

**MEETING SUMMARY  
PRESIDENT'S CANCER PANEL  
ENVIRONMENTAL FACTORS IN CANCER**

December 4, 2008  
Charleston, South Carolina

**OVERVIEW**

This meeting was the third in the President's Cancer Panel's (PCP, the Panel) 2008/2009 series, *Environmental Factors in Cancer*. The meeting focused on indoor/outdoor air pollution and water contamination as they relate to cancer risk. The agenda for the meeting was organized into two discussion panels.

**PARTICIPANTS**

***President's Cancer Panel***

LaSalle D. Leffall, Jr., M.D., F.A.C.S., Chair

Margaret Kripke, Ph.D.

***National Cancer Institute (NCI), National Institutes of Health (NIH)***

Abby Sandler, Ph.D., Executive Secretary, PCP, NCI

Beverly Laird, Ph.D., Vice-Chair, Director's Consumer Liaison Group

***Panelists***

Julia Brody, Ph.D., Executive Director, Silent Spring Institute

Kenneth P. Cantor, Ph.D., M.P.H., Senior Investigator, Division of Cancer Epidemiology and Genetics, National Cancer Institute

William L. Chameides, Ph.D., Dean, Nicholas School of the Environment, Duke University

Capt. Susan M. Conrath, Ph.D., U.S. Public Health Service, Office of Air and Radiation, Indoor Environments Division, U.S. Environmental Protection Agency

R. William Field, Ph.D., Professor, Department of Occupational and Environmental Health and the Department of Epidemiology, College of Public Health, University of Iowa

Marilie D. Gammon, Ph.D., Professor, Department of Epidemiology, University of North Carolina

Winifred J. Hamilton, Ph.D., Assistant Professor, Departments of Medicine and Neurosurgery, Baylor College of Medicine

Jay H. Lubin, Ph.D., Senior Investigator, Division of Cancer Epidemiology and Genetics, National Cancer Institute

John E. Vena, Ph.D., Head, Department of Epidemiology and Biostatistics, University of Georgia College of Public Health

Richard Wiles, M.A., Executive Director, Environmental Working Group

**OPENING REMARKS—LaSALLE D. LEFFALL, JR., M.D., F.A.C.S.**

On behalf of the Panel, Dr. Leffall welcomed invited participants and the public to the meeting. He introduced Panel members, provided a brief overview of the history and purpose of the Panel, and described the aims of the current series of meetings.

## PANEL I

**DR. JAY LUBIN:**

### **RADON EXPOSURE AND LUNG CANCER RISK**

#### **Background**

Dr. Jay Lubin is the principle statistician for the Agricultural Health Study, a prospective study of nearly 90,000 farmers and commercial pesticide applicators. He has been a member of several expert committees, governmental and nongovernmental, including the National Academy of Sciences Committee on the Biological Effects of Ionizing Radiation (BEIR-IV and -VI) and related workshops. Dr. Lubin is a Fellow of the American Statistical Association and an elected member of the National Commission on Radiological Protection and Measurements and the American Epidemiology Society. He is an adjunct scientist at McLaughlin Centre for Population Health Risk Assessment; an Affiliate Scientist at the Institute of Population Health, University of Ottawa; and a Senior Associate, Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health.

#### **Key Points**

- Radon, a noble gas generated by the natural decay of uranium-238, is ubiquitous in the crustal rock of the earth. Radioactive radon, specifically radon-222, is of particular interest in the public health realm because epidemiological studies have implicated it in the development of lung cancer. Radon-222 has a relatively long half-life—approximately 3.8 days—but several of its decay products have half-lives on the order of minutes.
- The alpha radiation released by radon-222 is unable to penetrate most surfaces; it can be blocked by clothing and skin. However, if radon or its short-lived decay products are inhaled into the lung, the radiation emitted can do considerable harm to the lung epithelium.
- Radon dissipates rapidly in air, but can accumulate in enclosed areas, such as mine tunnels and houses. Miners have been a valuable population for studying the effects of cumulative radon exposure. For miners, cumulative radon exposure is measured in Working Level Months (WLM). A WLM is calculated by measuring the alpha energy within a unit volume of air in a mine or area of interest (i.e., working level) and multiplying this by the number of working hours in a month (usually about 170 hours).
- In residential settings, cumulative radon exposure is measured by multiplying the number of years an individual has resided in a house by the number of alpha decays per second per cubic meter in the home. These measurements are often expressed using the standard international unit of the Becquerel ( $1 \text{ Bq} = 1 \text{ decay/sec/m}^3$ ), but the Environmental Protection Agency (EPA) has historically presented residential exposure using picocuries per volume ( $1 \text{ pCi/L} = 37 \text{ Bq/m}^3$ ).
- Because the health risks of radon exposure have been largely determined through studies of miners, calculations are often done to determine the equivalent WLM for residential exposures. For example, if an individual resides for 25 years in a home with radon levels of 1 pCi/L, he/she will receive a cumulative radon dose equivalent to 4 to 5 WLM.
- The EPA has established a recommended action level for radon of 4 pCi/L; individuals living in homes with levels of radon that exceed this concentration are strongly recommended to take steps to mitigate, or reduce, the levels of radon. It is estimated that 4 to 6 percent of homes in the U.S. exceed the EPA radon action level.
- In 1999, the National Academy of Sciences BEIR-VI Committee conducted a comprehensive evaluation of radon. This collaborative effort included pooled analysis of 11 cohort studies of

miners, including approximately 1.2 million person-years of observation and nearly 2,800 lung cancer deaths. The miners in these studies—who worked in tin, iron, and uranium mines across the world—had a mean radon exposure of 164 WLM. All of the studies showed a consistent pattern of increasing lung cancer risk with increasing radon exposure.

Interestingly, increased risk was seen even at 50 to 100 WLM exposures, suggesting that even the relatively low levels of exposure common in residential settings are likely associated with increased risk of lung cancer. An analysis was also conducted comparing the lung cancer risks of never-smoking with ever-smoking miners; radon exposure increased lung cancer risk for both groups, but the increase in risk associated with radon exposure was two-fold greater for never smokers than ever smokers. There have now been a total of 15 cohort studies of radon-exposed miners. Newer studies continue to confirm the BEIR-VI findings.

- Although studies of radon exposure among miners are informative, there are a number of reasons why it may not be appropriate to infer risks of residential radon exposure from these data. For example, most miners are men; it is possible that radon affects women and children differently than it affects men. Also, the mine environment is very different from home environments—miners at work tend to breathe heavier (i.e., move a larger volume of air per day) than people at home, and mines are generally dustier than homes. Thus, studies must be conducted to demonstrate whether residential radon exposure increases risk of lung cancer.
- There are several limitations to residential radon exposure studies. It is difficult to estimate how much radon a person has been exposed to as most people spend significant time outside their homes and also tend to live in different houses over their lifetimes. Furthermore, the risk of lung cancer associated with residential radon is likely very small, which necessitates large studies and/or data pooling.
- In the late 1980s, the U.S. Department of Energy and the Commission of European Communities (now the European Commission) sponsored a series of workshops to bring together principal investigators of 22 ongoing or planned studies of residential radon exposure. The goal of the workshops was to align the protocols of these studies to enable data pooling. Of these 22 studies, 19 have found an increased risk of lung cancer associated with residential exposures of 4 pCi/L (the EPA action level). Several pooled analyses, many of which have confirmed the increased risk of lung cancer, have also been published. There are plans to pool the data from all 22 studies for analysis.
- Based on data from studies of miners and residential exposure, BEIR-VI estimated that 10 to 14 percent of all lung cancer deaths per year in the U.S. are attributable to residential radon exposure; this translates to 16,000 to 23,000 deaths annually and makes radon the second leading cause of lung cancer in the U.S. It is estimated that one-third of lung cancer deaths caused by residential radon could be prevented if steps were taken to mitigate radon levels in homes above the current EPA action level of 4 pCi/L. If the EPA action level was reduced to 2 pCi/L and all homes in the U.S. were in compliance with this standard, up to 50 percent of radon-attributable lung cancer deaths could be prevented.

## **DR. WILLIAM CHAMEIDES:**

### **ENVIRONMENTAL FACTORS IN CANCER: FOCUS ON AIR POLLUTION**

#### **Background**

Dr. William Chameides has been Dean of the Nicholas School of the Environment since 2007. He was previously Chief Scientist at the Environmental Defense Fund and Regents Professor and Smithgall Chair at the Georgia Institute of Technology. He is a member of the National Academy of Sciences and a Fellow of the American Geophysical Union. Dr. Chameides' research focuses

on the atmospheric sciences, elucidating the causes of and remedies for global, regional, and urban environmental change and identifying pathways towards a more sustainable future. He is currently serving as Vice Chair of The National Academies' congressionally mandated study on America's Climate Choices.

## Key Points

- The connection between environmental factors and cancer risk is very complex. Public assumptions about risk factors may not be true; for example, many people assume that modernization and introduction of new chemicals into the environment are responsible for increased cancer risk. That may be true in part, but modernization and economic development can also improve the quality of the environment and reduce disease risk. This is apparent in China, where there has been a rapid rate of development and modernization over a short period of time. In traditional Chinese homes, solid fuels (e.g., wood, coal) were used for heating and cooking, contributing to indoor air pollution and lung disease. As modernization takes place within China, modern fuels such as natural gas, oil, and electricity are being used. As a result, the rates of lung cancer are likely to significantly decrease.
- Lifestyle changes associated with modernization can also have detrimental health effects. One study revealed a 20 to 30 percent increase in breast cancer among women in Shanghai over the past decade; it is thought that this may be due to diet and other lifestyle changes that have accompanied modernization.
- Much of the focus on the connection between air pollution and cancer stems from the “urban factor” observation in 1959: cancer mortality rates among urban populations were found to be double those of rural populations. At the time, it was assumed that this difference was due to air pollution; however, research since then has indicated that the difference was largely attributable to higher rates of smoking among urban populations. This example illustrates how the complicated interaction of factors that contribute to cancer risk makes it difficult to establish a connection between cancer and a single environmental factor.
- The most authoritative study on air pollution and cancer to date is the 1999 National-Scale Air Toxics Assessment (NATA 1999). This study looked at 133 of 188 known hazardous air pollutants (HAPs) and used a modeling system to extrapolate 1999 emissions data to estimate exposures. NATA 1999 estimated that the majority of Americans have an increased lifetime cancer risk from air toxics of between 1 and 25 in a million; this is a fraction of overall lifetime cancer risk and is considerably lower than the risk associated with radon exposure. The report found that mobile-source emissions are a primary concern, with benzene being the largest contributor to cancer risk. Diesel exhaust emissions were not included in the study due to lack of data. However, the EPA is cognizant of diesel exhaust's potential for harm and has created new emissions standards. Diesel engines typically have decades-long lifetimes so retrofit programs will be key in reducing emissions to meet the new EPA standards.
- NATA's assessment system is a combination of four different models. The first is a dose-response formula that utilizes epidemiological and/or animal study data and relates exposure to risk. The emissions modeling system for hazardous pollutants (EMS-HAP) produces estimates of geographic location and quantity of chemical emitted. This information is put into an atmospheric dispersion model called ASPEN (Assessment System for Population Exposure Nationwide), which links emissions to ambient concentrations across the U.S. Another model, HAPEM5 (Hazardous Air Pollutant Exposure Model, version 5), takes the ambient concentration estimates and links them to population exposures. These steps are combined to derive cancer risks. Most components of this model are based on calculations and assumptions rather than measurements and observations; thus, the data generated are estimates rather than actual exposure levels and risks.

- In the NATA 1999 report, the EPA states that the true cancer risk of air toxics is likely less than calculated in its assessment; this statement is based in part on the fact that the models used depended on extrapolation of data collected at high levels of exposure to estimate the effects of low-level exposures. However, systems similar to NATA’s do not accurately assess so-called “hot spots,” or microenvironments in which concentrations of chemicals are much higher than in the general environment. One example is school buses—buses with closed ventilation systems can have concentrations of particulate matter 10 to 100 times higher than ambient concentrations. It is important to make exposure assessments and predictions using actual measurements to capture hot-spot anomalies.
- The United States is not comprehensive in its study of hazardous air pollutants. As part of the 1990 amendments to the Clean Air Act, Congress gave EPA a list of 188 HAPs to study. Almost 20 years later, no new compounds have been added to this list though many new potentially toxic compounds are being added to the environment every year.
- There are many “emerging pollutants” that are not being regulated but could be problematic. Brominated fire retardants—known carcinogens—are one example. An Environmental Working Group study found much higher concentrations of brominated fire retardant in the blood and breast milk of U.S. women than in samples from women of Sweden, Japan, and Canada. This could be due to the more aggressive use of fire retardants in U.S. consumer products. However, fire safety must be balanced with the dangers of using potentially carcinogenic material. Similarly, a precautionary approach to nanotechnology may be appropriate. There is increasing industry use of nanoparticles in consumer goods; however, the health risks of this new technology have not been assessed.
- A more integrated framework for research and regulation of environmental pollutants is needed. Currently, separate EPA regulatory frameworks govern hazardous air pollutants, mobile-source air pollutants, particulate matter and other “criteria pollutants,” and water contaminants. Consumer products that could lead to indoor air pollution are not governed by EPA. This has created a regulatory maze that is difficult to navigate.

**CAPT. SUSAN CONRATH:**

**THE EPA’S RADON PROGRAM**

**Background**

Dr. Susan Conrath is a health and environmental professional with extensive experience in both the private sector and the U.S. Public Health Service Commissioned Corps, where she holds the rank of Captain. She holds an M.S. in microbiology, a master’s in philosophy, and a Ph.D. in human ecology from George Washington University, as well as an M.P.H. from the Johns Hopkins University Bloomberg School of Public Health. Dr. Conrath is considered an international expert on radon. She has served as a consultant to the World Health Organization; planned, organized, and chaired international meetings on radon; and is currently part of the editing committee for the Radon Handbook being developed by the World Health Organization’s International Radon Project.

**Key Points**

- Under Title III of the Toxic Substance Control Act (TSCA) (i.e., the Indoor Radon Abatement Act of 1988), EPA does have authority to regulate indoor radon; however, the Agency has chosen to rely on a voluntary program for controlling radon exposure. It has an active radon outreach effort to promote voluntary risk reduction and an extensive partnership network of stakeholders.

- Comparative risk assessments by EPA and its Science Advisory Board have continually ranked radon among the top four environmental risks to public health. Both the U.S. Department of Health and Human Services and the World Health Organization's International Agency for Research on Cancer (IARC) have identified radon as a known human carcinogen. It has also been identified as a serious public health risk by the U.S. Surgeon General's office, the Centers for Disease Control and Prevention (CDC), the American Medical Association, and the American Lung Association.
- There is no evidence of a safe level of radon exposure. Furthermore, exposure is cumulative: the more one is exposed the greater the health risks. EPA conducted a National Residential Radon Survey and found an average radon concentration of 1.25 pCi/L in U.S. homes. A map was created to illustrate the potential of homes within different counties to harbor radon in excess of the EPA action level (4 pCi/L). This action level is technology based (not health based), and the Agency recommends mitigation if radon levels are above 2 pCi/L.
- EPA administers the congressionally mandated State Indoor Radon Grant Program, which receives approximately \$8 million of federal funding annually. Participating states match 40 percent of federal contributions. Almost every state has a radon program, and more than half of the states have real estate disclosure laws related to radon (a seller must disclose the existence of radon in the home, if known). Between 15 and 20 states have regulations requiring professional certification of individuals performing radon testing or mitigation.
- EPA provided funding for the National Academy of Sciences BEIR-IV and -VI reports, which focused on radon. In consultation with the EPA Science Advisory Board and National Academy of Sciences panel members, EPA developed a single radon risk assessment model. The model includes all radon-related deaths and uses age-specific smoking data as well as updated census and mortality data. Using this model, EPA estimates that about 20,000 lung cancer deaths per year in the U.S. result from residential radon exposure.
- Progress has been slow in mandating radon testing, radon mitigation, and radon-resistant construction of homes, but EPA estimates that over 1.5 million homes have been built with new radon-resistant construction and over 700,000 homes have been mitigated since the late 1980s. According to EPA, this translates into more than 6,000 lives saved. However, the number of houses being built far outpaces efforts to mitigate or build radon-resistant homes.
- To accelerate progress against radon exposure and continue to save lives, EPA has partnered with the Conference of Radiation Control Program Directors (state program directors) and the American Association of Radon Scientists and Technologists (representatives from industry) to create the Radon Leaders Saving Lives Campaign, a new program to educate the public and encourage radon testing and mitigation. The main pillars of EPA's contributions to this effort are facilitation of stakeholder action (i.e., sponsoring state and regional stakeholder meetings), fostering continued collaboration with partners, and highlighting effective strategies for reducing radon exposure.
- The Radon Leaders program has created a knowledge gateway ([radonleaders.org](http://radonleaders.org)) to connect the public to radon-related resources across the World Wide Web. This online community for people interested in radon includes new resources and tools, forums, an events calendar, Webinars and presentations, and the latest community news.
- In the future, EPA would like to identify ways to increase action in the marketplace to reduce radon exposure. It also hopes to increase the number of builders using radon-resistant construction techniques and educate first-time homebuyers about radon.

## **DR. R. WILLIAM FIELD:**

### **ENVIRONMENTAL FACTORS IN CANCER: RADON**

#### **Background**

Dr. R. William Field is a Professor with joint appointments in the Department of Occupational and Environmental Health and the Department of Epidemiology at the University of Iowa College of Public Health. He directs the National Institute of Occupational Safety and Health-funded Occupational Epidemiology Training Program at the University of Iowa. Dr. Field currently chairs the measurement working group of the World Health Organization's International Radon Project.

#### **Key Points**

- Radon is a naturally occurring gas that can accumulate in homes that do not have proper mitigation systems. Builders usually do not build radon-resistant homes, although the technology is readily available. Radon enters the home and produces radon decay products over time. The most common radon decay products found in homes are polonium-218 and polonium-214. When radon or its decay products are inhaled, they release alpha particles in the lungs, which can directly damage the DNA of the respiratory epithelial cells.
- Alpha track detectors are used to monitor residential radon levels and can provide a visual representation of the damage induced by radon and its decay products. These plastic detectors are placed in a home for a period of three to four days; the damage to the detector caused by the impact of the alpha particles in homes with high radon levels can be visualized upon processing of the detector.
- Risk for all types of lung cancer is increased with protracted radon exposure. There are an estimated 161,000 lung and bronchus cancer deaths per year in the U.S.; approximately 21,000 of those deaths are attributable to radon. The number of radon-induced lung cancer deaths may seem small when compared with the number of lung cancer deaths caused by smoking, but the dangers of radon should not be dismissed.
- Susceptibility to radon-induced lung cancer varies among individuals. Mixed exposures to lung carcinogens (e.g., from smoking), a history of medical radiation exposure (e.g., x-ray therapy), and genetic variation all affect an individual's risk of lung cancer. An NCI study has found that individuals missing the GSTM1 gene (about half of the Caucasian population do not express this gene due to homozygous deletion) have a three-fold increase in lung cancer risk from radon. The product of the GSTM1 gene protects cells from oxidative stress by interacting with and neutralizing free radicals and other potentially harmful oxidative molecules.
- There is also evidence from miner-based epidemiological studies suggesting that prolonged radon exposure is linked to stomach, liver, and skin cancers as well as leukemia. Incidence of chronic lymphocytic leukemia (CLL) as well as all leukemias combined was positively associated with cumulative radon exposure in a miner-based incidence study. A recent study in Iowa using the Surveillance, Epidemiology, and End Results cancer registry noted an increased risk for CLL and chronic myeloid leukemia in counties known to have elevated levels of radon.
- The BEIR-VI pooled analysis of radon likely underestimates the true risk posed by radon. This is due to errors in detector measurements, failure to consider spatial and temporal radon variations within a home, and failure to integrate radon exposure from different sites (e.g., previous homes, the workplace). Also, measurement of radon gas is used as a surrogate for radon progeny exposure; it is the decay products—not radon itself—that cause cancer.

- Radon risk estimates increase with improved exposure assessment. When the North American Pooled Analysis data were restricted to individuals who: (1) resided in only 1 or 2 homes over a period of 5 to 30 years prior to recruitment; and (2) had at least 20 years covered by a year-long radon measurement, estimates of risk associated with radon exposure levels of 100 Bq/m<sup>3</sup> increased.
- The National Institute of Environmental Health Sciences (NIEHS) and NCI funded the Iowa Radon Lung Cancer Study (IRLCS), which incorporated the most advanced radon exposure assessment techniques ever used in a residential radon study. The study collected historical information on participant mobility within the home, time spent outside the home, and time spent in other buildings. Numerous radon measurements were performed on each level of the home; outdoor radon measurements and workplace radon exposure assessments were also performed. These measurements were integrated with information about the relative time each participant spent at the various locations (home, work, outdoors) to generate a more accurate estimate of cumulative radon exposure. Results showed that this robust method of modeling radon exposure produced higher risk estimates than did previously used methods (including those used for pooled analyses) that do not take into account how much time people spend in different locations.
- There are ways to reduce residential radon exposure. Homes can be fitted with radon mitigation system to help prevent accumulation of radon. One study showed that homes with an average radon level of 10 pCi/L could be reduced to an average level 1.2 pCi/L with the installation of radon mitigation systems. Mitigation systems have an added benefit of reducing moisture in lower levels of homes, which decreases chances for mold growth. Addition of radon-resistant barriers during new home construction costs about \$400, but retrofitting an existing home with a mitigation system costs about \$1,200; families unable to afford retrofitting are likely at increased risk for radon exposure.
- Future research should assess factors affecting individual susceptibility to radon-induced lung cancer (e.g., genetic polymorphisms such as GSTM1). Research should also be conducted on possible associations between radon exposure and extrapulmonary cancers. A cost-effective way of addressing these needs would be to include radon exposure measurements as part of prospective studies, such as the National Children's Study or the Agricultural Health Study. Systematic assessment of occupational radon exposures is also needed.
- A new type of radon detector developed with NCI and EPA funding may be useful for future studies of residential radon exposure; the glass-based detector measures a radon progeny with a half-life of 22 years. Data collected from the glass of picture frames or other keepsake items present in people's homes over several years (even if they have lived in several houses) can provide an approximation of their cumulative radon exposure.
- Legislation requiring radon-resistant construction of new homes needs to be explored. A voluntary program is insufficient to minimize construction of homes lacking radon mitigation systems; retrofitting these homes with mitigation systems will be three to four times as costly.

## **DR. MARILIE GAMMON:**

### **ENVIRONMENTAL TOXINS AND BREAST CANCER: UPDATE FROM THE LONG ISLAND BREAST CANCER STUDY PROJECT**

#### **Background**

Dr. Marilie Gammon obtained her Ph.D. from Yale University in 1989. She was a faculty member of the Department of Epidemiology at Columbia University from 1989 until 1999, at which time she moved to UNC-Chapel Hill. Her current research focuses on identification of risk

factors related to the incidence and survival of breast cancer (particularly estrogen-related factors that are potentially modifiable) as well as esophageal and gastric cancers. Dr. Gammon uses molecular epidemiologic techniques to elucidate inconsistent and/or modest effects. Dr. Gammon is currently Principal Investigator of the Long Island Breast Cancer Study Project (LIBCSP).

## Key Points

- Breast cancer incidence rates among U.S. women steadily increased 3 to 4 percent every year from the late 1970s until the late 1990s, when rates began to plateau. Increased mammography use (resulting in better detection) is thought to account for one-third of the increase and hormone replacement therapy (HRT) is also thought to have played a role, but the causes of the remaining increase in incidence are unknown.
- Between 50 and 67 percent of all breast cancers can be attributed to known risk factors: family history (genetics and shared environment), increased socioeconomic status, reproductive history, exogenous hormone use (i.e., HRT), and alcohol use. Any exposure to estrogen, including estrogen produced by the ovaries, increases an individual's risk for breast cancer. Therefore, the earlier a woman starts menstruation and the later menopause begins, the greater her risk for breast cancer. Lactation, which temporarily prevents ovulation and is associated with low levels of estrogen, decreases breast cancer risk.
- Higher breast cancer incidence and mortality rates occur in urban areas where there are high concentrations of women who have a higher socioeconomic status and a reproductive pattern less likely to protect them from breast cancer.
- The highest rate of breast cancer incidence in the U.S. is in white women. Breast cancer is a predominantly postmenopausal disease in the U.S., with the majority of cases occurring in women over the age of 50. In contrast, in Japan, breast cancer incidence rates decline after age 50. However, the longer Japanese immigrants live in the U.S., the more closely their incidence rates resemble those of white U.S. women. This suggests that breast cancer may be environmentally induced as well as associated with changes in reproductive patterns.
- The LIBCSP was funded by NCI and NIEHS in response to federal legislation passed in 1993; it was required to be a case-control study and include research on biomarkers of exposure to environmental toxins. Long Island community advocates were concerned about ambient pollutants including DDT (dichloro-diphenyl-trichloroethane) and other pesticides, air pollution, electromagnetic fields, chemical waste, and groundwater contamination.
- LIBCSP researchers identified a number of criteria for including environmental factors in the study. Candidate factors should have estrogenic effects *in vivo* or *in vitro* and exhibit carcinogenic effects in animal models. Their role in breast cancer should be consistent with previous epidemiological research and the epidemiology of the disease. The existence of a biomarker to measure exposure to the candidate was also considered an important feature. Finally, there had to be relatively high prevalence of exposure to the factor among women on Long Island.
- At the start of LIBCSP, the three environmental factors thought to have the strongest causal link to breast cancer were pesticides, electromagnetic fields, and polycyclic aromatic hydrocarbons (PAHs). LIBCSP found that DDT is not associated with breast cancer risk among women on Long Island; this is consistent with most published studies regarding DDT and breast cancer. There is ubiquitous exposure to electromagnetic fields from power lines, telephones, and computers, but LIBCSP has found no association with breast cancer risk.
- The primary source of PAH exposure is cigarette smoke, but these chemicals are also released upon burning of organic materials (e.g., wood, coal, gasoline, diesel) and are present

in grilled and smoked foods. The link between breast cancer and PAHs is unclear. Several studies have shown that active smoking is not associated with breast cancer.

- The LIBCSP conducted a multisource assessment of PAHs: vehicular traffic exposures, occupational exposures, active and passive smoke, diet, genetic pathways, and biomarkers of exposure were considered. Three thousand women (1,500 cases and 1,500 controls) participated in 2-hour interviews and provided blood samples and medical records. PAH adducts in the DNA of circulating lymphocytes were measured; the presence of detectable adducts was associated with a 29 percent increase in breast cancer risk. Active smoking was the best predictor of the presence of adducts, but former smokers also had detectable adducts.
- The LIBCSP also investigated whether exposure to PAHs in grilled and smoked foods has an effect on breast cancer risk. It was found that women who ate large amounts of grilled and smoked foods over their lifetimes had a 60 percent increased risk of breast cancer. In contrast, decreased incidence of breast cancer was observed among postmenopausal women who ate large amounts of fruits and vegetables; the largest reduction in tumor incidence was seen for estrogen receptor (ER)/progesterone receptor (PR)-positive tumors. Some studies are being conducted to determine whether high intake of fruits and vegetables could counteract the detrimental effects of consuming large amounts of grilled/smoked foods; results to date indicate that there may be a protective effect, but more data are needed.
- Studies were also conducted on the relationship between tobacco smoke and breast cancer. Similar to previously published studies, associations between active smoking and breast cancer were not observed. However, women passively exposed to tobacco smoke in the home for a long period of time were found to have a higher risk of breast cancer. Although controversial, the link between environmental tobacco smoke and breast cancer has been identified by other studies as well.
- Active smoking was associated with increased breast cancer risk only among women who were also passively exposed to environmental tobacco smoke; these women have an increased risk of developing ER/PR-positive breast tumors, but do not exhibit increased risk of developing tumors lacking these hormone receptors. ER/PR-positive tumors are the most common type of breast cancer in the United States and account for the majority of tumors in postmenopausal women; however, ER/PR-positive tumors are relatively uncommon among women in Japan.
- Studies were done to determine whether genetic variability in carcinogen metabolism genes influences breast cancer risk. Genetic variation in glutathione-S-transferases GSTM1, GSTT1, or GSTP1 was not associated with breast cancer risk; however, women who were current smokers and homozygous for the minor allele of GSTA1 exhibited an increased risk of breast cancer compared with never smokers homozygous for the GSTA1 major allele. Also, among women with PAH adducts above the median detectable level, those with a glutamine at both alleles of exon 23, position 751 of XPD appeared to have a higher risk of breast cancer, suggesting that this polymorphism may predispose women to the carcinogenic effects of PAH.
- LIBCSP is now interested in identifying environmental determinants of breast cancer survival. There is significant variation in survival rates of women diagnosed with breast cancer. There has been extensive research done on how clinical characteristics of a tumor (e.g., stage, size) influence survival, but little has been done to elucidate the role of non-clinical factors. LIBCSP is particularly interested in investigating the effects of organochlorines and environmental tobacco smoke as well as other sources of PAHs.

## **DISCUSSION AND CONCLUDING COMMENTS:**

### **PANEL I**

#### **Key Points**

- The EPA radon action level serves as a guideline; it is not a standard. Individuals can decide whether or not to comply with this recommendation.
- The radon action level was set as a technological action level—a level to which every home could feasibly be reduced. The action level is not based on the health effects of radon. In fact, there is no known safe level of radon exposure; even low levels of exposure can cause DNA damage, and exposure at levels below the EPA action level have been associated with health risks. Furthermore, several presenters agreed that studies to date have likely underestimated the health risks associated with radon. Thus, people must be strongly encouraged to mitigate radon levels in their homes to the lowest level possible.
- In order to reduce the EPA action level, it would be necessary to demonstrate that advances in mitigation technology have made it feasible to reduce residential radon levels below the current action level. The World Health Organization is currently considering recommendation of a radon action level lower than that of the EPA.
- Legislation at the federal and state levels should be considered to address radon. EPA should be encouraged to devise legislation requiring use of radon-resistant construction techniques. There are some examples of local legislation regarding radon. For example, some areas require use of radon-resistant construction techniques, and some states have enacted mandatory testing of radon levels in schools. Many of these requirements were created in response to community advocacy.
- The harmful consequences of radon exposure occur with cumulative exposure over many years. Requiring individuals to pay for installation of radon mitigation systems in homes in which they may reside for only a short period of time forces them to assume an unequal burden of the cost of reducing radon exposure for society as a whole.
- Very few epidemiological studies have examined whether individuals exposed to radon as children have higher risks of health consequences than those exposed as adults. One study of Chinese tin miners included a number of miners who had begun working in the mines before 13 years of age. The study identified radon as a risk factor for lung cancer, but lung cancer risk was not significantly different for miners first exposed to radon as children or young adolescents compared with those who began mining as adults.
- The public is generally unaware of, or apathetic to, issues related to radon exposure. However, there are examples of public outreach and advocacy. EPA partners with the National Environmental Health Association to sponsor annual workshops to train people to educate community leaders about environmental health issues, including radon. Also, an advocacy group called Cancer Survivors Against Radon (CanSAR), a community of people who believe their lung cancer (or that of their patient or loved one) was caused by radon exposure, speaks out about the importance of preventing exposure to radon in homes.
- Cancer risks due to the hazardous air pollutants studied as part of NATA 1999 are relatively small compared with all environmental risks of cancer. However, these risks are not insignificant, and it is likely that some subpopulations experience higher exposures and risks than the population as a whole; one example of this is the exposure of children to the high levels of air pollutants present in school buses. A more integrated regulatory structure for addressing air and environmental pollutants needs to be developed; the current regulatory structure is compartmentalized and inefficient.

- The fact that the LIBCSP did not find direct associations between breast cancer and the compounds on which it focused does not mean that there are no environmental causes of breast cancer. There are millions of pesticides and other toxins in the environment, but research has largely been limited to those compounds to which exposure can be measured. For example, exposure to toxins such as DDT and polychlorinated biphenyls (PCBs) can be easily measured because their half-lives in the human body are very long. Many pesticides are made to have short half-lives and thus are much harder to measure. Geographic modeling (i.e., using algorithms to predict historical exposure based on location) is one method that can help address this problem; this type of approach was used by LIBCSP to estimate exposure to PAHs.
- LIBCSP researchers did not begin interacting with community advocates until after the project received funding. The researchers and advocates met on a regular basis, and the advocates had strong opinions about how the study should be conducted. However, the research plan had already been laid out in the grant application, so many of the advocates' suggestions could not be incorporated. This caused some discontentment among the community advocates. A new collaboration funded by NIEHS and NCI called the Breast Cancer and Environment Research Centers specifically requires community advocate involvement.
- It is an enormous challenge to discern the effects of environmental exposures not only on individuals who are directly exposed but also on future generations, which could be affected through mechanisms such as gene imprinting. Diethylstilbestrol (DES) is an example of an agent that was found to increase cancer risk among those who were gestationally exposed. Once researchers are able to better understand mechanisms of action of various agents, it will be easier to make associations and address exposure effects.
- LIBCSP results have spurred approximately 40 substudies, which have been funded in part by private foundations, such as Susan G. Komen for the Cure and the Estée Lauder Company.
- Much research has been done on the relationship between radon exposure and lung cancer, but it is likely that radon also increases risk of other cancers as well. It may be possible to address this type of research question within the context of a large cohort study.

## **PUBLIC COMMENT**

### **Key Points**

- There was concern whether exposure to exhaust emitted from restaurants like McDonalds and Burger King might increase risk of breast cancer. A significant amount of fine particulate matter in the atmosphere in urban areas comes from the cooking of meat. Meat cooking within homes can also impact residential air quality.
- EPA has released several public service announcements (PSAs) regarding the dangers of radon exposure; however, these PSAs are generally not widely disseminated. The message that radon exposure is associated with health risks has not effectively reached the general public. This failure is similar to that seen in the area of environmental tobacco smoke.
- The possibility of requiring radon testing prior to the sale of a home was discussed. Currently, some states require the results be disclosed to a buyer if a radon test has been conducted. However, this actually provides a disincentive for homeowners to test for radon.
- Implementation of an enforceable standard for residential radon levels was discussed. In general, lawmakers have been reluctant to create regulations regarding people's homes, particularly pre-existing homes; however, it may be feasible to regulate use of radon-resistant techniques for new construction.

- NCI's Cancer Information Service (CIS) helps educate patients and the general public about issues related to cancer. Currently, CIS does not provide information about the influence of environmental factors on cancer; however, the existing structure of CIS should be used to relay this important information to the public.

## **PANEL II**

### **DR. KENNETH CANTOR:**

#### **CARCINOGENS IN DRINKING WATER: THE EPIDEMIOLOGIC EVIDENCE**

##### **Background**

Dr. Cantor is a Senior Investigator in the Division of Cancer Epidemiology and Genetics at NCI, where he has directed studies of cancer and environmental factors since 1977. His research interests focus on the epidemiologic investigation of cancer risks associated with occupational and environmental exposures, and their interaction with other risk factors and host factors. His particular areas of interest deal with water contaminants (nitrate, arsenic, disinfection byproducts), pesticides, electromagnetic radiation, and the role of genetic factors in susceptibility to these factors. Dr. Cantor received his B.A. from Oberlin College, a Ph.D. in biophysics from the University of California at Berkeley, and an M.P.H from the Harvard School of Public Health.

##### **Key Points**

- The EPA defines a community water supply as any system serving 25 or more persons or having 15 or more connections. More than 80 percent of the U.S. population receives its water from systems serving more than 10,000 people. There are nearly 30,000 water systems in the U.S. that serve fewer than 500 people each. In general, EPA regulations are first applied to large water supplies and then more widely imposed on all water supplies over time.
- The EPA regulates approximately 86 drinking water contaminants, which are organized into 5 main categories: microorganisms, disinfection byproducts, inorganic chemicals, organic chemicals, and radionuclides. Most suspected cancer carcinogens are in the organic chemical category. Arsenic is the only one of these 86 chemicals that is regulated based on human data; regulation of the remaining contaminants is based on extrapolation of data generated through animal studies.
- The link between arsenic and cancer was first discovered in the late 19<sup>th</sup> century. Dr. Jonathan Hutchison, who had been treating patients with Fowler Solution (a potassium arsenate solution used to treat a variety of ailments), published the first reports of arsenic-related cancer. Dr. Hutchison observed that patients treated with Fowler Solution for skin conditions later developed skin cancer.
- From 1942 to 2006, the Maximum Contaminant Level (MCL) issued by the EPA for arsenic was 50 µg/L. In February 2006, the MCL was decreased to 10 µg/L due to the results of several health studies conducted throughout the world.
- After studying 42 villages in Southwest Taiwan with high levels of arsenic exposure, C.J. Chen and colleagues published the first data in 1988 showing a cancer dose response to arsenic. This study compared cancer rates in groups of these villages with overall Taiwanese rates, confirming the dose-response relationships of arsenic with several cancers (i.e., skin, bladder, kidney, prostate, lung, liver). These results were replicated by studies in Chile and Argentina, with the exception of prostate and liver cancers, which were not elevated upon exposure to high levels of arsenic.

- Convincing evidence regarding arsenic-induced bladder, kidney, and lung cancers has been generated by studying populations that have been exposed to drinking water with levels of arsenic of 150 to 200 parts per billion. These data have led IARC to designate arsenic as a carcinogen; however, additional large studies with precise exposure assessment are needed to determine cancer risk in populations exposed to lower levels of arsenic. These kinds of studies tend to be very challenging and costly.
- Disinfection byproducts (DBPs) are a complex mixture of hundreds of different chemicals created when chlorine reacts with organic material commonly found in untreated water. Trihalomethanes (THM) and haloacetic acids (HAA) are the predominant DBPs found in drinking water. THM levels are used as a surrogate marker for total DBP exposure for both regulatory and research purposes. EPA regulations limit levels of THMs in water to 80 parts per billion and epidemiologists studying the effects of exposure to DBPs use THMs as an estimate for overall exposure.
- Several studies, including a pooled analysis, have shown that DBPs are linked to bladder cancer; however, few studies have been conducted on the potential link with other types of cancer. Where associations to cancer (including bladder cancer) have been observed, relative risks are modest (in the range of 1.3 to 2.6); however, given that a substantial portion of the population is exposed to DBPs, even a modest relative risk could have important public health implications. Furthermore, there is evidence that certain polymorphisms in genes whose products are involved in DBP metabolism may result in increased susceptibility to the carcinogenic effects of these compounds.
- Levels of nitrate, which is primarily a groundwater contaminant, have steadily increased in water sources over the past several decades. Approximately 42 percent of the U.S. population receives its water from a groundwater supply, which has an array of contaminants distinct from those found in surface water. The highest levels of groundwater contaminants are found in private wells, which are generally unregulated.
- A certain amount of nitrates in the soil are the result of natural nitrogen fixation by plants and other organisms; however, humans now contribute more nitrogen to soil than the total contribution of other living organisms. Human-produced nitrate comes primarily from fertilizers used for agriculture; fossil fuel combustion is another source.
- After being ingested, a portion of nitrate is converted to nitrite in the saliva. The nitrite is swallowed and can react with tertiary amines and amides in the gut to form nitrosamines and nitrosamides, which are highly carcinogenic. EPA has established an MCL for nitrate in drinking water; however, it is possible that nitrate is a human carcinogen at levels of exposure lower than the MCL. More research is needed to address this issue.

## **DR. JOHN VENA:**

### **AIR AND WATER POLLUTION AND RISK**

#### **Background**

Dr. John Vena is the newly appointed Head of the Department of Epidemiology and Biostatistics and Foundation Professor of Public Health in the College of Public Health at the University of Georgia. For the past five years he served as Professor and Chair of the Department of Epidemiology and Biostatistics at the Arnold School of Public Health at the University of South Carolina. Dr. Vena received his B.S. in biology from St. Bonaventure University and his M.S. and Ph.D. degrees in epidemiology from the State University of New York at Buffalo. Dr. Vena is a Fellow of the American College of Epidemiology and a member of the International Society for Environmental

Epidemiology, the Society for Epidemiologic Research, and the American Public Health Association (APHA), for which he currently serves on the Section Council for Epidemiology.

## Key Points

- Dr. Warren Winkelstein was the first to use air monitors to quantify air pollution in the U.S. He placed several monitors around Buffalo, New York, between 1959 and 1961 and correlated the data collected with the lung function of people in the area. The results of this study were used to establish dose responses for air pollution and ultimately led to the passage of the Clean Air Act. The acceptable level of air pollution identified at that time— $75 \mu\text{g}/\text{m}^3$ —is still recognized as the standard today.
- In the early 1980s, Dr. Vena conducted a case-control study of patients at Roswell Park Cancer Institute to examine the relationship between lung cancer and air pollution. He used Dr. Winkelstein's data to help determine historic levels of residential exposure to air pollution. It was found that individuals who had lived 50 years or more in Erie County, New York, an area with notably high levels of air pollution, had a two-fold increase in cancer risk. After adjusting for age and tobacco use, a 70 percent increase in cancer risk was still apparent. These study results also suggested that exposure to air pollution and smoking had a synergistic effect on lung cancer risk.
- Three U.S. cohort studies have subsequently been conducted to determine the health effects of air pollution—the American Cancer Society Study, the Harvard Six Cities Study, and the Loma Linda University Adventist Health and Smog Study. Each of these studies evaluated the relative risks of exposure to fine particulate air pollution. All three studies showed an increased risk of lung cancer.
- The exposure-response relationship between fine particles and lung cancer indicates that for every increase in exposure of  $10 \mu\text{g}/\text{m}^3$ , there is a 14 percent increase in cancer risk. Approximately 95 percent of U.S. cities have air pollution levels in the range of 10 to  $24 \mu\text{g}/\text{m}^3$ . Ultimately, reducing the amount of fine particles in the air will reduce the incidence of lung cancer.
- A prospective cohort study published by Paolo Vineis estimated exposure to environmental tobacco smoke (ETS) and air pollution in ten European countries over a period of eight years and correlated these data with rates of lung cancer. Of the lung cancer observed in never-smokers and former-smokers, 5 to 7 percent were attributed to air pollution and 16 to 24 percent were attributable to ETS.
- The link between cigarette smoking and breast cancer has been controversial; however, several studies and a recent meta-analysis have shown evidence that cigarette smoking increases risk of lung cancer among women with “slow acetylation” genotypes of N-acetyltransferase (NAT2), an enzyme that metabolizes many toxins, including those found in cigarettes.
- In one study, exposure to total suspended particulates (TSPs) was linked to an increased risk of breast cancer in postmenopausal women. Conversely, there was no correlation between high TSP exposure and increased breast cancer risk among premenopausal women.
- A study was also conducted on women exposed to high levels of PAHs from traffic emissions. Premenopausal women who had been exposed to high levels of traffic emissions at menarche and postmenopausal women exposed to high levels of traffic emissions at birth were found to be at higher risk for breast cancer; however, this correlation was only seen among nonsmokers. The data also suggest a stronger association between high traffic emission exposures and breast cancer risk among women with the GSTM1 null genotype.

- After adjusting for sex and age at enrollment, the New York State Angler Cohort Study found that risk for all cancers combined was 1.44 times higher among those who reported ever eating Lake Ontario fish compared with those who reported never eating Lake Ontario fish. In particular, incidence of breast cancer was also shown to be higher among female Lake Ontario fish consumers compared with nonconsumers.
- Studies of low-level exposure to carcinogens over a long period of time are burdened with methodological challenges that limit the ability to accurately estimate risks. However, the evidence to date indicates that a significant percentage of many types of cancer can be attributed to exposures to air and water pollution.

## **DR. JULIA BRODY:**

### **EVERYDAY EXPOSURES AND BREAST CANCER**

#### **Background**

Dr. Julia Brody is Executive Director of Silent Spring Institute and Principal Investigator of the Cape Cod Breast Cancer and Environment Study. Silent Spring Institute is a nonprofit research organization founded as a partnership of scientists and activists dedicated to studying the links between the environment and women's health with a goal of disease prevention. Dr. Brody earned her Ph.D. from the University of Texas at Austin and her A.B. from Harvard University. She is the lead author of *Environmental Factors and Breast Cancer*, a special issue of *Cancer*, a peer-reviewed journal of the American Cancer Society. The publication made headlines across the world, from the front page of the Los Angeles Times to news media in Korea and France.

#### **Key Points**

- Breast cancer is the leading cause of death among women in midlife. However, evidence shows that inherited genes account for only 27 percent of breast cancer risk and that only 5 to 10 percent of cases are associated with the high-risk inherited genes BRCA1 and BRCA2. Studies of twins and migrating populations have led to the conclusion that nongenetic factors play a predominant role in breast cancer incidence.
- There is a high level of interest in reducing breast cancer risk, particularly through primary prevention. A study team sponsored by Susan G. Komen for the Cure is reviewing scientific evidence about modifiable breast cancer risk factors. To date, the team has reviewed more than 450 human and animal studies looking at 216 chemicals and has published 5 review articles. A Science Review Database providing quick access to study information is available on the Silent Spring Institute Web site in order to facilitate public access to this information.
- Ionizing radiation is currently the only established environmental risk factor for breast cancer. Other modifiable risk factors such as consuming alcohol, being physically inactive, being overweight after menopause, and using pharmaceutical hormones have also been implicated in breast cancer.
- There is also evidence linking environmental pollutants (e.g., PAHs in vehicle exhaust and air pollution, persistent organic pollutants, PCBs, dioxin, and organic solvents) to breast cancer. While prior studies have shown no association between cancer risk and measures of exposure taken at diagnosis, a newer study has used blood samples collected during times of DDT use to link DDT exposure to subsequent breast cancer risk.
- It is difficult to definitively link environmental pollutants to breast cancer, in part because only a fraction of women exposed to environmental pollutants eventually develop breast cancer. Identifying and measuring exposure to various environmental factors across the lifespan is a complex undertaking. Adding to the complexity is the fact that the effects of

environmental exposures depend in part on other risk factors (e.g., genetic background, obesity).

- In biomedical research, clinical trials are often used to determine the effects of interventions on disease outcomes; however, this type of approach is not feasible for assessing the effects of environmental pollutants on breast cancer because it would be unethical to intentionally expose humans to a potentially toxic chemical.
- The National Cancer Program should fundamentally modify its approach for addressing environmental contributions to cancer and other long-latency diseases. Biological screening for chemicals and other environmental pollutants should be conducted in order to identify human exposures, and experiments in animals and other model systems should be used to elucidate the mechanisms of action of these pollutants. Data from these two approaches should be integrated and used as the basis for public policy; it is not judicious to delay action until definitive results from in-human studies can be generated.
- Environmental pollutants that may influence breast cancer risk were categorized based on mechanism of action: mammary gland carcinogens (i.e., chemicals that damage DNA and may act as tumor initiators), endocrine disruptors (i.e., chemicals that affect hormones and may act as tumor promoters), and developmental toxicants (i.e., chemicals that affect the developing breast and may increase susceptibility to the damaging effects of other factors).
- A review of published literature has identified 216 chemicals that cause mammary tumors in animal models; the public is widely exposed to at least 100 of these chemicals.
- There tends to be controversy regarding the translation of animal studies to humans; however, most chemicals to which the public is exposed have never even been studied in animals or cell culture. There is a need for modernization of test methods.
- Endocrine disruptors can be found in many commonly used products, including pesticides, food packaging, laundry detergent, hairspray, sunscreen, and soybeans. Many pharmaceutical agents, including oral contraceptives, are also endocrine disruptors. Silent Spring Institute conducted the most comprehensive study to date of endocrine disruptors in homes: 170 homes were tested for 89 endocrine disruptors. The Silent Spring study identified the presence of 67 endocrine-disrupting compounds and 27 pesticides (including DDT) in the homes tested. Phthalates, phenols, and parabens were found in 100 percent of homes and were among the most abundant contaminants. Flame retardants were present at levels ten times those in European homes. Every home had at least one compound present above established health guidelines; however, health guidelines do not exist for 28 of the detected endocrine disruptors.
- Cancer risks associated with exposure to chemicals in the environment should be taken seriously. Health assessments should be required for all synthetic chemicals, old and new, as a prerequisite for their use. Europe, Canada, and California currently have policies that can be adopted for the regulation of chemicals at a federal level. In order to implement new policies, better methods for chemical testing and exposure assessment need to be developed.

## **DR. WINIFRED HAMILTON:**

### **AIR POLLUTION AND CANCER: “HOT SPOTS”**

#### **Background**

Dr. Hamilton earned graduate degrees from the University of Michigan, Rice University, and the Harvard School of Public Health, the latter in environmental health epidemiology. She is Assistant Professor at Baylor College of Medicine, with joint appointments in medicine and

neurosurgery, and is Director of the Environmental Health Section, which she launched in 2002, of the Chronic Disease Prevention and Control Research Center. She is also a faculty member at Rice University, where she teaches a course on environmental health. Recent major projects include serving as Program Director and Principal Investigator for the 2007 symposium, “Environmental Health Is a VERB! Building Healthy Children;” chairing a Texas Medical Center committee to establish a regional Children’s Environmental Health Center; serving as Principal Investigator of a geospatial “hot spot” analysis of the relationships between multipollutant exposure and hospital admissions in Harris County; and serving as Principal Investigator of a recent geospatial analysis and report titled “Galveston Lead Poisoning in Galveston, Texas,” which stimulated national media attention and the creation of a Galveston lead task force.

## Key Points

- Minorities and low-income individuals are more likely to live, work, and attend school near major polluting facilities, freeways, and landfills, which increases their cancer risk. The existence of these types of documented, preventable disparities led President Clinton in 1994 to sign Executive Order 12898, which directs all federal agencies to address “disproportionately high and adverse human health or environmental effects of their programs, policy, and activities on minority and low-income populations.”
- Approximately two-thirds of all cancer is linked to environmental exposure; however, this estimate varies depending on the definition of environmental hazard (e.g., whether lifestyle choices are included). Many of these environmental exposures are at least theoretically preventable.
- Individuals are exposed to multiple pollutants—at the same time or in a sequence—that can interact to increase cancer risk. There are six “criteria” air pollutants (regulated by EPA), 187 hazardous air pollutants, 666 toxic release inventory chemicals (chemicals whose release or transfer is subject to public reporting), and about 50,000 other chemicals or pollutants of importance. Approximately 700 new pollutants are put on the market each year. The pollutants in food, water, and flora to which people are exposed every day must also be taken into account. Current research and policies address one pollutant and one exposure scenario at a time. This artificial separation undermines the ability to address the total burden of environmental hazards.
- Noncarcinogenic chemicals and weak carcinogens can play a major role in susceptibility to other carcinogens. The VA Normative Aging Study tested the tibias of 384 elderly men for lead levels. Lead exposure at any point in an individual’s life results in lead deposits in the teeth and bones. It was determined that higher levels of tibia lead were associated with increased sensitivity to ozone and sulfate pollution as well as cardiovascular autonomic dysfunction. Lead is currently listed by both the EPA and IARC as a probable carcinogen.
- The California Air Resource Board (CARB) defines a “hot spot” as a “location where emissions from specific sources may expose individuals and population groups to elevated risk of adverse health effects, including but not limited to cancer, and contribute to cumulative health risks of emissions from other sources in the area.” Specific actions are set forth by EPA for areas labeled as hot spots.
- Epidemiologists face many challenges when conducting hot spot research. Study design and statistical issues in spatial analyses, lack of good exposure data, and poor health effects data make it difficult to carry out this type of research.
- Steven Linder at the University of Texas School of Public Health used NATA census data to examine the cumulative cancer risk of people living in socially disadvantaged communities in Houston and Harris County, Texas. Those living in the poorest neighborhoods were found to have a cancer risk four- to ten-times greater than those living in other neighborhoods.

- Cumulative cancer risk is higher in areas with high rates of poverty. Lower socioeconomic status often equates with less desirable living conditions (nearby major industries, drycleaners, and gasoline stations) and hot spots of exposure that strongly correlate with cancer risk.
- U.S. regulation of air pollution is extremely fragmented with different government agencies mandating, researching, and educating on many of the same issues. Standards for some chemicals have been set by more than one agency with different levels mandated as safe. This has led many states and cities to implement their own regulatory structures.

## **MR. RICHARD WILES:**

### **Background**

Richard Wiles co-founded the Environmental Working Group (EWG) with Ken Cook in 1993 and now supervises all staff. He is a former senior staff officer at the National Academy of Sciences Board on Agriculture, where he directed scientific studies, including two that resulted in landmark reports: *Regulating Pesticides in Food: The Delaney Paradox* and *Alternative Agriculture*. Mr. Wiles is a leading expert in environmental risks to children, and under his direction EWG has become one of the most respected environmental research organizations in the country. EWG's exposure and risk assessment methods are recognized as state of the art and have been used by the EPA and the National Research Council. Mr. Wiles holds a B.A. from Colgate University and a M.A. from California State University at Sacramento.

### **Key Points**

- Babies in the United States are born “pre-polluted.” Fetal cord blood samples were drawn from 10 fetuses to test for 413 toxic chemicals. It was found that 287 of the tested chemicals—34 of which are known or suspected carcinogens—were present.
- The Environmental Working Group has estimated that there are 126 known or suspected carcinogens in tap water. This is a broad estimate that includes substances that have undergone just single animal studies; however, if tougher criteria are applied, 58 of these substances are listed as Proposition 65 carcinogens—those known to the state of California to cause cancer or reproductive toxicity.
- Many public water systems are not required by states to report levels of individual chemical compounds present in drinking water. This makes it difficult to set policy or conduct robust risk assessments.
- While it is desirable to eliminate exposure to carcinogenic, chlorination-generated DBPs, it is not necessarily a good idea to bypass treatment with chlorine in favor of treatment with other chemicals that have not been subjected to adequate safety testing. For example, in an effort to reduce levels of total THM in water systems, utility companies began using chloramination (treatment with a mixture of chlorine and ammonia) instead of chlorination to disinfect water. However, chloramination produced another set of byproducts, some of which are also suspected carcinogens. Additionally, the new approach altered the pH of many water systems, causing lead to be released from the insides of old pipes and creating additional health hazards.
- Atrazine, a pesticide/weed killer frequently used on corn crops, is a known endocrine disruptor and a suspected carcinogen. It has been present in the Midwest water supply for the past 35 years; approximately 23 to 25 million people have been exposed to atrazine through water supplies. Atrazine still enters many Midwestern water supply surface systems each year.

- The Safe Drinking Water Act is not a health-based law; it requires safety to be balanced with cost and feasibility of purification. For most carcinogens in tap water, EPA has a safe dose, or an MCL goal, of zero; however, the legal levels may be much higher, allowing tap water to remain full of pollutants.
- The risks associated with drinking tap water should be disclosed to the general public, and vulnerable populations should be protected. For example, tap water filtration within the home should be recommended for all pregnant women to help prevent babies from being born “pre-polluted.” Laws should be set in place to protect children from the pollutants currently found in tap water. However, the public must also recognize that there will always be a need to treat water to eliminate microbial contaminants; thus, tap water will never be completely free of pollutants.
- The bottled water industry is not regulated by the government: the water is not tested for contaminants. Therefore, bottled water is not necessarily an optimal alternative to public water systems. Nongovernment studies of bottled water have found the quality to be inconsistent; some brands were essentially the same as tap water. On average, the bottled water tested contained slightly lower levels of chlorination byproducts than most tap water, but the differences were not significant.
- The Environmental Working Group is supporting the Kid-Safe Chemicals Act, which is a proposed overhaul of the Toxic Substance Control Act. TSCA was intended to regulate chemicals in consumer products; however, most of the roughly 80,000 chemicals in commerce have been grandfathered under TSCA, despite the fact that little or no safety data exist for them. In addition, no health studies are required to bring a new product to market; TSCA does not require commercial chemicals to be proven safe. EPA has banned 5 chemicals or classes of chemicals in 31 years and has reviewed approximately 200 chemicals. TSCA has not been effective for reducing exposure to potentially harmful chemicals.
- Under the Kid-Safe Chemicals Act, chemicals found to be present in human blood (including cord blood), tissue, urine, or breast milk would be classified as chemicals of concern. Manufacturers of these chemicals would be required to generate and submit information on the safety of these chemicals. A risk assessment focused on vulnerable populations (e.g., children, babies) would be conducted for each of these chemicals of concern. The Act would also require regular biomonitoring, regular updates of health and safety data, provision of incentives for manufacturers to reduce health hazards, and public availability of all data.

## **DISCUSSION AND CONCLUDING COMMENTS:**

### **PANEL II**

#### **Key Points**

- For most organic compounds, evidence of carcinogenicity is based on animal studies, not human or epidemiologic studies. EPA regulatory levels are often based on results of these animal studies. The results of animal studies testing nitrates have been somewhat ambiguous, but there is stronger evidence for the carcinogenicity of nitrosamines.
- Chemicals (e.g., PAHs) in the environment adsorb to particulate matter in the air. There are particles of all different sizes in the air. It is the smaller particles (less than 10 microns in diameter) that are inhaled into the lung. Dr. Vena clarified that his early studies were based on data from stationary monitors that measured total suspended particulates in the air from all sources (this included both large and small molecules); thus, these monitors gave a crude measure of the air pollution to which people were exposed. The later cohort studies that

established a link between air pollution and lung cancer relied upon measurement of small particles (less than 10 microns).

- It is difficult to quantify risk associated with air pollution exposure due to people's constant movement in and out of geographic spaces every day. Urban areas are particularly complex because of the many sources of air pollution that must be considered.
- Indoor pollution tends to be higher than outdoor pollution. Pollutants accumulate indoors, even in houses that are relatively permeable (i.e., not sealed for weatherproofing purposes). Indoor pollution is higher in homes located near factories, oil refineries, and major highways, areas usually populated by lower-income populations.
- Most cancer registries provide information about incidence and mortality, but many lack information on other factors that may influence cancer risk, such as socioeconomic status, lifestyle, nutrition, and smoking. Furthermore, misclassification of cause of death is not uncommon in large databases, making it difficult to obtain accurate information on cancer-related mortality. Large databases are needed to carry out comprehensive studies; however, lack of funding and existing privacy legislation makes it almost impossible to obtain the necessary data.
- The best way to increase the safety of chemicals is to establish health-based standards. Green chemistry is one way to produce safer chemicals, but legislation should focus on the end goal—safer chemicals—rather than on the technology of green chemistry. If standards are established and enforced, manufacturers will be forced to be innovative to comply, and this will likely involve increased use of green chemistry.
- Under TSCA, EPA cannot directly request a study from chemical manufacturers. It is required to go through a formal rulemaking process to demonstrate the need for a study. The need must be justified by showing there is a health risk; however, the health risk cannot be shown unless a study has been conducted. This conundrum has resulted in little regulatory authority over chemical manufacturers. Additionally, the U.S. Food and Drug Administration (FDA) is prohibited by the Food, Drug, and Cosmetic Act from requiring premarket health studies for chemicals in cosmetics.
- There have been only a small number of studies of environmental pollutants and breast cancer. There is fairly strong evidence of the link between PAHs and PCBs and breast cancer among women with a particular genetic variant. There have also been a number of studies linking occupational exposure to organic solvents with breast cancer risk.
- For individuals, the best short-term solution for reducing exposure to tap water contaminants is the use of in-home filtration systems. These relatively inexpensive systems are readily available and can be installed under a sink or at the end of a water faucet. It is also beneficial to use a filtering pitcher (e.g., Brita).
- The water of most private wells is unregulated by the FDA so the risks of nitrate and arsenic exposure for the populations using these wells are unknown.
- The cancer burden caused by contamination of water with DBPs is currently not well characterized. A thorough review of current data is needed, as are resources for additional studies. Once enough data has been collected, decisions should be made to establish a balance between the risks of microbial contamination and the dangers of polluting water with carcinogenic compounds.
- Several priorities for research and monitoring were discussed. Future studies should continue to examine genetic susceptibility to the carcinogenic effects of environmental pollutants. Research agendas should be tailored to inform public policy. Infrastructure should be established so that populations—particularly vulnerable populations—can be monitored for exposure to contaminants.

- Although there is not definitive evidence regarding the health risks of certain environmental contaminants, policy decisions should be made based on present knowledge of human exposure and biological mechanisms.
- A significant portion of U.S. air pollution is due to use of combustion engines. The U.S. should enact policies to reduce pollution from these sources.
- Federal research and regulatory agencies should work together to protect the public from environmental pollutants.

## **PUBLIC COMMENT**

### **Key Points**

- The President's Cancer Panel was applauded for its recent work related to tobacco and encouraged to revisit the issue to help eliminate tobacco use in the United States.
- The new administration should be encouraged to promote availability of comprehensive prevention services. The medical system is not to blame for the existing disease-oriented paradigm; the primary problem is that not all insurance companies cover preventive services.
- Federal and state governments should establish stronger partnerships with advocates, which will promote better environmental monitoring and risk factor documentation as well as public health education.
- South Carolina has the lowest cigarette tax in the nation and ranks worst nationally in state funding for tobacco prevention and control with no state money dedicated to tobacco prevention. Grassroots efforts have helped pass several local ordinances, which collectively ensure that more than 20 percent of the residents of South Carolina have the right to breathe clean air in workplaces and public places. However, the tobacco industry is working at the state level to preempt the right of local governments to regulate tobacco smoke.
- The CDC Office on Smoking and Health has reported a decline in U.S. cancer rates for the first time; however, these improvements are not being enjoyed by all segments of the population. Communities with strong cancer prevention programs and smoke-free policies have shown the most progress. Many times this overshadows the work that still needs to be done in communities lacking the funding and support needed to address these concerns.
- Local governments should have the right to create stronger smoke-free ordinances than those established by the state; states should be permitted to establish minimum levels of protection, but should not be allowed to prevent local governments from strengthening these protections.
- Smoke-free legislation should continue to be implemented on the local level, not the federal level. Local governments are best equipped to handle enforcement of smoke-free ordinances and facilitate public awareness.
- Although it was one of the primary contributors to the Framework Convention on Tobacco Control, the U.S. has yet to ratify this treaty. One hundred-sixty countries have taken part in this treaty, which has been successful in limiting tobacco industry corruption and influence worldwide. The U.S. Senate should be encouraged to sign this treaty, as well as mandate cessation programs as part of all health care plans.
- The new administration should be urged to regulate port pollution. Port facilities are some of the largest unregulated sources of particulate pollution in the U.S. EPA has estimated that approximately \$70 billion dollars in health care costs could be saved if \$2 to \$4 billion is spent over the next 10 to 15 years cleaning up ports.
- EPA NATA data attributes up to 80 percent of the air pollution-related cancer risk faced by Americans to diesel exhaust. After being inhaled into the lungs, the tiny particles of diesel

exhaust travel into the bloodstream, causing cancer, stroke, high blood pressure, heart disease, and various other health issues. Pollution from diesel exhaust can be reduced by 90 percent with currently available technology.

- The South Carolina coast has much higher cancer rates than the national average, and one study showed that diesel air pollution creates harmful compounds when it mixes with the salty air and sunlight. This pollution has most recently been linked to brain cancer and neurological problems.
- Communities of poor and minority populations are more likely to be exposed to pollution from ports, trucks, and factories. Stringent national standards are needed to protect all communities from outdoor air pollution.

### **CLOSING REMARKS—DR. LEFFALL**

- Dr. Leffall thanked the attendees and panelists for making valuable contributions and assured them that the Panel would carefully consider the information collected at the meeting.

### **CERTIFICATION OF MEETING SUMMARY**

I certify that this summary of the President’s Cancer Panel meeting, *Environmental Factors in Cancer*, held December 4, 2008, is accurate and complete.

Certified by:

Date: April 14, 2009

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LaSalle D. Leffall, Jr., M.D.  
Chair  
President’s Cancer Panel