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DCEG Linkage

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DIRECTOR'S PAGE

New Fellowship Program for Radiation Epidemiology

Over the last decade, attention to radiation as a cause of cancer has been heightened by concerns about possible health risks associated with the Chornobyl nuclear facilities accident, radioactive fallout from nuclear weapons production and testing, indoor radon, medical diagnostic procedures, electromagnetic fields, and ultraviolet radiation. As the world's largest radiation epidemiology research program, DCEG's Radiation Epidemiology Branch conducts regional, national, and international studies of individuals exposed to medical, occupational, and environmental radiation.

Top: Peter Inskip, Sc.D., Kiyohiko Mabuchi, Ph.D., Bottom: Ruth Kleinerman, M.P.H., Elaine Ron, Ph.D.

There still remains many important unanswered questions about the carcinogenic and other health risks posed by radiation. It is therefore critical that there continue to be well trained and inspired researchers entering the field of radiation epidemiology. At present, however, there is a serious shortage of young researchers with such interests and training. The continued vitality of the field requires ongoing recruitment of capable investigators who understand the principles of epidemiology, biostatistics, and radiation biology, as applied to the quantitative study of radiation-induced tumors. In response to this need, DCEG has developed the Radiation Epidemiology Fellowship (REF), a postdoctoral fellowship program targeted to encourage promising, well-qualified scientists to enter the field of radiation epidemiology.

A unique aspect of the fellowship program is the opportunity to pursue research training at the Radiation Effects Research Foundation (RERF) in Hiroshima, Japan, for up to 3 years. The Radiation Epidemiology Branch has collaborated closely with RERF for over 25 years on studies of cancer risk among atomic bomb survivors. These studies have been the single most important source of information about the health effects of ionizing radiation in humans. Working at RERF will provide invaluable experience.

The Radiation Epidemiology Branch has developed the fellowship in collaboration with RERF and the Department of Epidemiology at The Johns Hopkins University

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Managing Editor
Michelle Renehan (renehanm@mail.nih.gov)

Photographer
Samantha Nhan (nhans@mail.nih.gov)

DCEG Linkage Reporters
Office of the Director, DCEG
Catherine McClave (mcclavec@mail.nih.gov)

Office of Division Operations and Analysis, OD, DCEG
Marianne Henderson (hendersm@mail.nih.gov)

Office of the Director, EBP
Katrina Wahl (wahlk@mail.nih.gov)

Biostatistics Branch, EBP, DCEG
B.J. Stone (stoneb@mail.nih.gov)

Clinical Genetics Branch, HGP, DCEG
Ruthann Giusti (giustir@mail.nih.gov)

Environmental Epidemiology Branch, EBP, DCEG
Patricia Madigan (madiganp@mail.nih.gov)

Genetic Epidemiology Branch, HGP, DCEG
Mary Fraser (fraserm@mail.nih.gov)

Laboratory of Population Genetics, HGP, DCEG
Jenny Kelley (kelleyj@mail.nih.gov)

Nutritional Epidemiology Branch, EBP, DCEG
Stephanie Weinstein (weinstes@mail.nih.gov)

Occupational Epidemiology Branch, EBP, DCEG
Judy Lichaa (lichaaj@mail.nih.gov)

Radiation Epidemiology Branch, EBP, DCEG
Ruth Kleinerman (kleinerr@mail.nih.gov)

Viral Epidemiology Branch, EBP, DCEG
Beth Maloney (maloneyb@mail.nih.gov)

DCEG Committee of Scientists
Tom O'Brien (obrient@mail.nih.gov)

DCEG Representative to the NIH Women Scientists Advisory Group
Martha Linet (linetm@mail.nih.gov)

DCEG Representatives to the NIH Fellows Committee
Dawn Elizabeth McNeil (mcneile@mail.nih.gov)
Joni Rutter (rutterj@mail.nih.gov)

DCEG Representative to the NIH pre-IRTA Committee
Tammy Shields (shieldst@mail.nih.gov)

Administrative Resource Center, OM, NCI
Melanie Keller (kellerm@mail.nih.gov)

Research Contracts & Acquisition Branch, OM, NCI
Sharon Miller (millersh@mail.nih.gov)

Contractor Support
Technical Editor
Jim Sontag (sontagj@hotmail.com)

Production Staff
Palladian Partners, Inc.
(mbarker@palladianpartners.com)

School of Hygiene and Public Health, along with the Radiation Oncology Sciences Program in NCI's Division of Clinical Sciences. Researchers at RERF, Johns Hopkins, and the NCI Radiation Oncology Sciences Program will actively participate in formal and informal teaching and mentoring and will provide access to relevant data. The fellowship program will provide opportunities to participate in all aspects of research, including protocol development, feasibility studies, data collection and analysis, and drafting of manuscripts for publication. The program will be guided by a steering committee composed of senior staff from the Radiation Epidemiology Branch and other units in DCEG, the Radiation Oncology Sciences Program, The Johns Hopkins University School of Hygiene and Public Health, and RERF.

During the first 2 years, fellows will attend one semester of didactic courses in radiation epidemiology, radiobiology, and risk assessment at NCI. The radiation epidemiology course will be directed by staff members of the Radiation Epidemiology Branch, the radiobiology course by scientists in the Radiation Oncology Sciences Program, and the radiation risk assessment course by researchers at Johns Hopkins. Fellows will also participate in seminars and conferences at NCI and Johns Hopkins. In addition to course work, fellows will explore research projects with their advisors and gain practical knowledge in writing study protocols. During this time, research plans will be developed, in conjunction with collaborators at RERF, for the fellows to pursue during their time in Hiroshima.

During years 3 and 4, many of the fellows will plan and conduct research at RERF, using atomic bomb survivor data, under the supervision of senior scientists from RERF and the Radiation Epidemiology Branch. In this setting, fellows will gain experience in conducting and analyzing epidemiologic radiation data, and they will develop a better understanding of radiobiological issues relevant to radiation carcinogenesis. Fellows will return to NCI for 1 year to complete manuscripts describing their research results for peer-reviewed scientific journals and to collaborate on other epidemiologic studies with investigators at NCI and

Johns Hopkins University. Fellows will continue to participate in seminars and conferences at NIH and Johns Hopkins. They will also have the option of spending their entire fellowship at NCI. Initial awards are for 2 years, with annual renewals up to 5 years. Fellows will receive job placement assistance from the steering committee and the DCEG Office of Education and Training.

Potential fellows must have an accredited doctoral degree in a discipline related to cancer etiology or prevention research (e.g., epidemiology, statistics, human or molecular genetics, or the biomedical, public health or behavioral sciences). Candidates with a Ph.D. typically will have less than 3 years postdoctoral experience. Applicants must be U.S. citizens or resident aliens eligible for citizenship within 4 years. Interested applicants should contact the Office of Education and Training, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Executive Plaza South, Room 8057, 6120 Executive Blvd., MSC 7242, Bethesda, MD 20892-7242. ■

DR. ROBERT MILLER: SCIENTIST EMERITUS AND BENEFACTOR OF NIH

At the March 3 DCEG Town Meeting, Dr. Robert Miller was honored for his many contributions to the Division, the Institute, and the NIH, and was presented with a certificate in recognition of his status as Scientist Emeritus, a position he has held since 1994. Dr. Miller also was presented with a plaque honoring him as an "NIH Benefactor" in recognition of his and Mrs. Miller's sponsorship of the NIH Astute Clinician Lectureship.

Dr. Robert Miller with Dr. Richard Klausner

Dr. Miller joined NCI in 1961 as Chief of the Epidemiology Branch, from which the current Division has evolved. On his appointment as Branch Chief, Dr. Miller promised to pursue entirely new scientific ventures. True to his word, he launched studies in two main areas: the link between cancer and congenital abnormalities, and pediatric cancer epidemiology. With a career spanning several decades, Dr. Miller is recognized as an international leader in epidemiologic research.

Dr. Miller's many contributions include groundbreaking research on atomic bomb survivors in Japan, and on inhabitants of the Marshall Islands who were exposed to fallout from nuclear testing. He was one of the first western scientists to visit China in the late 1970's and Chornobyl in the late 1980's. Dr. Miller has been a superb mentor to many scientists, a number of whom are now in leadership positions at NCI and elsewhere.

New insights into carcinogenesis, teratogenesis, and cancer biology have resulted from Dr. Miller's wisdom in pursuing research into rare pediatric cancers and cancer-malformation syndromes. His uncanny ability to integrate clinical, epidemiologic, and experimental observations provided an early model for the now burgeoning fields of genetic and molecular epidemiology. Today, Dr. Miller continues to contribute actively to DCEG research efforts, especially those of the Genetic Epidemiology Branch and the Clinical Genetics Branch, and to write original articles and analytical reviews that are models of clarity, fluency, and penetrating scientific insight.

An autobiographical profile of Dr. Miller can be found in the *American Journal of Medical Genetics* (1998;76:9-20). The paper is introduced by a very nice summary of Dr. Miller's accomplishments (1998;76:1-8) prepared by Dr. John Mulvihill, who headed the clinical genetics group in the epidemiology program for many years. ■

DR. KLAUSNER SPEAKS AT DCEG TOWN MEETING

Dr. Richard Klausner, Director of NCI, addressed the DCEG Town Meeting on March 3. After the presentation of awards, he commended the Division for establishing this annual event to recognize individual achievements for service, science, and mentoring. Dr. Klausner said that DCEG's research is widely acknowledged to be at the forefront of molecular and genetic epidemiology and that it serves as a model for the entire NIH intramural program.

Noting that he was nearing the completion of his fifth year as NCI Director, Dr. Klausner reflected upon a number of new challenges facing the Institute today. He remarked that his recent testimony at appropriation hearings was favorably received by Congress, whose generosity toward the Institute has made possible a period of sustained growth over the past few years.

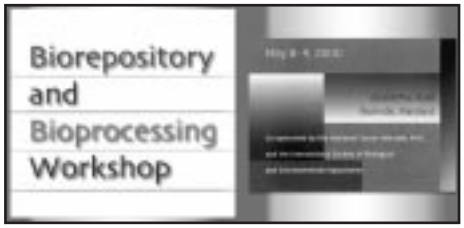
Dr. Klausner described a recent presentation to members of the Senate in which he summarized a 1944 report entitled "Science, the Endless Frontier." The report was commissioned by President Franklin D. Roosevelt to address the role of the Federal government in shaping the nation's nascent scientific research enterprise. Citing historical precedent, the report maintained that from its inception, the nation had always embraced the idea of exploration. It went on to suggest that this concept, once limited to physical and geographic boundaries, should be extended to the intellectual frontiers that were beckoning after the momentous victory achieved in World War II. The report argued that adequate support was essential for the success of the nation's research efforts and, rather than depend upon it from outside philanthropy, a firm commitment was required from the Federal government.

Dr. Klausner said that the report put forth a blueprint for the freedom of scientific inquiry by advocating a role for the government in providing research support to universities through grants and contracts. The report also recognized the central role of the government in providing a mechanism for meaningful peer review of scientific endeavors.

Dr. Klausner stressed that today, when Federal support for the National Cancer Program has never been greater, the Institute must ensure that it is living up to the responsibilities and the expectations of the American people. In particular, the issue of health disparities is still one of paramount concern. Dr. Klausner concluded by challenging the Division to use its expertise and creativity to develop new approaches to address this critical issue. ■

Catherine McClave

BIOREPOSITORY AND BIOPROCESSING WORKSHOP



On May 8 and 9, NCI and the International Society of Biological and Environmental Repositories (ISBER) cosponsored the Biorepository and Bioprocessing Workshop at the Rockville DoubleTree Hotel. A total of 275 attendees from 24 states and 8 foreign countries participated in the workshop, whose goals were to establish "best practices" for the creation and operation of NCI regional biorepositories; improve communication among biorepository personnel; set priorities for new studies of optimal specimen collection, processing, and storage conditions; disseminate information on the location of biorepositories and the availability of biologic and environmental specimens for research; and discuss and evaluate the latest regulatory guidelines for human specimen collection, shipping, and use for research.

Workshop speakers were from a variety of government agencies and commercial biospecimen management enterprises, including NCI, Centers for Disease Control and Prevention (CDC), National Bioethics Advisory Commission, RAND Corporation,


Dr. Montserrat Garcia-Closas

American Type Culture Collection (ATCC), International Agency for Research on Cancer, McKesson BioServices, Cryo Associates, and Gentra Systems. Drs. Jim Vaught, Richard Hayes, Montserrat Garcia-Closas, Mark Schiffman, and Neil Caporaso from DCEG were among the speakers. At the end of the workshop, a panel discussion expanded on the topics addressed by the speakers and proposed recommendations to improve and update NCI's approach to specimen management. The panel included the workshop session leaders as well as Drs. Ken Buetow and Regina Ziegler from DCEG and Dr. Christine Beiswanger from the Coriell Institute for Medical Research. The panel discussion focused on the issues of quality control in repository and laboratory settings, management of data exchange between repositories and high-throughput laboratories, and ethical issues related to specimen collection and subsequent use for research.


Drs. Richard Hayes, Mark Schiffman, and Neil Caporaso

The workshop included a commercial exhibit area, where vendors from 20 companies displayed products related to biological specimen processing and storage. Attendees were able to discuss their specimen processing and storage needs with representatives from the companies in more detail than is usually possible at larger scientific meetings.

ISBER, the workshop cosponsor, was formed in 1999 to provide a forum for discussing and sharing information concerning specimen processing and storage issues. The organization's initial membership came primarily from NCI, ATCC, National Institute of Standards and Technology, CDC, and local Washington-area biorepository companies. ISBER held its first general meeting and election of officers following the workshop on May 9. The first president of ISBER is Ms. Elaine Gunter of CDC, who has consulted with DCEG investigators for many years on projects involving specimen collection and biomarker assays. NCI's ISBER representatives are Dr. Vaught of DCEG and Dr. Roger Aamodt of the Division of Cancer Treatment and Diagnosis. Chosen as President-Elect at the ISBER meeting on May 9, Dr. Vaught will serve as President for 2001–2002. As the organization grows, it is expected that there will be valuable opportunities for exchange of information between ISBER and NIH scientists, repository managers, and contractors involved in biospecimen processing and storage.

DCEG's specimen collections at local contract biorepositories continue to grow at a rapid rate. During the past year, DCEG's total biorepository inventory has grown by over 800,000 specimens, or about 20 percent. This rate of growth is expected to continue for the foreseeable future as specimens from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial and other large ongoing or new studies continue to arrive at DCEG's biorepositories. From DCEG's perspective, many of the issues raised during the workshop should stimulate further discussion and research into methods and procedures that will result in more effective management of the growth of DCEG's contract biorepositories. Management of growth is especially critical at the Frederick Cancer Research and Development Center, where plans for expansion of the biorepositories and bioprocessing laboratories are expected to be implemented later this year or in 2001. ■

Jim Vaught


Dr. Jim Vaught

DCEG AWARDS

At the March 3 DCEG Town Meeting, Dr. Richard Klausner, Director of the NCI, presented awards to members of the Division.

DCEG Award for Exemplary Service

Dr. Robert Hoover, Director of the Epidemiology and Biostatistics Program, received the DCEG Award for Exemplary Service, which honors a scientist who combines sustained research accomplishments with outstanding service to the Division and to the Institute. He was honored for his critical role in developing scientific programs across all branches of the Division for nearly 30 years. The award cites his invaluable advice on scientific objectives, study design, interpretation of results, and presentation, and notes that these achievements were usually accomplished without any public credit. His selfless service in countless administrative capacities was also acknowledged, and he was credited with being a remarkable scientist and public servant, as well as a calming influence and generous mentor.

Dr. Robert Hoover with Dr. Richard Klausner

DCEG Outstanding Mentor Award

Dr. Jay Lubin won the 1999 DCEG Outstanding Mentor Award, which is given to a scientist deemed the most outstanding mentor by DCEG fellows. He was honored for his professionalism, patience, and manner of interacting with fellows as colleagues. An internationally renowned statistician, Dr. Lubin mentors with enthusiasm, teaches on an understandable level, and fosters independence and responsibility.

Dr. Jay Lubin with Dr. Richard Klausner

DCEG Award for the Outstanding Research Paper by a Fellow

Dr. Eric Engels received the 1999 Award for the Outstanding Research Paper by a Fellow, published during the past calendar year. Dr. Engels' winning paper, "Plasma HIV viral load in patients with hemophilia and late-stage HIV disease: A measure of current immune suppression," describes the implications of viral load measurements late in HIV disease, and shows how load predicts disease progression independent of CD4 cell counts. ■

Dr. Eric Engels with Dr. Richard Klausner

ASSESSING RADON EXPOSURE

Residential radon kit

A cruise through the aisles at the nearest Home Depot or any other home improvement center will turn up a rather common item: home radon testing kits.

Radon causes its mischief by emitting alpha particles. Skin usually provides a reasonable barrier to the effects of these alpha particles. But when radon is inhaled, this colorless, odorless, radioactive gas comes into close contact with susceptible lung epithelia, where the alpha particles cause the genetic damage that leads to lung cancer.

Although testing for radon is a routine part of home ownership today, it was not until the early 1980's that most people became concerned about this carcinogen in their homes. The need to consider the potential of high levels of radon in homes across the country came into clear view when a nuclear power plant worker in Pennsylvania set off radioactivity contamination detectors—not when he was leaving work, but when he was coming in to start his shift. A test of his brand new home revealed high radon levels, considered astonishing at the time. With the publicity surrounding this event, the average American became aware of the potential risks associated with radon in their homes.

Exposure to a gas is extremely difficult to quantify. For radon exposure, most researchers have focused their studies on uranium miners. Miners are usually chosen because within certain types of underground mines, they are faced with relatively high concentrations of radon gas that they breathe in deeply. In trying to assess the radon exposure these miners experience, researchers have faced the challenge of estimating risk based on work records and area measurements of radon or its decay products. However, work histories typically have been incomplete, if they exist at all, and radon measurements have been of limited use. In addition, most studies of miners have not accounted for other known risk factors for lung cancer, such as smoking and exposure to arsenic.

Jay Lubin, Ph.D.

Attempting to tease out the array of complexities surrounding radon exposure, Dr. Jay Lubin, a biostatistician in the Biostatistics Branch and principal investigator for a series of studies of miners in China, and Dr. Michael Alavanja, an epidemiologist in the Occupational Epidemiology Branch specializing in lung diseases, are taking a number of approaches to quantify the risk of lung cancer associated with different types of exposure to radon gas.

"I view the radon issue as the archetypal way epidemiology evolves," Dr. Lubin said. "First, you assess associations in an occupational setting where there are high levels of exposure, then try to use what you learn about the potential problem for the exposed population at large."

Because many of the exposures in miner studies have been misclassified, Dr. Lubin and his colleagues jumped at an opportunity to conduct a study of radon exposure and lung cancer in Chinese miners working for the Yunnan Tin Corporation in southern China. There were three important reasons for undertaking the China study: it was a very large cohort with a large number of lung cancer patients; it was conducted in a tin mine rather than a uranium mine, and workers tended to have very long duration of exposure and; unique to this cohort, there were a large number of workers who were exposed as children. The China study was the largest study of lung cancer cases ever conducted.

The study followed a cohort of 17,000 workers, 981 of whom had died of cancer. The researchers also conducted a case-control study of lead-210, which

is a long-lived decay product of radon that tends to deposit in bone. By measuring skeletal lead-210 *in vivo*, the researchers had a more accurate way of quantifying radon exposure.

The researchers found that exposure in childhood did not impart any added lung cancer burden in adulthood. In addition, they discovered that the risk of lung cancer as a result of exposure to radon was higher if radon exposure and tobacco use overlapped. The skeletal lead study showed that lead-210, as measured by a whole-body counter, only weakly correlated with radon exposure as calculated by work history. The air in underground mines is typically dust filled, which Dr. Lubin says may be somewhat protective because the alpha particles can attach to particles too big to be inhaled deeply into the lungs. However, the risk of lung cancer increased sharply with the measured lead-210 activity.

With the risks associated with radon exposure in the mine becoming clear, Dr. Lubin and his colleagues looked to the studies of radon exposure in the home to estimate directly the effects of indoor radon on the risk of lung cancer, and to compare those risks patterns found in miner studies.

"The question really is one of 'How do you extrapolate from the mine environment to the home?'" Dr. Lubin said. "When we looked at the exposures in the home over time, we found they weren't that much lower than the exposures among some miners. This means the amount of extrapolation between exposure in the mine and in homes is relatively small."

Dr. Lubin and his colleagues looked for a means to extrapolate the exposures from the miner studies and apply them to the home environment by recalculating radon exposure in several studies published in the literature. When they compared results from the miner studies with those from the residential studies, they found that they could estimate the risk for home exposure by using a model based on the miners.

Although the extrapolation model works well, Dr. Lubin acknowledges that the model is still far from perfect. Assessing home exposure has proven difficult. Radon levels in the home vary widely over time, as a function of weather, among other things. Simply taking a single measurement, even for an entire year, and multiplying that exposure by the number of years in the house leads to an imprecise estimate. In addition, few people live in the same home their entire lives, making a lifetime exposure estimate for most people next to impossible to obtain.

In an attempt to estimate risk more accurately, Dr. Lubin is involved with two separate efforts—one in North America and one in Europe—to pool data from several studies to determine risk related to home radon exposure. The North American study will pool data from nine indoor radon case-control studies of nearly 6,000 lung cancer cases in the United States and Canada. The European study will include 11 case-control studies of 10,000 lung cancer cases.

"The data pooling provides the large number of cases needed to get definitive results," Dr. Lubin said. "It's the best we can do. Even so, there is still a gap between exposure levels of the miners and that found in homes. But, we are completing the analysis on a study in China that may bridge that gap for us."

In the Gansu province in North Central China, there is a group of people whose homes are underground. The mean radon level found in their homes is four times higher than the mean radon level in the United States. Half of the houses had radon levels that exceeded the U.S. Environmental Protection Agency action level for remediation. As a reference, only 5 percent of U.S. residences exceed this level. Dr. Lubin, Radiation Epidemiology Branch member Ms. Ruth Kleinerman, and several Chinese investigators are collaborating on the case-control study, which they expect to be completed shortly.

Dr. Alavanja believes that Dr. Lubin's efforts to


Michael Alavanja, Dr.P.H.

extrapolate low-dose exposures are important. Dissatisfied with the current methods of estimating residential exposure, which assume that radon levels are constant, Dr. Alavanja latched onto a technology developed by physicists to measure radon. Called the surface monitor method, this technology detects long-lived radon decay products embedded in glass.

Radon gas, as it decays, has enough momentum to permanently imbed itself in glass in the form of lead-210, which has a half-life of 22 years. The lead is not visible to the eyes or to the touch, but it can be detected when it decays into polonium-210 and releases alpha particles. As a result, an unleaded piece of glass that has followed a person from move to move, like a mirror or a picture frame, can serve as a long-term retrospective exposure meter. In a study of women in Missouri, most of whom did not work outside the home, Dr. Alavanja was able to get a good estimate of cumulative radon exposure by examining pieces of glass they had had since they were married.

Dr. Alavanja chose women for this study because only 80 percent of lung cancer cases in women can be explained by a smoking habit, whereas in men, it is between 90 to 95 percent. With 20 percent of lung cancer cases unexplained, radon in the home may be an especially important factor for these women. The Missouri study included 372 cases of lung cancer and 471 controls. Dr. Alavanja and his colleagues used both standard radon gas detectors and the surface monitor method to estimate radon exposure. With the standard detectors, the risk of lung cancer did not increase with the increase in estimated radon concentration. However, the surface monitor method of estimating lifetime radon exposure showed a correlation between increased risk of lung cancer and increased exposure to radon.

The surface monitor method has been validated only in the laboratory. As a result, Dr. Alavanja is now conducting a validation study in homes in an area just outside Helsinki, Finland, where the rate of residential radon is very high. Because many of these homes have had standard radon measurements for a few years, Dr. Alavanja now has the opportunity to see if he can reproduce the radon exposure history using the surface detector method. He also plans to validate the method in Minnesota, where 40 homes have had full year radon measurements for the past 15 years.

Should the surface monitor method prove to more accurately estimate radon exposure, the research community may be able to come up with a more definitive assessment of the risk of residential exposure. With that risk assessment in hand, Dr. Alavanja can start to examine more detailed questions, such as how radon interacts with genetic material and whether there is a genetic predisposition to radon susceptibility. ■

Lisa Seachrist

A PROFILE: DR. MUSTAFA DOSEMECI

Mustafa Dosemeci, Ph.D.

When determining the risk of cancer associated with a particular exposure, the risk estimate is only as good as the accuracy of the estimate of exposure. Exposure assessment is limited by the nature of the exposure measurement, which is usually estimated retrospectively.

Dr. Mustafa Dosemeci, a recently tenured senior investigator in the Occupational Epidemiology Branch, has applied his background in chemistry and industrial hygiene to create exposure assessments for a variety of exposure situations. Dr. Dosemeci grapples with methodological issues that concern approaches for yielding the most accurate assessment of exposure.

"It's important to think about the best ways to ask questions to understand exposure assessment," Dr. Dosemeci said. "Because exposures for each discipline are different, the way you determine the exposure is different. The main purpose is to correctly assess the extent of an exposure."

After receiving an undergraduate degree in chemistry, Dr. Dosemeci earned a Ph.D. in occupational health from Hacettepe University in his native Turkey. He applied his training in exposure assessment to epidemiology while working as a visiting scientist at the T.U.C. Centenary Institute of Occupational Health at the London School of Hygiene and Tropical Medicine. Dr. Dosemeci joined NCI in 1986.

"I went to London to learn more about exposure assessment," Dr. Dosemeci said. "At NCI, there were opportunities to use my training in epidemiology and industrial hygiene to carry out studies bridging these two disciplines."

In developing appropriate methods for assessing exposure, Dr. Dosemeci has created job exposure matrices for more than 40 chemical and physical hazards. He has also developed methods for assessing exposure to benzene and other industrial chemicals, silica, diesel exhaust, and electromagnetic fields.

"Currently, one of my main interests is evaluating the impact of genetic factors on the biologically effective dose of environmental hazards," Dr. Dosemeci said. "Although people may have the same environmental exposure, our models for risk need to take into account genetic variability. I really like this interdisciplinary approach."

In an attempt to integrate environmental exposure with genetic information, Dr. Dosemeci and a number of his colleagues have initiated a case-control study of bladder cancer, the largest to date, in Spain. The study involves 1,500 cases and 1,500 controls from 20 hospitals. The researchers are conducting personal interviews using a computer-assisted technique to obtain information on occupational, environmental, clinical, and dietary risk factors. In addition, blood samples are being collected to examine genetic susceptibility markers. Dr. Dosemeci expects to begin analyzing the data in 2001.

Dr. Dosemeci also initiated an autopsy-based interdisciplinary, multisite, case-control study of lung cancer in Russia. He and his colleagues identified 500 lung cancer cases and 500 controls from 88 hospitals where autopsies are performed on almost 95 percent of the decedents. The researchers collected full work and residential histories, measurement data on more than 100 occupational and environmental hazards, and normal and tumor tissue samples to identify genetic susceptibility markers. Data from the study are currently under analysis.

In addition to conducting exposure assessments, Dr. Dosemeci chairs the DCEG Exposure Assessment Working Group, which facilitates the exchange of ideas and experiences about exposure-related issues for various risk factors. The group considers methods for assessing exposures related to diet, viruses, hormones, occupation, the general environment, radiation, and other areas. The group also organizes seminars and provides exposure databases to be used by other DCEG investigators. ■

Lisa Seachrist

HELICOBACTER PYLORI INFECTION AND INTERLEUKIN-1 POLYMORPHISMS


Emad El-Omar, M.D.

When a person is infected with *Helicobacter pylori*, three things can result: an ulcer, gastric cancer, or an asymptomatic, trouble-free infection. What is almost certain is that this person will develop inflammation somewhere in the stomach and that how that inflammation develops and progresses will determine the outcome of the infection. When the inflammation is confined to the antrum (bottom area), copious amounts of acid are produced, which can lead to a peptic ulcer. But when the inflammation occurs throughout the stomach, the infection can take hold in the corpus (middle area), where acid-producing cells reside. The stomach then makes the mistake of producing less acid.

"The primary purpose of the acid in the stomach is to sterilize the food we eat," said Dr. Emad El-Omar, a visiting scientist in the Viral Epidemiology Branch and Professor of Gastroenterology at the University of Aberdeen in Scotland. "If we don't have enough acid in our stomachs, bugs can colonize and start to produce toxins. That leads to more inflammation and more damage and finally the destruction of the acid-producing cells." The destruction of acid-producing cells, called gastric atrophy, is irreversible and leads to chronically low levels of stomach acid. As a result, the gastric mucosa faces continual assault from the cancer-causing toxins produced by bacteria it can no longer kill.

What tips the balance between developing an ulcer or stomach cancer remains a mystery. Interestingly, if an ulcer develops as a result of *H. pylori* infection, stomach cancer will not develop, and vice versa. Because the bacteria's characteristics do not appear to influence the development of either outcome, Dr. El-Omar decided to examine whether a genetic polymorphism known to enhance inflammation played a role in developing stomach cancer.

"I was interested in host genetic factors involved with making people susceptible to gastric cancer," said Dr. El-Omar, who clarified the link between *H. pylori* and gastric cancer.

What Dr. El-Omar and his colleagues found was a classic combination of environmental exposure and a genetic predisposition leading to cancer. The researchers discovered that two known genetic polymorphisms that are associated with overexpression of a cytokine that promotes inflammation, predispose a person infected with *H. pylori* to develop gastric cancer over a peptic ulcer. In particular, the researchers implicated the proinflammatory cytokine interleukin-1 (IL-1) and its receptor antagonist (*Nature* 2000;404:398-402).

Dr. El-Omar and his colleagues became interested in IL-1 because it is not only a potent stimulator of inflammation, but also a very powerful acid inhibitor. Polymorphisms that increase expression of the cytokine have been implicated in other inflammatory conditions, such as systemic lupus erythematous, psoriasis, and ischemic heart disease.

To determine whether two polymorphisms—one in the *IL-1b* gene and one in its receptor antagonist, the *IL-IRN* gene—played a role in developing gastric cancer over a peptic ulcer, the researchers studied a group of first-degree relatives of gastric cancer patients infected with *H. pylori* and a group of unselected newborns as population controls. The researchers also analyzed data from a case-control study in Warsaw, Poland, where there were 393 cases of gastric cancer and 430 controls with DNA samples. Overall, they found the polymorphisms to be associated with risk of low acid production, gastric atrophy, and gastric cancer.

"In any other system, increasing inflammation would work because it would help clear the infection," Dr. El-Omar said. "But, because IL-1 activity also decreases stomach acid production, it causes the unintended problem of allowing the infection to spread. The destruction of gastric acid-producing cells is really an inadvertent effect. Basically, you have these genes that are probably irrelevant unless you get this exposure."

Although these polymorphisms are implicated in the risk of gastric cancer, Dr. El-Omar says further research is needed to refine the genetics before implementing a screening approach. He notes that "we would end up testing far too many people." Even so, Dr. El-Omar says that people who have had a first-degree relative with stomach cancer should be tested for *H. pylori* infection. If the test is positive, treatment can be initiated before it causes too much damage.

Dr. El-Omar and his colleagues at DCEG are continuing to examine genetic factors associated with risk of gastric cancer. They plan to maintain their collaborations after Dr. El-Omar returns to the University of Aberdeen in July. ■

Lisa Seachrist

NURSES' ROLE IN CANCER GENETICS AND CLINICAL STUDIES

Mary Fraser, R.N., M.A.

Nurses in DCEG serve as the initial point of contact between potential participants in oncology clinical studies and both the Genetic Epidemiology Branch (GEB) and the Clinical Genetics Branch (CGB). For persons interested in participating in familial cancer research studies, the nurse must initially obtain information on the family and the number and types of cancers that have occurred. "Since one in three people eventually develops some form of cancer, most families have at least one or two members who have had cancer," said Ms. Mary Fraser, a Clinical Nurse Specialist in GEB. "For our studies, it's crucial to know about the primary cancer types, ages of diagnosis, whether any cancers developed in bilateral organs, and whether there are any family members with multiple primary cancers."

From this point, a clinical nurse specialist draws a pedigree of the extended family. Because some genetic traits skip a generation, the pedigree includes at least three generations, although something important can appear for only two generations. Then, at a joint meeting between the GEB and CGB, the nurse presents the information collected on the families. If a Branch decides to collect more information about a family, the research team requests pathology slides and reports to document the cancers.

When a Branch decides that a family fits the criteria for inclusion in a study, the research team invites the family to NIH for a clinical evaluation. The clinical nurse specialist is usually the first member of the research team to contact the family to explain the study, describe and send informed consent documents, answer questions, and schedule clinic times. When the family members arrive at NIH, they sign the informed consent documents, undergo a clinical evaluation, and have blood drawn and other biological specimens collected.

"It's the nurse's responsibility to make sure the family understands the aims of the study and that participation is entirely voluntary. Family members need to understand that they may choose not to participate in any aspect of the study," said Ms. Fraser. The nurse also urges family members to seek routine medical care in their home communities, as the clinical evaluations in the research protocols should not serve as substitutes for comprehensive cancer screening.

But the clinical nurse wears many other hats, including those of advocate, educator, and source of psychosocial support for participants. For example, Ms. Fraser and her coworkers have educated families that are predisposed to melanoma about how to avoid sunburns and administer monthly skin self-examinations for precursor lesions and risk markers. The nurses' extensive educational efforts have led to the increased likelihood of prevention or, if a melanoma develops, early detection. "It's . . . gratifying when you can give specific information that can help a person lower their cancer risk or detect a cancer early," said Ms. Fraser.

Much of the work done by Ms. Fraser and other nurses involved in clinical cancer research is fast

becoming applicable to oncology nurses (Wujcik D, Fraser MC. The National Cancer Program. *Semin Oncol Nurs* 2000;16:65-75). In the past 10 years, approximately 20 inherited cancer susceptibility genes have been identified. As a result, many oncology nurses are enrolled in educational programs so they can play greater roles in conducting family risk assessments, implementing comprehensive cancer risk management plans, and providing genetic education. The challenge for both clinical and oncology nurses is to keep up both with the influx of new genetic information and with the ever-increasing sophistication of patients. "We often get a flurry of inquiries and referrals when results of cancer genetics research make the headlines," said Ms. Fraser.

Because much of the information from genetic evaluations is for research and requires extensive analysis and interpretation, it may not have relevance to clinical care. Ms. Fraser noted that for some of the cancers being studied, such as melanoma, the results of genetic testing for alterations in melanoma susceptibility genes are not yet clear enough to make it a valuable clinical tool. For others, such as for retinoblastoma and *BRCA-1/2*-related breast cancer, the information could be valuable to both the families and clinicians. GEB and CGB are now developing protocols to offer genetic testing and risk notification when the results may benefit the study participants' clinical care.

As genetic predisposition testing continues to move rapidly from the research arena to the clinic, clinical and oncology nurses will increasingly find themselves involved in obtaining family histories, drawing pedigrees, and working with families rather than individuals in order to manage familial cancer. In addition, they can expect to be faced with a number of continuing challenges related to complex psychosocial, legal, and ethical issues surrounding predisposition testing.

Ms. Fraser notes that the Branches are indebted to the families that participate in the studies. "Without the families," she says, "we couldn't do the research that allows us to make more progress in understanding the mechanisms and management of hereditary cancer." ■

Lisa Seachrist

DR. THOMAS O'BRIEN'S SLANT ON HIV

Thomas O'Brien, M.D.

Research on the complex interplay between host genetic factors and susceptibility to viral infection is the main focus of Dr. Thomas O'Brien, a recently tenured senior investigator in the Viral Epidemiology Branch. He feels fortunate to be able to carry out this work at NCI.

"I think the environment and research resources here are optimal for doing cutting-edge work," Dr. O'Brien said. "And I have been lucky to work with very good people both inside and outside of DCEG. Resources, such as well-established cohorts of HIV-infected persons, have let me explore interesting questions."

Dr. O'Brien received undergraduate and medical degrees from the University of Michigan, and an M.P.H. from the Harvard School of Public Health. He joined NCI in 1992, after 7 years at the Centers for Disease Control and Prevention, where he initially studied Agent Orange exposure in Vietnam veterans. In 1988, at the height of the AIDS epidemic, he started studying the epidemiology of HIV-1 and conducting surveillance of HIV-2. In 1996, Dr. O'Brien used a newly available, highly sensitive, quantitative test for HIV-1 RNA to show that the early measurement of this nucleic acid level could predict long-term risk of AIDS among HIV-infected hemophiliacs. A follow-up study found that measurement of HIV RNA levels over time were even more predictive of outcome.

"Since our work and that of other groups showed that the virus can be present at high levels very early in the course of infection, it forms the basis for trying to knock down viral replication as soon as possible," Dr. O'Brien said.

The work helped lay the foundation for using HIV-1 RNA assays to monitor a patient's response to

highly active antiretroviral therapy (HAART). Dr. O'Brien credits the dramatic decrease in HIV-related deaths in the United States to the development of HAART at the same time diagnostic labs devised viral RNA assays. "Either one by itself wouldn't have been nearly as helpful," he said.

Dr. O'Brien became particularly interested in the interplay of host genetic factors and viral infection when he and his colleagues discovered an HIV-positive hemophiliac whose HIV receptor gene carried mutations thought to protect against infection.

The major coreceptor required for HIV infection of T-cells is CC-chemokine receptor 5 (CCR5). In 1996, researchers discovered a 32-base pair deletion ($\Delta 32$) in the *CCR5* gene that made the gene nonfunctional. A study of people who failed to become infected with HIV, despite multiple exposures to the virus, found that they were homozygous for *CCR*Δ*532*.

Dr. O'Brien led a team evaluating an HIV-infected hemophiliac who was homozygous for *CCR*Δ*532*. They found that this individual was infected with an HIV strain that invaded T-cells through the CX-chemokine receptor 4 (CXCR4).

"Although being homozygous for *CCR*Δ*532* provides very strong protection against HIV infection, it is not absolute protection," Dr. O'Brien said. In fact, having no CCR5 receptor may actually abet infection by more virulent HIV strains. Strains of HIV capable of entering T-cells via the CXCR4 receptor are typically more specific, more pathogenic, and syncytium-inducing strains that emerge in late-stage infection. Dr. O'Brien thinks that drug developers need to consider this issue in designing therapies to block the CCR5 receptor.

Because people who were homozygous for *CCR*Δ*32* appeared to be healthy, Dr. O'Brien, along with Howard Hughes-NIH Research Scholar Dr. Giang Nguyêñ, studied 15 people who were homozygous for *CCR*Δ*532* but were not infected with HIV. They found that compared with people carrying wild-type copies of *CCR5*, people homozygous for *CCR*Δ*532* exhibited a higher prevalence of hypertension, higher lymphocyte counts, and higher enzyme levels in those people infected with hepatitis C virus.

One of the curiosities of AIDS is that homosexual men often develop Kaposi's sarcoma, while it occurs rarely in other individuals infected with HIV. Dr. O'Brien and his colleagues documented that an epidemic of human herpesvirus-8 (HHV-8) occurred at the same time as the HIV epidemic. In addition, they found that men who were coinfected with HHV-8 and HIV-1 were at highest risk of Kaposi's sarcoma, thus linking HHV-8 etiologically to the sarcoma. This study provided evidence that the epidemic of Kaposi's sarcoma among U.S. homosexual men in the early 1980's was due to the dual epidemics of HIV-1 and HHV-8.

Together with collaborators at the University of California at San Francisco, Dr. O'Brien is also investigating host genetic factors that protect against infection by hepatitis B virus and hepatitis C virus. The researchers are studying a group of injection drug users who remain free from infection by these viruses, despite their high-risk behavior. Chemokine receptors and HLA genes initially will be examined, and later genome-scanning techniques will be used to identify other target genes. Because hepatitis B and C infections are associated with hepatocellular carcinoma, Dr. O'Brien hopes the results of this investigation will offer new insights into the etiology of this cancer. ■

Lisa Seachrist

RECENT SCIENTIFIC HIGHLIGHTS

Biostatistics Branch

Two-stage Case-control Study with Cluster Sampling of Controls

A pseudolikelihood approach is presented for analysis of a two-stage, population-based case-control study with cluster sampling of controls. The methods were developed to analyze data from a nonmelanoma skin cancer study that evaluated the role of ultraviolet radiation while adjusting for age group and other risk-related factors known only for participants in the case-control study. The methods yielded estimates of relative and absolute risk, with standard errors and naturally accounted for the two-stage sampling of the cohort and cluster sampling of controls. (Fears TR, Gail MH. Analysis of a two-stage case-control study with cluster sampling of controls: Application to nonmelanoma skin cancer. *Biometrics* 2000;56:190-198)

Prostate-specific Antigen Testing and Prostate Cancer Mortality

An analysis of U.S. prostate cancer mortality rates in white men less than 85 years of age found a decline in levels lower than those existing in 1986, the year in which prostate specific antigen testing was approved as a diagnostic tool. For men 60 to 79 years of age, mortality rates were lower in 1997 than in any year since 1950. Stage-specific survival rates suggest that a rapid decrease in mortality may be explained by the large number of high-grade prostate cancers detected before metastasis. (Tarone RE, Chu KC, Brawley OW. Implications of stage-specific survival rates in assessing recent declines in prostate cancer mortality rates. *Epidemiology* 2000;11:167-170)

Crohn's Disease and Risk of Cancer

A record-linkage study of cancer incidence among patients in Denmark with Crohn's disease detected no increased risk for colorectal cancer, whereas an 18-fold excess was observed for cancer of the small intestine (3 adenocarcinomas and 2 carcinoids). (Mellemkjaer L, Johansen C, Gridley G, Linet MS, Kjaer SK, Olsen JH. Crohn's disease and cancer risk (Denmark). *Cancer Causes Control* 2000;11:145-150)

Inhaled Arsenic Exposure and Mortality

A study of copper smelter workers, who were followed for up to 50 years, found a significantly increased standardized mortality ratio (SMR) for all causes (SMR=1.14), all cancers (SMR=1.13), respiratory cancer (SMR=1.55), diseases of the nervous system and sense organs (SMR=1.31), nonmalignant respiratory diseases (SMR=1.56), and emphysema (SMR=1.73). Further analyses revealed a significant, linear increase in the excess relative risk of respiratory cancer with increasing exposure to inhaled airborne arsenic. Other causes of death were not related to inhaled arsenic exposure. (Lubin JH, Pottern LM, Stone BJ, Fraumeni JF. Respiratory cancer in a cohort of copper smelter workers: Results from more than 50 years of follow-up. *Am J Epidemiol* 2000;151:554-565)

Shipyard Counties and Lung Cancer Mortality

An analysis updating lung cancer mortality through 1994 found rates generally higher in counties that had World War II shipyards, which were associated with substantial exposure to asbestos, than in all U.S. counties without shipyards and in coastal counties without shipyards. Rates increased markedly from 1950–1969 to 1970–1994, with the changes more pronounced in females than males. Pleural mesothelioma mortality rates among males were also significantly higher in shipyard counties than coastal counties without shipyards. (Jemal A, Grauman D, Devesa S. Recent geographic patterns of lung cancer and mesothelioma mortality rates in 49 shipyard counties in the United States, 1970-94. *Am J Ind Med* 2000;37:512-521)

The Burden of Cancer in the Elderly

In 1990, 63 percent of all new cancers in the United

States occurred in the population aged 65 years and older. As more people live longer, the absolute burden of cancer in this age group will increase. This chapter examines time trends in mortality and incidence rates for specific cancer types that are prevalent in the elderly. It also displays trends in the risk factors that influence rates, such as obesity, smoking, and screening practices. (Devesa SS, Hunter CP. The burden of cancer in the elderly. In: Hunter CP, Johnson KA, Muss HB, eds. *Cancer Among the Elderly.* New York: Marcel Dekker, 2000, pp. 1-24) ■

Environmental Epidemiology Branch

Cervical Lesions and Human Papillomavirus DNA Testing

This study investigated whether testing women with low-grade squamous intraepithelial lesions (LSIL) of the uterine cervix for human papillomavirus (HPV) DNA is useful as a triage strategy. Overall, cancer-associated types of HPV DNA were detected in cervical samples from 532 (83 percent) of 642 women. Because a very high percentage of women with an LSIL diagnosis from Pap smears are positive for cancer-associated types of HPV DNA, there is limited potential for this assay to direct decisions about the clinical management of women with LSIL. (Koutsky LA. The Atypical Squamous Cells of Undetermined Significance / Low-Grade Squamous Intraepithelial Lesions Triage Study (ALTS) Group. Human papillomavirus testing for triage of women with cytologic evidence of low-grade squamous intraepithelial lesions: Baseline data from a randomized trial. *J Natl Cancer Inst* 2000;92:397-402)

Human Papillomavirus Type and Cervical Disease

A study of the prevalence of type-specific human papillomavirus (HPV) infection in relation to cervical disease in a high-risk population found that infections among women with normal cytology peaked at ages younger than 25 years and again at 55 years and older. Seventy-three percent of low-grade squamous intraepithelial lesions (LSIL), which decreased with age, were HPV positive. The prevalence of high-grade squamous intraepithelial lesions (HSIL) peaked around age 30 years and again at age 65 years and older. The majority of HSIL (89 percent) and cancers (88 percent) were HPV positive. HPV16 was predominant in LSIL, HSIL, and cancers. (Herrero R, Hildesheim A, Bratti C, Sherman ME, Hutchinson M, Morales J, Balmaceda I, Greenberg MD, Alfaro M, Burk RD, Wacholder S, Plummer M, Schiffman M. Population-based study of human papillomavirus infection and cervical neoplasia in rural Costa Rica. *J Natl Cancer Inst* 2000;92:464-474)

Characteristics of Women with Breast Implants

A study comparing the characteristics of women with breast implants with women who received other types of plastic surgery did not find differences with respect to family income, number of pregnancies, alcohol consumption, cigarette smoking, or histories of previous gynecologic surgeries or operations for benign breast disease. However, implant patients were significantly more likely to be white, have low educational levels, have early ages at first birth, be thin, and be screened frequently for breast disease. Implant patients also reported greater use of exogenous hormones and familial histories of rheumatoid arthritis. (Brinton LA, Brown SL, Colton T, Burich MC, Lubin J. Characteristics of a population of women with breast implants compared with women seeking other types of plastic surgery. *Plast Reconstr Surg* 2000;105:919-927) ■

Genetic Epidemiology Branch

Mosaicism in von Hippel-Lindau Disease

Two individuals with clinical von Hippel-Lindau (VHL) disease were negative for the VHL mutation by standard testing methods. However, the mutation was detected in a portion of their lymphocytes with the use of more stringent methods. Each person had an offspring with VHL disease and a germline mutation in the VHL tumor-suppressor gene. These findings have clinical screening and counseling implications for families with a member who is potentially mosaic for VHL disease. (Sgambati MT, Stolle Cm, Choyke PL, Walther MM, Zbar B, Linehan WM, Glenn GM. Mosaicism in von Hippel-Lindau disease: Lessons from kindreds with germline mutations identified

in offspring with mosaic parents. *Am J Hum Genet* 2000;66:84-91)

Laboratory of Population Genetics

BRCA Mutations in Male Breast Cancer Patients

Pathological tissue from men in Israel with breast cancer was screened for three founder mutations in the *BRCA1* and *BRCA2* genes. None of the 14 Arab patients carried the mutations. Of the 110 Jewish patients, none had the *BRCA1* 5382insC mutation, although 4 carried the 185delAG mutation in the gene. The 6174delT mutation in the *BRCA2* gene was detected in 15 patients. These results suggest that at least 17 percent of Jewish males diagnosed with breast cancer in Israel carry a founder mutation in the *BRCA1* or *BRCA2* gene. (Struewing JP, Coriaty ZM, Ron E, Livoff A, Konichezky M, Cohen P, Resnick MB, Lifzchiz-Mercerl B, Lew S, Iscovich J. Founder *BRCA1/2* mutations among male patients with breast cancer in Israel. *Am J Hum Genet* 1999;65:1800-1802) ■

Nutritional Epidemiology Branch

Dietary Intervention and Recurrence of Colorectal Adenomas

A dietary intervention study found that adopting a diet low in fat and high in fiber, fruits, and vegetables does not influence the risk of recurrence of colorectal adenomas. A similar percentage of subjects in the intervention and control groups had at least one recurrent adenoma. Among subjects with such lesions, the mean number of adenomas did not differ significantly between the two groups. Similar also were their rates of recurrence of large adenomas and advanced adenomas. (Schatzkin A, Lanza E, Corle D, Lance P, Iber F, Caan B, Shike M, Weissfeld J, Burt R, Cooper MR, Kikendall JW, Cahill J. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group. *N Engl J Med* 2000;342:1149-1162)

Dietary Quality and Mortality among Women

A prospective cohort study of breast cancer examined the association of mortality from all causes with overall dietary quality. With the use of a multifactorial index accounting for foods recommended by current dietary guidelines (i.e., fruits, vegetables, whole grains, low-fat dairy, and lean meats and poultry), it was found that women in the highest intake level of recommended foods had a 30 percent lower risk of multivariate-adjusted all-cause mortality, compared with those in the lowest level. These findings suggest that a dietary pattern characterized by consumption of foods recommended in current dietary guidelines is associated with decreased risk of mortality in women. (Kant AK, Schatzkin A, Graubard BI, Schairer C. A prospective study of diet quality and mortality in women. *J Am Med Assoc* 2000;283:2109-2115)

Measuring Urinary Estrogen Metabolites by Enzyme-Linked Immunosorbent Assay

An evaluation of a new, sensitive enzyme-linked immunosorbent assay (ELISA) kit to measure levels of urinary estrogen metabolites from premenopausal and postmenopausal women found the assay to have good reproducibility for 2-hydroxyestrone and 16 alpha-hydroxyestrone. For the latter metabolite, however, batch-to-batch variability was not negligible. An excellent correlation was obtained for measurements made by ELISA and gas chromatography-mass spectroscopy for the ratio of metabolites. (Falk RT, Rossi SC, Fears TR, Sepkovic DW, Migella A, Adlercreutz H, Donaldson J, Bradlow HL, Ziegler RG. A new ELISA kit for measuring urinary 2-hydroxyestrone, 16 alpha-hydroxyestrone, and their ratio: Reproducibility, validity, and assay performance after freeze-thaw cycling and preservation by boric acid. *Cancer Epidemiol Biomarkers Prev* 2000;9:81-87) ■

Occupational Epidemiology Branch

Serum DDE and Polychlorinate Biphenyl and Non-Hodgkin's Lymphoma

A comparison of 1,1-dichloro-2,2-bis (O-chloro-phenyl) ethylene (DDE) and polychlorinate biphenyl serum levels among non-Hodgkin's lymphoma patients before and after chemotherapy found pretreatment and posttreatment concentrations to be highly correlated. Levels of the organochlorine

compounds were significantly lower between initiation and completion of chemotherapy, decreasing between 25 and 29 percent. The results were not affected by adjustment for weight, age, histologic type, or change in lipid concentrations. (Baris D, Kwak LW, Rothman N, Wilson W, Manns A, Tarone RE, Hartge P. Blood levels of organochlorines before and after chemotherapy among non-Hodgkin's lymphoma patients. *Cancer Epidemiol Biomarkers Prev* 2000;9:193-197)

Butadiene Genotoxicity among Exposed Workers

An examination of genotoxic outcomes associated with butadiene, a carcinogen in laboratory rodents, found that exposed workers in China had higher levels of hemoglobin *N*-(2,3,4-trihydroxybutyl) valine (THBVal) adducts and greater lymphocyte and platelet counts than unexposed workers had. Among exposed workers, neither the *GSTT1* nor the *GSTM1* genetic polymorphism of glutathione S-transferase predicted urinary mercapturic acid butanediol formation, THBVal adducts, uninduced sister chromatid exchanges, aneuploidy, or mutations in the *glycophorin A* or *hprt* genes. (Hayes RB, Zhang L, Yin S, Swenberg JA, Xi L, Wiencke J, Bechtold WE, Yao M, Rothman N, Haas R, O'Neill JP, Zhang D, Wiemels J, Dosemeci M, Li G, Smith MT. Genotoxic markers among butadiene polymer workers in China. *Carcinogenesis* 2000;21:55-62)

Gastroesophageal Reflux Disease and Cancer Risk

Using data from a large, population-based case-control study, an analysis was carried out to evaluate whether gastroesophageal reflux disease or treatment-related medications are associated with the risk of esophageal or gastric cancer. Excess risk of non-cardia gastric adenocarcinoma was associated with a history of gastric ulcer. Risk of esophageal adenocarcinoma increased with frequency of gastroesophageal reflux disease symptoms. Risk was not related to ever having used H-2 blockers, though nonsignificant increases were observed in users of 4 years or more. (Farrow DC, Vaughan TL, Sweeney C, Gammon MD, Chow WH, Risch HA, Stanford JL, Hansten PD, Mayne ST, Schoenberg JB, Rotterdam H, Ahsan H, West AB, Dubrow R, Fraumeni JF, Blot WJ. Gastroesophageal reflux disease, use of H-2 receptor antagonists, and risk of esophageal and gastric cancer. *Cancer Causes Control* 2000;11:231-238)

N-acetyltransferase 2 Genotype and Risk of Bladder Cancer

A meta-analysis of case-control studies examining the relation between the gene encoding *N*-acetyltransferase 2 and bladder cancer found a 40 percent increased risk among slow acetylators compared with rapid acetylators. An analysis by geographic region revealed that studies conducted in Asia generated a summary odds ratio of 2.1, in Europe of 1.4, and in the United States of 0.9. (Marcus PM, Vineis P, Rothman. NAT2 slow acetylation and bladder cancer risk: A meta-analysis of 22 case-control studies conducted in the general population. *Pharmacogenetics* 2000;10:115-122)

Sexual Behavior and Risk of Prostate Cancer

A population-based case-control study of prostate cancer found an elevated risk associated with a history of gonorrhea or syphilis and with serological evidence of syphilis. Risk increased with increasing occurrences of gonorrhea among subjects with three or more events. Patterns of risk for gonorrhea and syphilis were similar for black men and white men. (Hayes RB, Pottern LM, Strickler H, Rabkin C, Pope V, Swanson GM, Greenberg RS, Schoenberg JB, Liff J, Schwartz AG, Hoover RN, Fraumeni JF. Sexual behaviour, STDs and risks for prostate cancer. *Br J Cancer* 2000;82:718-725) ■

Radiation Epidemiology Branch

Mortality among Catholic Nuns Certified as Radiologic Technologists

Within a large cohort of certified radiologic

technologists, Catholic nuns had an almost 3-fold greater risk of tuberculosis and a 20 percent excess of breast cancer compared with other U.S. females. However, compared with other female technologists, nuns were at significantly increased risk of dying from all causes, stomach cancer, diabetes, ischemic heart disease, all digestive diseases, and gastric and duodenal ulcers. Nuns also had a significant deficit of lung cancer, no deaths from cervical cancer, and a breast cancer risk 10 percent lower than expected for technicians. (Doody MM, Mandel JS, Linet MS, Ron E, Lubin JH, Boice JD, Fraumeni JF. Mortality among Catholic nuns certified as radiologic technologists. *Am J Ind Med* 2000;37:339-348)

Electromagnetic Fields Studies and Risk of Acute Lymphocytic Leukemia

A large-scale, case-control study of childhood acute lymphocytic leukemia (ALL), carried out in collaboration with the Children's Cancer Group, found no association between risk of disease and distance from transmission lines or with an exposure index accounting for contributions of nearby power lines. (Kleinerman RA, Kaune WT, Hatch EE, Wacholder S, Linet MS, Robison LL, Niwa S, Tarone RE. Are children living near high-voltage power lines at increased risk of acute lymphoblastic leukemia? *Am J Epidemiol* 2000;151:512-515) When "partial participants," who allowed only measurements outside the door and who tended to be of lower socioeconomic status (LSES), were excluded from an analysis of electric power line wire codes and direct in-house measurements of magnetic fields, the odds ratio for ALL among subjects living in homes with very high current configurations increased between 11 and 23 percent, suggesting a possible selection bias associated with LSES in epidemiologic studies of magnetic fields. (Hatch EE, Kleinerman RA, Linet MS, Tarone RE, Kaune WT, Auvinen A, Baris D, Robison LL, Wacholder S. Do confounding or selection factors of residential wiring codes and magnetic fields distort findings of electromagnetic fields studies? *Epidemiology* 2000;11:189-198) ■

Viral Epidemiology Branch

Human Papillomavirus and Risk of Prostate Cancer

Using serum samples obtained at enrollment 12 to 32 years (average 12 years) earlier in a health plan, a case-control study of prostate cancer found no significant excess risk related to the prevalence of antibodies to human papillomavirus type 16 (HPV-16) in either white or African American men. After adjusting for age at serum sampling and race, HPV 16 antibody positivity was associated with a slightly increased risk. (Hisada M, Rabkin CS, Strickler HD, Wright WE, Christianson RE, van den Berg BJ. Human papillomavirus antibody and risk of prostate cancer. *J Am Med Assoc* 2000;283:340-341)

HIV and Hepatitis C Virus Load and Sexual Transmission

A study of HIV and hepatitis C virus loads in men with hemophilia and the risk of viral transmission to their female partners found higher loads of both viruses associated with increased transmission risk. The hepatitis C virus load was higher among dually infected men than in those infected with this virus alone. (Hisada M, O'Brien TR, Rosenberg PS, Goedert JJ. Virus load and risk of heterosexual transmission of human immunodeficiency virus and hepatitis C virus by men with hemophilia. *J Infect Dis* 2000;181: 1475-1478)

Sexual Transmission of Hepatitis G Virus

A study of sexual transmission of hepatitis G virus (HGV) in female sexual partners of men with hemophilia (n=161 couples) found an infection prevalence of 48 percent among men and 21 percent among women. Among men, infection prevalence was 99 percent for hepatitis C virus, 94 percent for hepatitis B virus, and 86 percent for HIV. Among women, these rates were 3 percent, 11 percent, and 12 percent. An adjusted odds ratio for HGV infection for women with an HGV-positive male sexual partner was 2.77. (Yeo AET, Matsumoto A, Shih JW, Alter HJ, Goedert JJ. Prevalence of hepatitis G virus in patients

PEOPLE IN THE NEWS

In April, **Dr. Michael Alavanja,** a member of the Occupational Epidemiology Branch, received the Blue Cross/Blue Shield Distinguished Federal Employees Award for his outstanding educational, civic, religious, and humanitarian contributions to the community. Dr. Alavanja has volunteered as the Friday night coordinator for a soup kitchen in Frederick for the past 11 years, served on several advisory committees for the Superintendent of Education in Frederick County, and participated on a civic association board. In addition, he has taught religious education classes for more than a decade.

At this year's George Washington University's commencement celebration, **Alina Brenner**, a member of DCEG's Radiation Epidemiology Branch, received the Excellence in Special Projects Award for Epidemiology and Biostatistics. Her project involved an evaluation of lung cancer and previous lung disease. Jay Lubin, Biostatistics Branch, was her NCI Advisor.

Capt. Rochelle Curtis, a member of the Radiation Epidemiology Branch, has been awarded the PHS Commission Corps Meritorious Service Medal. The award recognized her efforts in bringing to fruition a series of landmark studies of cancer risk following bone marrow transplantation.

Dr. Mustafa Dosemeci, a member of the Occupational Epidemiology Branch, has been awarded tenure in the NIH intramural research program. Dr. Dosemeci received a Ph.D. in occupational health from Hacettepe University in Ankara, Turkey, where his research focused on industrial hygiene practices and occupational cancer epidemiology. Afterwards, he did postdoctoral research at the London School of Hygiene and Tropical Medicine. In 1986, Dr. Dosemeci joined NCI as an industrial hygienist, specializing in assessing historical exposures in the workplace and evaluating exposure-response relationships. (See page 10).

Dr. Joseph Fraumeni, Director of DCEG, has been awarded the 2000 DHHS Secretary's Award for Distinguished Service. The award recognizes Dr. Fraumeni for his leadership in creating an exceptionally productive national program of population-based studies to identify environmental and genetic determinants of cancer. The Secretary's award is given to persons who demonstrate teamwork and partnerships that significantly advance the Department's mission.

Dr. Thomas O'Brien, a member of the Viral Epidemiology Branch, has been awarded tenure in the NIH intramural research program. Dr. O'Brien received undergraduate and medical degrees from the University of Michigan, and an M.P.H. from the Harvard School of Public Health. He joined NCI in 1992, after 7 years at the Centers for Disease Control and Prevention. Since joining NCI, Dr. O'Brien has focused on understanding the interaction between host genetic factors and susceptibility to infection by viruses, including HIV, human herpesvirus 8, and hepatitis B and C viruses. (See page 13).

Dr. Alice Sigurdson, a member of the Radiation Epidemiology Branch, will participate in the newly formed Tenure-Track Investigation Committee.

Dr. Rashmi Sinha, a member of the Nutritional Epidemiology Branch, received an NCI Technology Transfer Award for her work on developing methods for assessing exposure to heterocyclic amines by using questionnaires and biomarkers.

Dr. Joni Rutter, a member of the Laboratory of Population Genetics, and **Dr. Elizabeth Dawn McNeil,** a member of the Genetic Epidemiology Branch, have been selected as representatives to the NIH Postdoctoral/Clinical Fellows Committee. The Committee works to foster communication among fellows and to enhance the intramural training program through a series of programs designed for fellows.

Dr. Wendy Wang will give up her position on the Committee as she moves from the Laboratory of Population Genetics to a position in the Division of Cancer Prevention.

BOOK ANNOUNCEMENTS

Infectious Causes of Cancer

Recent scientific advances, particularly in molecular biology, have produced fresh insights into the role of infectious agents in the etiology of cancer. In *Infectious Causes of Cancer: Targets for Intervention*, **Dr. James Goedert,** Chief of the Viral Epidemiology Branch, and other leading experimental and clinical researchers provide a critical survey of the viruses, bacteria, and parasites known to contribute to the risk of cancer. The authors focus on human infection by herpes viruses, retroviruses, papillomaviruses, hepatitis viruses, and *Helicobacter pylori*, and the malignancies associated with these biological agents. The book also addresses new diagnostic technologies and the promise of targeted therapeutics and vaccines in the prevention and treatment of cancer. (Goedert, J, ed. *Infectious Causes of Cancer: Targets for Intervention.* New Jersey: Humana Press, 2000)

Women and Health

This book on women's health is targeted to members of the medical and scientific community, as well as to health care consumers. It synthesizes the latest research on the full range of conditions and diseases that affect women. The book contains 100 chapters grouped into 14 sections. The section devoted to cancer is edited by **Dr. Louise Brinton,** Chief of the Environmental Epidemiology Branch. The chapter "Cancers in Women" was written by **Dr. Susan Devesa,** Chief of the Descriptive Studies Section in the Biostatistics Branch. **Dr. Shelia Zahm,** Deputy Director of DCEG, was editor of the section on occupational health. She also wrote the chapter on occupational cancer with **Dr. Debra Silverman** and **Dr. Mary Ward** of the Occupational Epidemiology Branch. **Dr. Rebecca Troisi,** a member of the Environmental Epidemiology Branch, and **Dr. Patricia Hartge,** Deputy Director of the Epidemiology and Biostatistics Program, contributed to the chapter "Ovarian Cancer." The chapter "Cervical Cancer Screening" was written by Dr. Diane Solomon, a member of the NCI Division of Cancer Prevention, with **Dr. Mark Schiffman,** Chief of the Interdisciplinary Studies Section in the Environmental Epidemiology Branch. Other sections of the book include reproductive health, sexually transmitted diseases, international women's health, occupational health, environmental exposures, cardiovascular disease, mental disorders, and aging. (Goldman MB, Hatch MC, eds. *Women and Health.* San Diego, CA: Academic Press, 1999)

Environmental Engineering and Health Sciences

This book contains 42 papers presented at an international symposium for the interdisciplinary exchange of views on environmental engineering and health sciences, which was held in October 1998 in Mexico. The papers are grouped into four sections: fundamentals of environmental engineering and health sciences, exposure assessment, risk assessment, and environmental engineering applications. **Dr. Mary Ward,** a member of the Occupational Epidemiology Branch, served as an editor of the book. (Raynal JA, Nuckols JR, Reyes R, Ward eds. *Proceedings of the International Symposium on Environmental Engineering and Health Sciences: A Joint Effort for the XXI Century*. Englewood, CO: Water Resources Publications, LLC, 2000) ■

WORKSHOP REPORT: PHAKOMATOSES REVISITED

DCEG and the NIH Office of Rare Diseases sponsored a workshop, which was held in Rockville in March, 1999, on phakomatoses. Motivation for the workshop came from the cloning of the genes for 10 dominantly inherited disorders that are classified as phakomatoses. These are congenital and hereditary developmental anomalies having in common selective involvement of the tissues of ectodermal origin and development of disseminated glial harmartomas in the tissues. The phakomatosis genes constitute about one third of the hereditary cancer genes that have been cloned thus far. The workshop report was recently published in the *Journal of the National Cancer Institute* (Tucker M, Goldstein A, Dean M, Knudson A. 2000;92:530-533)

The phakomatosis disorders for which genes have been cloned are neurofibromatoses 1 and 2, tuberous scleroses 1 and 2, von Hippel–Lindau disease, nevoid basal cell carcinoma syndrome, Cowden disease, Peutz–Jeghers syndrome, juvenile polyposis, and familial adenomatous polyposis. The workshop included four sessions: clinical medicine and pathology, chaired by Dr. Margaret Tucker, Genetic Epidemiology Branch; genetics, chaired by Dr. Alisa Goldstein, Genetic Epidemiology Branch; molecular biology, chaired by Dr. Michael Dean, NCI's Division of Basic Sciences; and general features of the phakomatoses, chaired by Dr. Alfred Knudson, Fox Chase Cancer Center, and who at the time of the workshop was also a member of DCEG.

In the clinical medicine and pathology session, workshop participants reviewed the concept of phakomatoses and discussed mutation types and patterns and the functional roles of specific genes. The genetics session focused on mosaicism, new mutations, homozygotes, and one-hit and two-hit lesions. In the molecular biology session, discussion topics emphasized the molecular features of the phakomatoses. The final session considered the general features of the phakomatoses and expansion of the definition to include the gene for multiple endocrine neoplasia type 1, *MEN1*, in the list of cloned phakomatosis genes, since most patients with the disorder have multiple facial angiofibromas and a variety of skin findings seen in other phakomatoses. ■

RESEARCH CONTRACTS & ACQUISITION BRANCH: THE CONTRACTOR PERFORMANCE SYSTEM

Federal Acquisition Regulations require that project officers prepare a report of contractor performance at least annually. To provide a mechanism for performance information to be gathered systematically, NIH developed the Contractor Performance System, which has been embraced by eight other federal agencies. The system promotes cooperation and partnership with the other agencies and facilitates the selection of the best contractors to provide goods and services.

The system's database is expanding rapidly, with a 117 percent increase in the number of contractors added in 1999. The system is an internet-based, shared-file system for capturing, maintaining, and disseminating contractor performance evaluations on quality of service, cost control, timeliness, and business practices. The database is password-protected to ensure the security of confidential information.

DCEG project officers are using past performance information in selecting new contractors, and taking advantage of performance reports for improving the performance of current contractors. The reports also provide a means of informing contractors of problems or suggestions for improvement. To ensure that the system provides meaningful information, project officers must be candid when evaluating contractor performance. There is no legal liability associated with ratings given by project officers, as long as evaluations are not arbitrary or capricious.

The system has been upgraded to allow project officers and contractors to directly access it and prepare and submit reports electronically. NIH is currently training government contractors on using the system, and is pilot testing the contractor-use upgrade. These two upgrades will eliminate errors from reentry of information, as well as expedite the process.

Project officers who are interested in obtaining a password to directly submit performance reports should contact Ms. Sharon Miller at 435-3783. Training classes are offered on the use of the system, and a 15-minute training module can be accessed at *http://cbtcpstrg.od.nih.gov*. ■

Sharon Miller

NEWS FROM THE TRENCHES

Biostatistics Branch

At the annual meeting of the American Association for Cancer Research, held in April in San Francisco, **Dr. Susan Devesa** presented a poster on the *Atlas of Cancer Mortality in the United States, 1950–1994,* and cochaired a session on cancer epidemiology. While at the meeting, **Mr. Dan Grauman** had attendees field test a new web-based system for producing U.S. cancer mortality maps at different levels of detail and methods of rate selection.

In March, **Dr. Mitchell Gail** gave a presentation on survival analysis at the Eastern North American Regional Biometrics Society meeting in Chicago.

At the March meeting of the German Region of the International Biometric Society, **Dr. Michael Hauptmann** delivered a paper on imputing missing values in exposure histories. While in Germany, Dr. Hauptmann also gave a seminar at the School of Medicine of the University of Erlangen on exposure–time-response relationship between occupational asbestos exposure and risk of lung cancer.

At a January seminar at the George Washington University Department of Statistics, **Dr. Ruth Pfeiffer** spoke about inference for environmental effects on the basis of family data that accounts for ascertainment and genetic effects. ■

Clinical Genetics Branch

In March, **Dr. Mark Greene** spoke about recent advances in hereditary ovarian cancer research at the Ovarian Cancer Symposium of the Society for Gynecologic Investigations, which was held in Chicago. At the City of Hope Comprehensive Cancer Center's Workshop on Hereditary Cancer Syndromes, held in February in Duarte, California, he gave presentations on an NCI perspective of cancer genetics research and on the clinical and genetic aspects of hereditary melanoma and nevi. ■

Environmental Epidemiology Branch

In April, **Dr. Louise Brinton** and **Dr. Catherine Schairer** participated in a meeting in Oxford, England, to discuss future plans of the Collaborative Groups on Aetiological Factors in Cancers of the Breast and Female Genital Tract. In February, Dr. Schairer also gave a lecture on hormone replacement therapy and risk of breast cancer at George Washington University.

At the April meeting of the American Association for Cancer Research, **Dr. Montserrat Garcia-Closas** presented a poster on the collection of genomic DNA from buccal cells by mouthwash and buccal cytobrush.

At the American Association for Cancer Research meeting, **Dr. James Lacey** presented a poster on differential effects of smoking on risks of squamous cell carcinomas and adenocarcinomas of the cervix. He also spoke on this topic at the Keystone Molecular Epidemiology Symposium, held in February in Taos, New Mexico.

At the American Association for Cancer Research meeting, **Dr. Katherine McGlynn** presented a poster on methylenetetrahydrofolate reductase, methionine synthase, folate, alcohol, and breast cancer. In March, she also gave a talk at the Fox Chase Cancer Center on international trends and patterns of primary liver cancer incidence and mortality.

In March, **Dr. Mark Schiffman** spoke to several groups on new developments in using human papillomavirus DNA testing for cervical cancer prevention. The meetings included the American Society of Colposcopy and Cervical Pathology, held in Orlando; the British Society of Colposcopy and Cervical Pathology, held in Birmingham, England; the International Union Against Cancer Conference on Cervical Cancer Prevention, held in Chicago; and a Kaiser Family Health Foundation-sponsored press conference, held in New York. ■

Genetic Epidemiology Branch

In April, **Dr. Margaret Tucker** and **Dr. Maria Theresa Landi** gave presentations at the annual meeting of

the American Association for Cancer Research. Dr. Tucker spoke at the "Meet-the-Expert" sunrise session about secondary tumors related to cancer treatment. Dr. Landi presented a poster on dioxin-related markers of exposure and effect.

In February, **Dr. Tucker** presented a paper on dysplastic nevi as a biomarker for melanoma risk at a symposium entitled "Common Frontiers in Cancer Research," which was sponsored by NCI and the Japan Society for the Promotion of Science. In February she also spoke at an educational conference titled "The Future is Now! Clinical and Ethical Implications of Cancer Genetics," about NCI's efforts to protect patient privacy and confidentiality and to maintain data security in cancer research involving genetic testing. Dr. Tucker also discussed the Health Insurance Portability and Accountability Act proposed by the Secretary of the Department of Health and Human Services. The conference was hosted by the McLaughlin Research Institute and Benefits Healthcare Alliance for Education and Research, and was held in Big Sky Mountain Village, Montana. ■

Nutritional Epidemiology Branch

At the April meeting of the American Association for Cancer Research, **Dr. Rashmi Sinha** gave a seminar on developing biologic measures of exposure as part of a symposium on "Molecules, Genes, and the Pathway to Cancer: New Methods and Approaches in Epidemiology." Her abstract on high intake of PhIP associated with increased risk of breast cancer was also presented at the meeting in a symposium on "Epidemiology of Breast and Other Cancers." In another talk, Dr. Sinha presented her findings on heterocyclic amines and risk of cancer at a symposium on molecular epidemiology, which was sponsored by the Environmental Mutagen Society in April in New Orleans.

In April, **Dr. Stephanie Weinstein** presented a paper titled "Risk of invasive cervical cancer is decreased with a common (C677T) methylenetetrahydrofolate reductase polymorphism" at the Experimental Biology meeting in San Diego.

Occupational Epidemiology Branch

At the April meeting of the American Association for Cancer Research, presentations were given by **Dr. Qing Lan** on the connection between glutathione S-transferase and the risk of stomach cancer in Warsaw, Poland, **Dr. Xeng Xie** on the expression of p53 and p21 proteins in esophageal and gastric carcinomas, **Dr. Capri-Mara Fillmore** on thyroid nodules and cancer related to the intake of I-131 in dairy products of northeastern Kazakhstan, **Dr. Dalsu Baris** on a linkage study of cancer among acromegaly patients, and **Dr. Aaron Blair** on exposure to organophosphate pesticide and risk of non-Hodgkin's lymphomas. Also at the meeting, **Drs. Richard Hayes** and **Bu-Tian Ji** presented a poster on tobacco use and risk of colorectal adenomas and cancer in the prostate, lung, colon, and ovarian cancer screening trial.

During April, **Dr. Mustafa Dosemeci** presented a series of talks on exposure assessment in cancer epidemiology studies at the University of California at San Francisco, the Lawrence Livermore National Laboratory, the University of North Carolina, and the National Institute of Environmental Health Sciences. In May, he spoke about exposure assessment at the plenary session of the Workshop on Occupational Cancer in Ontario. Also at the plenary session, **Dr. Blair** gave a talk titled "Occupational cancer epidemiology: Past, present and future."

At the annual meeting of the American Epidemiological Society, which was held in March in Tampa, **Dr. Debra Silverman** presented a paper titled "Why do black Americans have a higher risk of pancreatic cancer than white Americans?"

In April, **Dr. Mary Ward** participated in a workshop on women's health and the environment, which was held at the Kennedy School of Government at Harvard University. Dr. Ward has been appointed as a member of the Oversight Committee for the Long Island Breast Cancer Study Project.

The Branch hosted a number of short visits by foreign scientists to discuss ongoing projects. Among the visitors in February was **Dr. Aage Anderson**

from the Cancer Registry of Norway, who met with Dr. Blair and Dr. Larry Engel to discuss the JANUS; in March were **Dr. Judith Guernsey** from Dalhousie University in Nova Scotia, who met with Dr. Blair, Dr. Patricia Stewart, and Ms. Joanne Colt to discuss a steel workers study, and **Dr. Bengt Jarvholm** from Umea University in Sweden, who met with Drs. Blair, Silverman, Baris, and Dr. Wong-Ho Chow to discuss studies of construction workers; in April were **Dr. Elsebeth Lynge** from the Cancer Registry of Norway, who met with Dr. Blair and Dr. Stewart to discuss dry cleaner studies, **Dr. Reul Vermeulen** from Wageningen Agricultural University in the Netherlands, who met with Dr. Stewart and Dr. Rothman to discuss biologic monitoring in the rubber industry, and **Dr. Paolo Boffetta** from the International Agency for Research on Cancer in France, who met with Dr. Wong-Ho Chow to discuss renal cell cancer studies. ■

Radiation Epidemiology Branch

Last December, **Dr. Charles Land** gave talks on sources of uncertainty for radiation-related risk estimates at an international conference on Bridging Radiation Policy and Science, held in Leesburg, Virginia, and at the annual meeting of the Society for Risk Analysis in Atlanta. At a January workshop sponsored by the NCI and Centers for Disease Control and Prevention and held in Rockville, he presented his work on estimating thyroid cancer risk to the U.S. population from exposure to I-131 in fallout from the Nevada test site. At a March meeting at the National Academy of Sciences in Washington, D.C., Dr. Land spoke to the Biological Effects of Ionizing Radiation (BEIR) VII Committee about current revisions to the 1985 NIH Radioepidemiological Tables.

At the March meeting of the American Epidemiological Society, which was held in Tampa, **Dr. Martha Linet** participated in a debate on the risk of childhood leukemia associated with electromagnetic field exposure.

In April, **Dr. Ihor Masnyk** gave a talk at the Foreign Service Institute of the U.S. Department of State in Arlington. The topic of his address was nuclear energy and health issues in the Ukraine following the accident at Chornobyl.

Dr. Elaine Ron and **Dr. Terry Thomas** gave talks at the International Conference on Chronic Radiation Exposure, which was held in March in Chelyabinsk, Russia. Dr. Ron spoke about the epidemiology of thyroid cancer, while Dr. Thomas spoke on stochastic effects of environmental radiation exposure in populations living near the Mayak industrial association. In February, Dr. Ron also gave a talk on thyroid cancer and radiation exposure to the Department of Experimental Radiation Oncology at MD Anderson Cancer Center in Houston.

At the April meeting of the American Association for Cancer Research, **Dr. Alice Sigurdson** presented a talk on sex hormones correlated with the risk of testicular cancer. ■

COMINGS … GOINGS

In March, **Ms. Laura Beil** spent 3 weeks working in the Division under a Knight Medical Science Journalism Fellowship. She has been a science reporter for the Dallas Morning News since 1992. Through discussions with DCEG scientists, Ms. Beil focused on learning more about how research data are generated, analyzed, and interpreted. Her visit also allowed staff members to gain insights into the news media from a reporter's perspective.

Dr. Deirdre Hill has joined the Radiation Epidemiology Branch as a postdoctoral fellow under a Cancer Research Training Award. She received a Ph.D. in epidemiology in 1997 from the University of Washington, where she investigated the role of menopausal hormones in the etiology of endometrial cancer. Dr. Hill subsequently completed a fellowship in the Department of Preventive Medicine at the University of Southern California School of Medicine, where she evaluated effect modification of family history on radiation-related risk of breast cancer. She

is collaborating with other Branch investigators in analyzing data from studies of retinoblastoma, adult brain tumor, and cancer in Down's syndrome patients. Dr. Hill is located in EPS/7085, and can be reached at 496-6600.

Dr. Kiyohiko Mabuchi has joined the Radiation Epidemiology Branch as a special expert for radiation studies. He retired as Chief of the Epidemiology Department at the Radiation Effects Research Foundation, where he directed an active, international research program of cancer risk in atomic bomb survivors. Dr. Mabuchi serves on the Executive Board of the Japanese Association of Population-Based Cancer Registries, as a member of the International Committee on Radiological Protection, and as an advisor to the United Nations Scientific Committee on the Effects of Atomic Radiation. He will collaborate with Branch members on several epidemiologic projects, including investigations of radiation-induced thyroid cancer among atomic bomb survivors, the preparation of an updated Life Span Study cancer incidence report, and the design and development of an international non-melanoma skin cancer study involving time trends, incidence, and case-control components. Dr. Mabuchi is located in EPS/7013, and can be reached at 594-7649.

Dr. Ulrike Peters has joined the Nutritional Epidemiology Branch as a postdoctoral fellow. She received a Ph.D. in nutrition from the University of Kiel, Germany, where she conducted case-control and incidence studies of celiac disease. More recently, Dr. Peters received an M.P.H. from the Department of Epidemiology at the University of North Carolina School of Public Health. She is particularly interested in nutritional epidemiology and genetic susceptibility. Dr. Peters is working with Dr. Rashmi Sinha on a study of colon cancer involving vitamin D intake and vitamin D receptor polymorphisms. She is located in EPS/7030, and she can be reached at 594-7079.

Dr. Steven Simon has joined the Radiation Epidemiology Branch as a special expert for radiation dosimetry. He received a Ph.D. in radiological health sciences from Colorado State University, and was formerly employed as a senior staff officer of the Board of Radiation Effects Research at the National Academy of Sciences. Dr. Simon is working on ways to make information used by NCI for the radiation fallout study more accessible, including modifying computer programs, upgrading web-based maps and other graphics, and archiving scientific and technical information in an easily retrievable format. He will also participate in efforts by scientists from the United States, Russia, and Kazakhstan to compare methodologies for estimating radiation doses received by the public from nuclear weapons tests conducted at the Nevada and the Semipalatinsk test sites. Dr. Simon is located in EPS/7015, and can be reached at 594-1390.

Ms. Katrina Wahl has joined the staff of the Office of the Director, Epidemiology and Biostatistics Program, as a secretary. Ms Wahl holds a B.A. in political science from Ohio University. She is located in EPS/8093, and she can be reached at 594-7837.

Ms. Ifetayo White, a secretary in the Occupational Epidemiology Branch, has moved to South Carolina, where she is working as a massage therapist.

Dr. Shinji Yoshinaga has been appointed a special volunteer in the Radiation Epidemiology Branch. He received a Ph.D. from the Department of Epidemiology and Biostatistics at the University of Tokyo. Dr. Yoshinaga is a researcher at the National Institute of Radiological Sciences in Chiba, Japan, where he is studying the health effects of occupational exposure to radiation and radiation-induced cancers, as well as working on data analysis methods. While visiting the Branch, Dr. Yoshinaga is evaluating the health effects from low-dose radiation exposure experienced by radiological technologists in Japan. He is located in EPS/7045 and can be reached at 496-5285.

Dr. Tongzhang Zheng is spending 5 months in the Occupational Epidemiology Branch while on sabbatical from the Yale University School of Public Health. He is an associate professor in the Division of Environmental Health Sciences, where his research interests focus on occupational and environmental exposures in the etiology of Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, and breast cancer. Dr. Zheng is located in EPS/8110, and he can be reached at 435-4710. ■

CALENDAR OF EVENTS

Date	Event
June 26	DCEG Seminar: Prospective Follow-up Studies of Cancer in Populations Screened Twice (1975, 1985) prior to Diagnosis of Cancer Dr. Kathy Helzlsouer 10:30 am–11:30 am, EPN / J Women Scientists Advisory Group Lunch: The Art of Juggling Dr. Kathy Helzlsouer 12:00 pm, EPS / 7101
July 14	DCEG Town Meeting and Committee of Scientist Forum Dr. Fraumeni 10:30 am–12:00 pm, EPN / C,D,E,F
July 20	Senior Advisory Group Retreat Glenview Mansion
July 24	Board of Scientific Counselors Conf. Rm. 10, Bldg. 31
September 7	Senior Advisory Group Meeting 1:00 pm–4: 00 pm, EPN / G
September 11–13	National Cancer Advisory Board Conf. Rm. 10, Bldg. 31
September 26	Nutritional Epidemiology Branch Site Visit
October 5	Senior Advisory Group Meeting 1:00 pm–4:00 pm, EPN / G
October 12–13	DCCPS / DCEG Prostate Cancer Workshop
November 9	Senior Advisory Group Meeting 1:00 pm–4:00 pm, EPN / G
November 27–28	Board of Scientific Counselors Conf. Rm. 10, Bldg. 31
December 4–6	National Cancer Advisory Board Conf. Rm. 10, Bldg. 31
December 7	Senior Advisory Group Meeting 1:00 pm–4:00 pm, EPN / G