
- disseminate existing knowledge to help reduce the burden of environmentally related disease.





from the director's desk

As the University of North Carolina-Chapel Hill Center for Environmental Health and Susceptibility (CEHS) approaches its sixth anniversary, we are building upon our traditional strengths in the basic sciences and epidemiology by enhancing the role of physician-scientists in the Center's activities. In this way, we will raise the profile of clinical environmental medicine, which is essential if we are to successfully translate our basic science and epidemiological research from the laboratory bench to the patient's bedside and beyond to inform and shape public health policy.

To this end, the CEHS is deeply involved with the UNC Clinical and Translational Science Award (CTSA) project, an ambitious, university-wide initiative that will, with funding from the National Institutes of Health, accelerate the pace at which scientific discoveries are translated into improved care for patients and communities. The UNC CTSA will provide an academic home — a new, state-

of-the-art clinical research facility — for biomedical clinical and translational researchers and will help sustain, and increase, the work of interdisciplinary research teams. CEHS and CTSA leaders are working closely to maximize the role of the CEHS Facility Cores (Molecular Epidemiology, Biostatistics and Epidemiologic Methods, Biomarkers and Nutrient Assessment) and to promote a strong emphasis on environmental medicine within the new initiative.

We are also leveraging our CEHS Pilot Project Program grants to encourage young physician-scientists to pursue environmental health research; two MD/PhDs are recipients of this year's grants. These pilot grants are intended to help investigators generate the initial data needed so they can then apply for larger research grants. In addition, the CEHS has just announced two \$40,000 Pilot Project Program grants designated specifically for physician-scientists to encourage research on the environmental

aspects of disease. We are advertising these new grants widely to potential investigators throughout the UNC School of Medicine. (If interested, contact CEHS Scientific Coordinator Jorge Izquierdo.)

And finally, we are working with three UNC physician-scientist teams who are submitting applications for DISCOVER (Disease Investigation through Specialized Clinically Oriented Ventures in Environmental Research) grants, a new research initiative funded by the National Institutes of Health (NIH). CEHS members are also developing ideas for the Genes and Environment Initiative, another new NIH research program.

We are encouraged by the many upcoming opportunities for the CEHS to enhance our own mission and to assist other UNC research groups to achieve their scientific goals. The ultimate beneficiaries of these collaborative efforts, we hope, will be patients and society.

James Swenberg
Director, CEHS

An international collaboration to explore the interaction between genes, environment and melanoma

Researchers at the UNC-Chapel Hill Center for Environmental Health and Susceptibility are conducting several studies to better understand the genetic and environmental basis of skin cancer. UNC-Chapel Hill is part of a large, international study of Genes, Environment and Melanoma (GEM) funded by the National Cancer Institute to bring together melanoma experts from around the world to improve

our understanding of the causes of malignant melanomas. In particular, the GEM group is studying how genes interact with sun exposure to increase the risk of melanoma.

Over a period of four years, GEM enrolled 3,700 individuals from the U.S., Canada, Italy and Australia, giving researchers the ability to understand melanoma in both the Northern and Southern hemispheres, in cloudy and sunny climates, and in regions with

different ethnic backgrounds. UNC researchers, through the North Carolina Melanoma Study, enrolled 316 people with malignant melanomas from 42 counties spanning the western mountains to the coastal region of the state.

UNC CEHS member Dr. Robert Millikan, UNC Department of Dermatology faculty member Dr. Nancy Thomas and Department of Epidemiology faculty member Dr. Kathleen Conway-Dorsey are

The UNC CEHS's Pilot Project Program provides seed grants to jump-start research and help young investigators catapult this initial funding into larger, outside grants. This year, six UNC principal investigators were awarded grants of \$25,000 each toward their promising projects:

Susceptibility to Prenatal Dieldrin Exposure in a Model for Anxiety/Aggression Disorders

Jean M. Lauder, PhD, professor of cell and developmental biology

Environmental Agents and Early Onset of Aging and Age-Related Diseases

Paul Chastain II, PhD, postdoctoral research associate, Department of Pathology and Laboratory Medicine

Purines in Exhaled Breath Condensate as Biomarkers of Inflammation

Charles R. Esther Jr., MD, PhD, assistant professor, Division of Pediatric Pulmonology, Department of Pediatrics

Dr. Charles Esther Jr. is working on a sensitive marker for inflammation of the lungs that can be measured simply by having a patient breathe into a tube. Esther, a physician-scientist, then analyzes the sample with the aid of the CEHS Biomarker Facility Core's mass spectrometry instruments and staff. Once fully developed, Dr. Esther's technique could give physicians a noninvasive, highly sensitive way to assess the severity of airway disease.



Dietary α -tocopherol Supplementation as a Way to Decrease Neuroinflammation Following Exposure to Environmental Agents

Patricia A. Sheridan, PhD, postdoctoral fellow, Department of Nutrition

Effects of Cadmium on DNA Synthesis, Cell Cycle Control and Microsatellite Mutation Rate in Human Cells in Culture

Jayne C. Boyer, PhD, assistant professor of pathology and laboratory medicine

Comparison of two measures of oxidative DNA damage, the comet assay and 7-hydroxy-8-oxo-2-deoxyguanosine, in healthy African-American and white adults

Jessie Satia, PhD, MPH, assistant professor of epidemiology and nutrition

For more information on the research taking place at the UNC-Chapel Hill CEHS, or to view current publications, visit <http://cehs.sph.unc.edu/>

co-investigators on the North Carolina Melanoma Study.

“By studying the occurrence of melanoma around the world, we were able to investigate how people with similar genetic makeups develop melanoma in different environments: that is, how genetic makeup interacts with the environment,” notes Millikan.

Preliminary results from the GEM study indicate that some people may be at increased risk for melanoma because of differences in how they repair DNA when it is damaged by UV exposure. Researchers also found that there are at least three different types of melanoma, based on the type

of DNA damage that occurs. UNC scientists continue to study changes in the DNA that occur in melanoma and whether these genetic changes may be caused by sunlight.

“The types of mutations that we found in melanoma help explain why traditional chemotherapy is not successful for melanoma patients, and points to new types of treatments that need to be tested,” Millikan explains. “Our results on DNA repair suggest that some people are more susceptible to sunlight than others, so they need to take special precautions against sunburns when they are young.”

At this time, there are no commercially available genetic tests

to determine individual genetic susceptibility for melanoma. However, people should be aware of their families' experience with skin cancer, and if melanoma is common, are advised to consult a dermatologist.

UNC's CEHS brought to the international GEM study a high degree of expertise in DNA repair, as well as experts in how the skin responds to environmental exposures to sunlight and chemicals.

“Both the GEM study and the CEHS demonstrate how important it is for scientists to work together and combine their areas of expertise,” adds Millikan. “Collaboration is the best way to find answers to important research questions.”

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immunology, the multidisciplinary CEMALB research team includes medical specialists in pediatric and adult pulmonology, cardiology and pediatric critical care, as well as PhDs and master's and doctoral students in toxicology, immunotoxicology, environmental sciences and physiology.

The CEMALB team is working on a wide range of research initiatives to shed light on the links between environmental factors and asthma. They study airborne pollutants, having volunteers sit in an exposure chamber where, for instance, they might be exposed to the same level of exhaust as someone driving through New York's Holland Tunnel.

"Twenty-four hours after a region has an increase in air pollution, there are more visits to doctors and to the emergency room and increased use of asthma medications. That suggests that the air pollutants either directly cause asthma exacerbation, or increase sensitivity so that when people are exposed to other things

they're allergic to, they're more reactive. So someone who is allergic to cats will have more of an allergic response to a cat after they are exposed to low level ozone or another pollutant."

CEMALB researchers believe that the pollutants cause an increase in monocyte cells in the airway, and these cells enhance someone's allergic response, such as an increased asthma exacerbation. This presents a potential new cell type to target in the treatment or prevention of pollutant-induced exacerbations. Investigators are studying whether pre-treatment with antioxidants or combinations of vitamin E and vitamin C could inhibit the activity of the monocyte cells in the airway and protect people with asthma against the effects of air pollution.

CEMALB is also funded by the National Institutes of Health to explore how pollutants enhance airway inflammation in both asthma and chronic obstructive pulmonary disease. The Center is also collaborating

with the National Institute of Environmental Health Sciences on genetic research to determine whether genetic variations play a role in increasing someone's risk from environmental pollutants. And, because viral infections are a leading cause of an asthma exacerbation, CEMALB investigators are exploring how diesel exhaust and tobacco smoke change the way that people respond to these infections.

Peden and the CEMALB research team also work closely with the CEHS, using the resources of the Facility Cores (particularly epidemiology and biostatistics), collaborating on grant applications and mentoring graduate students who assist in research. "We'd like to offer to other CEHS researchers an opportunity to do more direct clinical research in humans through our facilities, and likewise we'd like our CEHS colleagues' help to move our research efforts from our human exposure chamber data into studying real people in real environments." ❄



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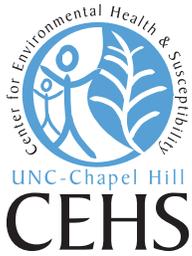
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COMMUNITY OUTREACH AND EDUCATION

News from the

Community Outreach and Education Program of the UNC Center for Environmental Health and Susceptibility



Asthma in North Carolina

More than 451,000 North Carolinians have been diagnosed with asthma, a condition that disproportionately affects Native Americans, African Americans, women, children, the elderly and the poor. One in ten adults in this state has been diagnosed with asthma.

Asthma is a leading chronic illness

among children in the United States. Families of children with asthma, in addition to dealing with increased medication use, are often faced with frequent visits to the doctor's office or emergency room, and increased school absences. Unfortunately, in North Carolina, asthma rates for children

and adolescents are higher than the national median.

Air pollution has many harmful health effects. CEHS researchers are investigating how air pollution may make someone asthmatic, and once someone already has asthma, how air pollution makes it worse.

How you can help improve North Carolina's air quality

Ozone and particle pollution, the two biggest air quality concerns in North Carolina, come primarily from motor vehicles and industry, including power plants. Each of us has the power to improve air quality through our actions. Here are a few ways you can make a difference:

- **Leave your car.** Take the bus, car pool, van pool, walk or ride your bike.
- **Drive smart.** When you do drive, use cruise control and stay within the speed limit. Avoid sudden stops and starts. Plan your trips to combine short trips. And avoid idling, since idling for more than one minute wastes gas and increases pollution, compared to shutting off and re-starting your engine.
- **Conserve electricity.** Set your thermostat to the highest comfortable temperature in the summer (try 78°F) and, during winter, try a setting of 65–68°F. Use ceiling fans to increase both cooling and heating efficiency. Look for the Energy Star label when purchasing major appliances.
- **Cut it out.** The engines in lawn care equipment are major polluters. Use hand-powered or electric lawn care equipment, and consider natural landscaping to reduce the amount of lawn.

For more tips, visit N.C. Air Awareness at

daq.state.nc.us/airaware/

How the COEP is helping North Carolinians breathe easier

The Community Outreach and Education Program (COEP) informs the public of CEHS research on air pollution and health and **how they can improve air quality in North Carolina:**

- UNC-Chapel Hill is part of the nationwide Health Observances and Public Education (HOPE) Partnership, **a project designed to enhance scientific literacy and improve public understanding of the impact of research on human health.** The HOPE project team is developing educational materials for Asthma and Allergy Awareness Month and two other national health observances.
- **The COEP serves on the Asthma Project Management Team for the N.C. Asthma Program of the Division of Public Health.** The team is developing a State Asthma Plan to effectively address asthma in all ages, ethnic groups, backgrounds and settings. The COEP is also part of the Asthma Alliance of North Carolina, a statewide partnership of local and state government agencies, academic institutions, local asthma coalitions, nonprofits and private industry working to reduce the impact of asthma.
- **The CEHS COEP led an Air Pollution and Asthma workshop for high school students at the North Carolina Museum of Life and Science** to foster interest in environmental science careers in underserved youth, particularly minorities and females.
- This summer, the **CEHS co-sponsored a three-day Environmental Science Institute for teachers and environmental educators** with the U.S. EPA to help educators better integrate information about asthma and air pollution into their classroom activities.

Skin cancer in North Carolina

Skin cancer is the most common type of cancer in the United States: one in five Americans will develop some form of skin cancer (melanoma and non-melanoma) during their lives, and one million will be diagnosed this year alone.

North Carolina has one of the highest rates of skin cancer in the country, and North Carolinians are more likely to die from malignant melanoma than the average American, particularly in our rural areas.

There are many risk factors for developing skin cancer, including environmental factors such as sunlight and tanning booths, and genetic factors such as a family history of skin cancer. Among these, ultraviolet radiation (UV) from sunlight is considered the major risk factor for skin cancer, since UV exposure can cause DNA damage, which can lead to uncontrolled cell growth. The interaction of environmental factors with a person's genetic makeup can increase an individual's risk for developing skin cancer.



Stay Safe in the Sun

Children are especially susceptible to the damaging effects of the UV radiation. Research has shown that exposure to UV, especially in childhood, increases the likelihood of developing the most deadly form of skin cancer, melanoma. However, it is also important for adults to be safe in the sun as well. Protect yourself from UV radiation in the following ways:

- Seek shade during peak sun hours (10 am to 4 pm).
- Use a sunscreen with a sun protection factor (SPF) of 15 or higher — and reapply often. The higher the SPF, the better.
- When outdoors, wear a long-sleeved shirt and pants, a hat to shade the ears, face, and eyes, and sunglasses to protect the skin around the eyes.
- Pay attention to the EPA's UV index, which predicts the next day's ultraviolet radiation levels on a 1–11+ scale, to help you plan sun-safe activities. To find out the UV Index for your area, visit the EPA SunWise UV Index website at www.epa.gov/sunwise/uvindex.html.
- Avoid tanning beds, which can lead to skin cancer and premature aging of the skin.

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Reaching Out to the Community

The Community Outreach and Education Program (COEP) of the UNC-Chapel Hill Center for Environmental Health and Susceptibility translates Center research into knowledge that can be used to improve public health and educates the public about how individual and group susceptibilities interact with environmental and occupational factors to cause disease.

The COEP has compiled a report that highlights the latest research on skin cancer and its environmental and genetic risk factors. The COEP is also collaborating with the N.C. Department of Public Instruction and the North Carolina Parent Teacher Association to develop educational materials and increase public awareness about the dangers of skin cancer and how to reduce risks.