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SHEDDING NEW LIGHT ON RISK FACTORS FOR MELANOMA

Although many of the risk factors for malignant melanoma—the deadliest form of skin cancer—are known, they are not well understood. Recent findings by DCEG researchers are providing new insights into the genetic and environmental factors that increase the risk for the disease. About 10 percent of malignant melanomas occur among persons who have an affected family member. Other known risk factors for melanoma are the presence of atypical moles, total number of moles, skin sensitivity to the sun, freckling, and hair, eye, and skin color.

It has long been known that occurrence of melanoma is higher in southern regions of the United States where sunshine is more intense. However, relating an *individual's* melanoma risk to his or her sun exposure has been hard to do. The main difficulty has been in determining precisely how much sunlight a person has been exposed to and how much of that exposure is from the midrange, ultraviolet B (UVB) wavelengths that are most closely associated with skin cancer.

A group of DCEG researchers led by **Thomas R. Fears, Ph.D.,** Biostatistics Branch, addressed this problem by devising a new method of estimating a person's lifetime sun exposure based on past residence. In a collaborative study conducted with the University of Pennsylvania and the University of California at San Francisco, information was collected from subjects with and without melanoma on the places they had lived. Robertson-Berger (RB) meters, which measure the amount of solar radiation received in a particular location, were used to estimate the UVB intensity. The RB meters had been in place for 11 years at 30 locations around the country as part of another NCI/National Oceanic and Atmospheric Administration study. A person's cumulative intensity of exposure was estimated by adding up the RB counts for each residence location in six-month increments. Average annual intensity was determined by dividing the cumulative intensity by the person's age in years. The study, published in the July 15 issue of *Cancer Research,* revealed that melanoma risk increased with increasing average intensity of UVB exposure: a 10 percent increase in average lifetime intensity was associated with a 19 percent increase in risk of melanoma for males and a 16 percent increase for females.

Dr. Margaret Tucker Using a Dermatoscope To Examine Dysplastic Nevi

One surprising finding was that intensity of sun exposure in adulthood was as important to melanoma risk as was intensity of exposure in childhood. The researchers also noted that the risk of melanoma increased with time spent outdoors, regardless of skin type. "Childhood exposure is important, but we have shown that it's total sun exposure—and the intensity of that exposure—over a lifetime that affects melanoma risk," noted Fears. "And,

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even for people who tan well, melanoma risk increases with time spent outdoors."

This study was conducted among persons not selected for a genetic predisposition to develop melanoma and included only non-Hispanic whites. The main known cause of inherited susceptibility to melanoma is mutation of the *CDKN2A* gene, which was discovered in high-risk families by DCEG staff and their collaborators. Functioning as a tumor suppressor gene, mutations in *CDKN2A* have been found in about 20 percent of multiple-case families.

Penetrance of the *CDKN2A* mutation—the likelihood that someone with this mutation will develop melanoma—appears to be influenced by geographic location, according to research published in the June 19 issue of *Journal of the National Cancer Institute* by DCEG scientists and other members of the International Melanoma Genetics Consortium. The consortium studied 80 families in Australia, Europe, and the United States who had documented *CDKN2A* mutations and at least two cases of cutaneous malignant melanoma.

Among mutation carriers, the estimated risk of developing melanoma by age 80 years was 91 percent in Australia, 76 percent in the United States, and 58 percent in Western Europe. Since penetrance was highest in the areas with a high incidence of melanoma, it appears that "the same risk factors that affect melanoma risk in the general population—sun exposure, fair skin, and so on—also influence penetrance in the families we studied," explained **Alisa Goldstein, Ph.D.,** of the Genetic Epidemiology Branch (GEB), one of the study's authors. "Although possession of a mutation is a strong risk factor, other risk factors are also important for the development of melanoma in individuals from high-risk families."

A second gene, *CDK4,* has also been discovered by DCEG researchers and their collaborators to increase susceptibility to melanoma in rare families. Mutations in other genes, as yet unidentified, may also increase risk. Even so, in a paper in the June 15 issue of *Cancer* that describes the natural history of melanoma and dysplastic nevi in high-risk families, **Margaret A. Tucker, M.D.,** Chief of the GEB, and her colleagues, showed that the pattern of disease appears to be very similar in all melanoma-prone families, no matter which susceptibility state is involved. For example, age at diagnosis and thickness of melanomas do not vary between families with different mutations.

DCEG staff and their colleagues have shown that atypical or dysplastic moles—precursor lesions that may develop into melanoma—are an important risk factor in familial melanoma. However, the majority of atypical moles in this longitudinal study either remained stable or regressed; few moles changed in a manner suggestive of developing melanoma. "This is good news because it means that, with regular skin examinations, most melanomas can be found early when the disease is most treatable," observed Dr. Tucker.

Melanoma is considered an epidemic cancer because its incidence and mortality are increasing rapidly. In the United States, the incidence has more than doubled and deaths have increased about 44 percent since 1973. Future research should help to further refine measures of exposure to solar radiation and clarify the relationship between sunlight exposure and melanoma risk. Researchers also hope to elucidate the genetic and other susceptibility factors involved in dysplastic nevi and their progression to melanoma and to identify appropriate interventions. ■

—Eleanor Mayfield

MAUREEN HATCH HEADS THE CHORNOBYL RESEARCH UNIT

In May, **Maureen C. Hatch, Ph.D.,** was appointed Chief of the Chornobyl Research Unit (CRU) in DCEG's Radiation Epidemiology Branch. Dr. Hatch joins NCI after faculty appointments at Columbia University and Mt. Sinai Medical Center, New York, where she served as Director of the Division of Epidemiology.

Dr. Hatch is a New York native who received her Ph.D. from Columbia University in 1985. Her research interests include environmental and radiation epidemiology, the reproductive effects of environmental toxins, and environmental and work-related factors affecting women's health. Dr. Hatch has coedited several books, including *Women and Health,* a comprehensive text that received the 1999 Award of Excellence in Medical Science from the Association of American Publishers.

DCEG Linkage spoke with Dr. Hatch about her past accomplishments and her plans for CRU.

What led you to pursue a career in epidemiology?

My undergraduate degree was in English, with a minor in mathematics. When I graduated, I wanted to do something "relevant" … so I entered the urban planning field. I was interested in the ideas that are central to urban planning—such as how the physical environment impinges on how we live and work—but I became discouraged about the actual practice of it.

Even in my experience as a planner, I was always attracted to the area of health. I've always had a yearning to delve into biology. I had done some quantitative research as an urban planner, and I kept hearing about this field called epidemiology. Eventually I went back to school and got my Ph.D.

How did you become involved in the field of radiation exposure?

While I was getting my Ph.D., I was interested in environmental epidemiology in the broadest sense, although not specifically radiation exposure. Then, one of the first projects I became involved with after receiving my degree was a series of health studies related to the Three Mile Island accident. [The studies ultimately found no clear association between radiation exposure and cancer incidence following the 1979 incident at the Pennsylvania nuclear power plant.]

There's something about radiation epidemiology … it becomes a sort of constant attraction. You may get involved in other areas, but you're still always interested in it. While much of the work I'd done between Three Mile Island and today focused on women's health and reproductive issues, I maintained the connection to radiation work by serving on the science advisory committee of the thyroid cancer study at the Hanford Nuclear Site in Washington state as well as the National Academy of Sciences Committee on Radiation Epidemiology Studies.

When the opportunity to head the CRU arose, I found I was very interested in returning to the topic. The Chornobyl study of persons who were exposed *in utero* is coming to fruition now, and that played to my palette of interests.

Could you talk more about the *in utero* study?

So far, the Chornobyl studies have focused on individuals who were

Dr. Maureen Hatch

exposed to radiation as children or adults. There's a study of leukemia risk among cleanup workers in the Ukraine and two parallel studies of thyroid cancer risk among people exposed to the radiation as children: one study is in Belarus and one in the Ukraine.

There appears to be an inverse relationship between age at exposure and risk of thyroid cancer. And one of the unanswered questions is whether this relationship extends to the prenatal period. People have hypothesized that the prenatal period is one of heightened sensitivity, and studies have linked prenatal x-ray exposure to risk of childhood cancer. However, a recent report on atomic bomb survivors did not clearly show a difference in cancer risk between those exposed prenatally and those exposed postnatally.

The question is still an open one, and one to which we think we can contribute. We'd also be contributing to the question of effects of radioiodide exposure in utero, which has barely been addressed. We estimate that there are about 2,000 individuals who were exposed in utero that we can recruit into the study.

What interested you in joining DCEG and the CRU in particular?

DCEG is a national treasure: It is a group of world-class scientists who are so productive. The opportunity to become part of it was immensely appealing. In and of itself, the CRU is comprised of distinguished individuals and is a wonderful team to join. I also was interested in becoming a part of the CRU because of the multiple countries, disciplines, and institutions involved in its work, the fact that the research has broad public health implications, and the potential to scientifically contribute.

What is your plan for the CRU?

Getting the in utero study underway is the main aspect of my plan. I have been here three months and have had a chance to visit all three ongoing studies. My plan is to do everything I can to make sure our collaborations with Columbia University and the Belarussians and Ukrainians continue to be successful. If time permits, I'm also hoping that I'll be able to collaborate with others in the Division on other research related to women's health. ■

—Nancy Volkers

INDOOR AIR POLLUTION PLAYS A ROLE IN LUNG CANCER IN CHINA

Indoor air pollution resulting from the incomplete combustion of coal and other materials used to heat homes or cook food is a major public health concern in developing countries. Although the relationship of certain risk factors, such as tobacco and asbestos, to lung cancer has been well examined, the role of other types of exposures is less clearly understood. Because of unique environmental exposures in two rural areas in China—the Gansu Province in the north and the Yunnan Province in the south—DCEG researchers focused on these regions as places to study risk factors for lung cancer.

Within the Yunnan Province, researchers observed particularly high lung cancer mortality rates in Xuanwei County. Even though few women have smoked in that region, lung cancer rates among Xuanwei women are the highest in China. Past research identified the use of smoky coal in unvented indoor stoves or firepits as a possible culprit.

Qing Lan, M.D., Ph.D., of the Occupational Epidemiology Branch, first started studying this question in 1990. After joining NCI in 1999, she continued to work on the project, recently focusing on changes from unvented to vented stoves and the impact on lung cancer. The study, published in the June 5 issue of the *Journal of the National Cancer Institute,* compared lung cancer rates in 17,184 farmers in Xuanwei who switched to vented stoves with rates in 4,048 farmers who continued to use unvented stoves or firepits. Stove use and smoking rates were similar between the groups, and men and women were represented in about equal numbers.

Looking at data from 1976 to 1992, Dr. Lan, along with colleagues at the Environmental Protection Agency and the Chinese Academy of Preventive Medicine, found that use of vented stoves reduced lung cancer risk by 41 percent in men and 46 percent in women. They also found that installing a vented stove could cut indoor levels of air pollution by more than 65 percent.

"This paper was the first to show that the change to vented stoves actually had an impact," observed **Nathaniel Rothman, M.D., M.P.H.,** of DCEG's Occupational Epidemiology Branch. Ironically, the increase in stove ventilation has led to increased levels of outdoor or ambient air pollution: "At dinnertime you see black smoke rising and the air starts turning dark," Rothman said. "The good news is that people are getting less

Chinese Woman Cooking on an Indoor Stove Heated by Coals

smoke exposure in their homes, but now there is potential for continuing exposure in the outdoors."

Drs. Lan and Rothman are also seeking to understand cofactors related to lung cancer in this region, in particular, the role of genetic susceptibility. Their previous work in the Xuanwei region found a two-fold increase in the risk of developing lung cancer among people who carried a homozygous deletion in the *GSTM1* gene, which codes for an enzyme that detoxifies polycyclic aromatic hydrocarbons (PAHs), such as those found in coal smoke. In addition, there was evidence of a gene-environment interaction between these two risk factors (reported in 2000). In a second study, they showed that exposure to large amounts of smoky coal was strongly associated with lung tumors that overexpressed the p53 protein, as measured in sputum. Mutations in the *p53* gene are the most common genetic change associated with human cancers. The effect of smoky coal exposure was particularly striking in women, being more than three times higher among p53 overexpressers than among those who did not overexpress the protein.

Drs. Lan and Rothman hope to study gene-environment interactions in more detail among this group of people and they recently returned from a site-visit to Xuanwei, where they explored new research opportunities in the region. "There are few places in the world where we could study a population that has lung cancer caused not by tobacco or occupational exposure, but primarily by environmental PAH exposure," says Rothman. "It could provide insight into the mechanisms relating air pollution and lung cancer in general, regardless of geographical region."

Another group of DCEG researchers has provided further insights into the effects of indoor air pollution. **Jay Lubin, Ph.D.,** of the Biostatistics Branch and **Ruth Kleinerman, M.P.H.,** of the Radiation Epidemiology Branch, along with **Alina Brenner, M.D., Ph.D., Katherine Chen,** and **Catherine Metayer, M.D., Ph.D.,** worked with scientists in the United States and China to study lung cancer in the rural Gansu Province. In this area, many residents live in underground homes that are heated by coal or wood. In contrast to Xuanwei, all of the homes in Gansu have chimneys and ventilation rates are higher, yet pollutant levels are high when stoves were in use and when kangs (raised brick sleeping platforms) were heated in the evening. NCI researchers found an array of independent risk factors for lung cancer in this population: high radon levels in the homes, the use of coal for heating and cooking, cooking oil fumes from rapeseed and linseed oil, and prior lung diseases (tuberculosis, asthma, and emphysema/bronchitis).

In a study published in the April issue of the *Journal of Occupational and Environmental Medicine,* Ms. Kleinerman, Dr. Lubin, and others showed that coal use increased lung cancer risk by about 30 percent in the Gansu region, and risk increased relative to the percentage of time that coal was used over the past 30 years. Study participants also used biomass (sticks and twigs) for heating and cooking, but no relationship was found with lung cancer risk.

The radon study, published in the March 15 issue of the *American Journal of Epidemiology,* involved nearly 900 people with lung cancer and about 1,750 matched control subjects. Radon levels were measured in each household and used to characterize radon concentrations over the past 30 years. Researchers found that as radon levels increased, so did the risk of lung cancer.

Radon levels in the study were nearly five times the average level for U.S. homes and more than four times higher in Chinese underground dwellings than in aboveground dwellings. However, said Dr. Lubin, "The problem of high radon levels in underground houses is becoming less acute because the Chinese government has been encouraging people to move to aboveground houses and dwellings."

The Gansu study is unique because of the exposure of the population to high indoor radon levels, which are intermediate between levels experienced by uranium miners and by the general population. NCI researchers plan to further clarify the risk of lung cancer from residential radon in an international project that will pool all studies dealing with this relationship. ■

—Nancy Volkers

SEMINAR SERIES ADDRESSES PSYCHOSOCIAL ASPECTS OF CANCER

Dr. Susan McDaniel

The Clinical Genetics Branch of DCEG and the Behavioral Research Program of the Division of Cancer Control and Population Sciences have started a seminar series focused on the psychosocial aspects of cancer. The first seminar, which took place October 3, was given by Dr. Susan McDaniel and dealt with the experience of genetic testing in two families. Dr. McDaniel is Professor of Psychology and Family Medicine at the University of Rochester School of Medicine. The idea for the seminar series arose from the shared interest of the two Divisions in the behavioral aspects of genetic research. The joint seminars will take place approximately three times a year.

BLANCHE ALTER WINS LIFETIME ACHIEVEMENT AWARD

Blanche Alter, M.D., M.P.H., of the Clinical Genetics Branch (CGB), recently received the Lifetime Achievement Award from the Fanconi's Anemia Research Fund (FARF).

The organization, founded in 1989, has given out only one previous Lifetime Achievement Award, and Dr. Alter is the first active investigator honored.

"Dr. Alter's work has truly been a steady foundation throughout the years for the Fund, both in terms of her knowledge of Fanconi's anemia (FA), and now cancer epidemiology, as well as her ability to connect with families," commented Mary Ellen Eiler, Executive Director of the FARF. The FARF is a patient advocacy organization that provides support to FA families and raises money for scientific research. It sponsors an annual family camp, an annual scientific symposium, and publishes *FA—A Handbook for Families and Their Physicians,* a text that has become the standard resource for information about the diagnosis and management of this rare disorder.

The award was presented at the FARF annual family meeting, held in August at Camp Sunshine in Casco, Maine, which Dr. Alter attends on a regular basis. The inscription on the plaque reads:

With profound gratitude for pioneering greater understanding of Fanconi's anemia and for tireless dedication to helping FA patients and families worldwide. Your gift of self as a resource for FA families and to the FA Research Fund as a teacher, physician, scientist, and friend has value beyond measure.

Dr. Alter has devoted her career to the clinical, laboratory, and etiologic investigation of FA and other inherited bone marrow failure disorders of childhood. She joined the staff of CGB two years ago and started enrollment in the first comprehensive, epidemiologically-oriented study of FA and its companion diseases in January 2002.

Dr. Blanche Alter Accepts Award from FARF Founder David Frohnmayer

"This is a fabulous acknowledgment of the contributions she has made to the field in the past, as well as a ringing endorsement of the work she is doing with DCEG," remarked **Dr. Mark Greene,** Chief of the CGB. ■

—Maria Sgambati, M.D.

STUDY LAUNCHED ON RARE INHERITED BONE MARROW FAILURE DISORDERS AND CANCER RISK

The Clinical Genetics Branch recently launched a large-scale study of persons with inherited bone marrow failure syndromes (IBMFS). This study will follow patients and their immediate relatives over a long period of time, examine the specific underlying genetic disorders, and analyze factors that can affect the course of these syndromes and increase the risk of cancer.

IBMFS, most often diagnosed during childhood, are relatively rare disorders that involve some form of aplastic anemia. People with these syndromes are at increased risk of leukemia and various solid tumors. Of special interest will be the study of family members for cancer risk, since they may carry one of the altered genes related to these diseases.

"By looking at a large group of patients and family members who may be cancer-prone, we hope to learn more about these issues and to evaluate techniques for cancer screening and prevention," comments **Blanche Alter, M.D., M.P.H.,** lead investigator. To provide a truly comprehensive evaluation to persons with these complex, multisystem disorders, Dr. Alter has teamed with a number of associate investigators in various medical specialties at the NIH Clinical Center and at several extramural institutions.

The study is enrolling families in which at least one member has or had an IBMFS such as:

- Fanconi's anemia
- Diamond-Blackfan anemia
- Shwachman-Diamond syndrome
- Dyskeratosis congenita
- Severe congenital neutropenia
- Thrombocytopenia absent radii
- Amegakaryocytic thrombocytopenia
- Pearson's syndrome
- Bone marrow failure other than acquired.

A major worry for families living with these conditions is the impending threat

of cancer in young patients. With this study, researchers hope to gain an understanding of why cancer develops in people with IBMFS, why it occurs earlier than in the general population, the role of IBMFS genes in carcinogenesis, and the potential means for risk reduction.

All North American families with these syndromes are eligible for the study. There are two subgroups—those who are evaluated as part of the NIH Clinical Center Cohort and those who provide medical information as part of the Field Cohort. Currently, Dr. Alter sees a family every other week at the Clinical Center. Affected individuals and their immediate family receive comprehensive physical and laboratory examinations by a team of specialists over the course of a several day visit, along with information and advice regarding the management of any newly identified clinical problems that are detected.

For further information about this study, visit the study web site online at: *http://marrowfailure.cancer.gov.* ■

—Rhonda DeJoice

SENIOR ADVISORY GROUP HOLDS ANNUAL RETREAT

The DCEG Senior Advisory Group gathered for its fifth annual retreat, held on July 18 at Rockwood Manor in Potomac, Maryland. In his opening remarks, DCEG Director **Joseph Fraumeni, Jr., M.D.,** highlighted the importance of team-building and accountability. This year's retreat presented an opportunity for the Division to consider ways of increasing the scientific impact of our epidemiologic studies in terms of advancing etiologic insights and biologic concepts, identifying preventive measures, and improving clinical practice. Dr. Fraumeni placed particular emphasis on forming partnerships with NCI's Center for Cancer Research and extramural research programs that will advance the Institute's research agenda. He encouraged investigators to strengthen their involvement with the NCI faculties as a way to enhance molecular epidemiology and emphasized the need to develop mechanisms that more closely link laboratory efforts to epidemiologic projects.

Fostering High-Impact Research

Patricia Hartge, Sc.D., the retreat Program Chair, moderated a lively discussion about the Division's 2001 publication portfolio. **Aaron Blair, Ph.D.; Robert Hoover, M.D., Sc.D.; Margaret Tucker, M.D.; Mark Schiffman, M.D., M.P.H.,** and **Joanne Colt, M.P.H., M.S.,** presented various analyses of the portfolio as a measure of scientific productivity. The research portfolio attempts to strike a balance between high-impact science and the need to investigate areas of special interest to the general public and the Congress. Not surprising was the direct correlation seen between the originality and creativity of the work and its publication in a high-impact journal. Concern was expressed over the need to amass a sizable publication record at the expense of more fruitful collaborations that may not always result in numerous first or senior author publications. The experience of younger investigators in designing and conducting long-term field studies was also cited as an issue with future implications.

The Division faces critical decisions regarding which of its large cohort studies should add or expand their collection of biospecimens. Methods to enhance the quality of research while using resources wisely were discussed, including strengthening concept reviews, improving cost estimates, and strategic planning. A working group will be convened to address these issues.

Addressing Personnel Issues

DCEG Deputy Director, **Shelia Zahm, Sc.D.,** facilitated a discussion on a variety of personnel issues and their long-range implications, including the recruitment and retention of fellows, the increasing number of staff scientists, and the mentoring of all investigators, including senior staff.

A recent poll of DCEG postdoctoral fellows revealed that personal recommendations from mentors, friends, and past or current DCEG fellows were the recruitment methods that drew them to the Division. Ways to increase the fellow applicant pool included encouraging senior and junior investigators to give talks at graduate school departments in epidemiology and biostatistics, improving advertisements, and the better utilization of DCEG alumni.

DCEG's Office of Education (OE), headed by **Demetrius Albanes, M.D.,** will take the lead in improving current recruitment and mentoring practices. The OE will ensure that all fellows undergo annual performance reviews and promote effective mentoring by formalizing DCEG mentoring guidelines, offering a mentoring workshop in the fall, and developing additional ways to recognize and reward good mentoring practices. Another aim of the OE is to establish a DCEG Visiting Scholars program to foster interactions with outside scientists. **Arthur Schatzkin, M.D., Dr.P.H.,** led a discussion focused on

issues unique to tenure track investigators. The group stressed the need for a senior mentor, not necessarily the Branch Chief, as well as having a formal tenure plan that is reviewed biannually by the Branch Chief, Program Director, and Division Director.

Louise Brinton, Ph.D., described the changing role of staff scientists within the Division, in terms of increasing numbers and seniority that allows them to take the scientific lead on various studies. The importance of equitable salaries and other means of recognizing outstanding performance for all staff was also discussed.

Maximizing Molecular Epidemiology Data

Another major topic under deliberation was how to manage the impending wealth of data from molecular epidemiology studies. A key concern was the cost and information technology challenges of processing numerous biospecimens from large studies at the NCI Core Genotyping Facility (CGF). Developing database structures with enough flexibility to be used for multiple current studies as well as future studies is critical. A working group will examine these issues and explore available assistance through existing NIH programs, including the Center for Information Technology, the Cancer Genome Anatomy Project, and the NCI Center for Bioinformatics, and the NCI Faculty on Bioinformatics, Biostatistics, and Computational Biology.

Enhancing Laboratory Collaborations

The last part of the retreat centered on issues surrounding the storage and processing of biologic samples. DNA extraction was singled out as the current major bottleneck to molecular epidemiology studies in the Division. The discussion explored ways to improve DNA processing efficiency, including moving DNA quantification activities to CGF. Other topics focused on standardizing and simplifying aliquotting schemes as well as ensuring ease of sample retrieval from biorepositories. The related issue of offering a laboratory experience for epidemiology postdoctoral fellows was also discussed.

Jim Vaught, Ph.D., and **Marianne Henderson, M.S.,** will oversee DCEG's efforts to support an expansion of the capacity at NCI Frederick for proteomics, molecular pathology, cytogenetics, nanotechnology, and hormonal assays, while continuing to request more timely cost estimates for SAIC services. Dr. Vaught will also pursue the means for conducting quality control research on biospecimen and storage issues.

In closing remarks, Drs. Fraumeni and Hoover complimented the group on their efforts, noting that the day had resulted in many productive discussions of key topics that will contribute to the future success of the Division. They underscored the need for the Division to take all necessary steps to maximize the use of available resources, to enhance productivity and the pursuit of high-impact and high-quality research, and to establish benchmarks for measuring performance. ■

—Cathy McClave, M.S.

FIRST BEEBE SYMPOSIUM HELD; FELLOWSHIP ESTABLISHED

Gilbert Wheeler Beebe, Ph.D., one of the world's leading authorities on radiation effects, recently retired from the National Cancer Institute at age 89. To commemorate the occasion, the National Academy of Sciences Board on Radiation Effects Research held the first annual Gilbert Beebe scientific symposium on Tuesday, June 18, 2002, at the new National Academies Science Building in Washington, DC. Collaborators and colleagues from Japan and the United States gathered to honor Dr. Beebe's contributions over the course of his 68-year career.

Dr. Beebe's forte was in establishing extremely valuable cohort studies. After World War II, he played a key role in creating the Medical Follow-up Agency, with the goal of examining and following veterans for the after-effects of war-related injuries and diseases. Dr. Beebe helped organize 18 million Army records that covered 1.5 million feet of floor space in St. Louis, Missouri. Since its inception in 1946, studies from this gold mine of army medical experience have yielded information on a variety of conditions including psychoneurosis, peripheral nerve damage, vascular injuries, and infectious hepatitis.

Drs. Burton Bennett of the RERF and Gilbert Beebe (Photograph by Ben Hamlin, NAS)

Dr. Beebe also played a leadership role in creating a long-term research strategy for the Atomic Bomb Casualty Commis-

sion (ABCC) in Japan. **Robert Miller, M.D., Dr.P.H.,** DCEG Scientist Emeritus, remembered Dr. Beebe's six-day work week, famous "pink note sheets," and whistling of tunes that were undecipherable by his colleagues. Several important cohorts grew from the ABCC, including the Life Span Study for mortality follow-up, the Adult Health Study for clinical examination, and the Pathology Study.

The ABCC was reorganized into the Radiation Effects Radiation Foundation (RERF) in 1975 and became a cooperative endeavor between Japan and the United States. Dr. Beebe served as the first Chief Scientist. Dr. Burton G. Bennett, the current Chairman of RERF, commented on Dr. Beebe's contributions. "In many ways in a long and distinguished career you have made a difference," he noted. "Thank you with sincere appreciation and gratitude for all you have done for us."

Joseph Fraumeni, Jr., M.D., DCEG Director, recalled the excitement in 1977 when Dr. Beebe, a "bona-fide legend," agreed to join NCI. At NCI, Dr. Beebe continued to evaluate the atomic bomb survivor data with a focus on quantitative analysis, statistical modeling, and differential sensitivity of tissues to carcinogenic effects.

In 1986, after the world's worst nuclear power accident in Chornobyl, Drs. Beebe and Miller helped forge a tri-national partnership among scientists from the Ukraine, Belarus, and the United States, to study the affected populations. "Gil is truly a star and a gentleman—it has been an honor and education to have him as a colleague and a friend," reflected Dr. Geoffrey R. Howe, of Columbia University, who has worked on the Chornobyl projects for many years.

The Department of Energy, National Academy of Sciences, NCI, and RERF announced the establishment of the Gilbert W. Beebe Radiation Fellowship in honor of Dr. Beebe's distinguished career in radiation epidemiology and statistics. The fellowship will provide support for recipients to work at the Radiation Epidemiology Branch and the RERF. ■

—Chitra Mohla, M.S.

HPV EXPERTS GATHER TO IDENTIFY PROMISING RESEARCH DIRECTIONS

Persistent infection with oncogenic human papillomavirus (HPV) causes virtually all cases of cervical cancer. Fully exploring the natural history of HPV infections and evaluating the effectiveness of HPV vaccines and diagnostic tests are major research foci in the Environmental Epidemiology Branch (EEB). In June, DCEG coordinated a workshop aimed at identifying promising directions for future epidemiological and prevention studies related to HPV. In addition to cervical cancer, HPV infections have been implicated in the etiology of other cancers involving the anogenital tract in men and women, as well as oropharyngeal and possibly other sites. The workshop brought together 30 experts in the field of HPV epidemiology from more than a dozen countries.

HPV Experts at Monograph Planning Meeting

Mark Schiffman, M.D. (EEB), Dr. Diane Solomon (Division of Cancer Prevention), and Dr. Xavier Bosch (Catalan Institute of Oncology in Barcelona) are now preparing a monograph based on the workshop presentations and discussions. Although the monograph will mainly cover cervical cancer, other putative HPV-related malignancies will also be discussed. The publication will provide an up-to-date summary of current knowledge and future directions for research, with chapters covering a broad range of topics, including disease burden, natural history, etiologic cofactors, immunity, vaccinology, screening, diagnostic techniques, treatment, and novel hypotheses. ■

—Mark Schiffman, M.D.

SUMMER STUDENTS GAIN RESEARCH EXPERIENCE IN DCEG

DCEG mentors made a big impact on the 17 students who were hosted this year as part of the NIH Summer Research Program. This program provides an opportunity for students to enhance their knowledge and understanding of the world of biomedical research and contributes to their personal academic goals. High school students may want to get a taste of research, whereas college or graduate students may be looking for practical applications of course work or the honing of a career path.

Aside from having a "wonderful experience," Kate Kirby, a second year graduate student at the University of Michigan, School of Public Health said, "I was able to apply the knowledge that I learned in my graduate program to real-world data and to manage all the inherent complications that such data supply. My mentor, **Bob Biggar** [an M.D. in the Viral Epidemiology Branch (VEB)], was excellent at directing my work and helping me to determine trends and associations in my study that needed further analysis."

A summer fellowship gives students a first-hand opportunity to see how the academic theories are applied in a research setting. Working with **Michael Alavanja, Dr.P.H.,** Kendra Khawaja, a graduate student in the M.P.H. Epidemiology Program at Columbia University, remarked, "It was an outstanding experience to work with cancer experts on my first 'real' analysis. The 11 weeks proved more fruitful than I had imagined."

While immersed in graduate school, it is easy to lose sight of the practical applications of the academic concepts, especially with a dissertation looming and student loans mounting. The summer experience can inject a new sense of purpose to a student's studies. "My summer experience at NCI allowed me to see the practical importance of the material I've learned in graduate school," noted Eric Maiese, a student at the Johns Hopkins Bloomberg School of Public Health. "It brought classroom knowledge into the 'real world' through use of exciting, cutting edge hands-on training. My mentor, **Michie Hisada** [an M.D. Sc.D., Ph.D. in VEB], was an invaluable asset to the progression of my project and for insight into the research community. The internship has reinforced my desire to pursue a career in public health research."

The mentoring summer students receive is vitally important to shaping their career decisions. For Christine Masters, a nursing student at Ohio State University, her summer experience provided a unique opportunity for her to learn about clinical research. "My mentor, **Jennifer Loud** [a C.R.N.P., M.S.N. in the Clinical Genetics Branch] has been exceptionally generous, obliging, and encouraging. She urged me to ask questions, offered advice, and served as an excellent role model. Jennifer has actively introduced me to peers in the nursing and research fields from who I have received enormously helpful information. This experience has me considering a doctorate degree."

The program, coordinated by the NIH Office of Education, begins each year in mid-May and concludes in late August. Highlights for the students include the Summer Lecture Series and the Research Poster Day. VEB summer students have been well represented at the NIH Poster session. **James Goedert, M.D.,** VEB Branch Chief, promotes student participation in this academic event. "Without exception, every one of our summer students over the years has found the development and presentation of their research project at Poster Day to be valuable and memorable," he observed. "Poster Day is one of the rare opportunities for students to glimpse the breadth and depth of the NIH Intramural Research Program, which can only be termed awesome."

Since completing the program, several students are considering dissertation projects with DCEG investigators. The summer program wouldn't be possible without the active participation of DCEG researchers to serve as mentors. Thanks go out to the DCEG mentors who worked hard to provide educational and productive opportunities in cancer epidemiology and genetics research to the summer students. More information on the NIH Summer Research Program can be found online at: *http://www.training.nih.gov.* ■

—Kris Kiser, M.H.A.

DCEG Hosts Summer Research Interns: (front row) Kristin Kiser, Dr. Joseph F. Fraumeni, Jr., Dr. Shelia Hoar Zahm; (back row) Cheryl Pendergrass, Christine Masters, Jennifer Fergenbaum, Jim McClave, Kate Kirby, Laveta Stewart, Caroline Hoffman, Kendra Khawaja, Gayle Baker, Katrina Trivers, Eric Maiese, Meredith Fosters, Leonard Rodman, Vanessa Shaw, Amy Proctor, Sarah Daugherty, Eric Faden, and Kristen Cummings

CHORNOBYL COLLABORATORS MEETING ON LEUKEMIA TAKES PLACE

Chornobyl Leukemia Study Collaborators and Advisors

More than 35 participants from the United States and Ukraine met to discuss the binational study of "Leukemia and other hematologic diseases among cleanup workers at the Chornobyl Nuclear Plant." Participants from the DCEG Chornobyl Research Unit included **Gilbert Beebe, Ph.D., Andre Bouville, Ph.D., Maureen Hatch, Ph.D., Nickolas Luckyanov, Ph.D., Ihor Masnyk, Ph.D.,** and **Kathleen Stine, M.B.A.** Leukemia study collaborators from the Research Centre for Radiation Medicine in the Ukraine were also present, as were Columbia University collaborators including Drs. Stuart Finch, Geoffrey Howe, and Mr. David Burch, as well as scientists from the U.S. Department of Energy.

The major project involves a case-control study of leukemia risk among 110,000 Chornobyl cleanup workers in the Ukraine. Because of the large-scale exposure at relatively low doses, the study should help to reduce the uncertainty about risk of leukemia from such exposures. Recruitment has begun with the interviews proceeding at a brisk pace. The study is scheduled for completion in 2004.

In addition to scientists and administrators involved with the project, attendees at the meeting included members of the newly formed Leukemia Advisory Group to DCEG, comprised of Drs. Bruce Chabner (hematology), Harvey Checkoway (epidemiology), Lennie Wong (biostatistics), and Keith Eckerman (dosimetry). The NIH Office of Rare Diseases, NCI, and the U.S. Department of Energy sponsored the meeting, which was held in Bethesda in May. The Advisory Group intends to meet on an annual basis, with next year's meeting possibly taking place in the Ukraine.

—Kathleen Stine, M.B.A.

UPDATED POWER PROGRAM NOW AVAILABLE

Version 3.0 of the POWER program is now available online. The computer software program, initially developed in 1998 by **Jay Lubin, Ph.D.** (Biostatistics Branch) and **Montserrat Garcia-Closas, M.D., Dr.P.H.** (Environmental Epidemiology Branch), allows the user to determine the statistical power or sample size for epidemiological studies that test for marginal effects of a single exposure or interactions between two exposures. The program is particularly useful for determining sample sizes needed for studies of gene-environment interactions.

Enhancements in the new version include the following:

- Power/sample size calculations for one exposure (binary or categorical factors with multiple levels);
- Power/sample size calculations for two exposures, the specification of a dependent joint probability distribution for the exposures;
- Entry of values for either marginal odds ratios or main effects odds ratios for the specification of the alternative hypothesis; and
- Improved handling of program log and output files.

The program is available online at: *http://dceg.cancer.gov/POWER.*

DCEG ALUMNUS, WILLIAM BLATTNER, WINS 2002 JOHN SNOW AWARD

William Blattner, M.D., a former DCEG scientist, has won the American Public Health Association (APHA) John Snow Award. The award, presented at the APHA annual meeting held in Philadelphia during November, recognizes an outstanding epidemiologist who has made contributions of enduring value to the improvement of human health. It is named after Dr. John Snow (1813–1858), a legendary figure in the history of public health, who was the first to link the spread of an 1854 outbreak of cholera in central London to the use of a sewage-contaminated water pump.

Dr. Blattner spent 22 years in the epidemiology program at NCI. His research played a key role in establishing the link between human T-lymphotropic virus type 1 and a T-cell leukemia/lymphoma that is endemic in the Caribbean and parts of Japan. In the early 1980's, when AIDS was emerging, he helped track the disease and identified its relation to HIV infection and to AIDS-related malignancies. Dr. Blattner helped found the Institute of Human Virology in Baltimore and now serves as its Director of Epidemiology and Prevention. He is also a professor in the Department of Medicine at the University of Maryland School of Medicine. ■

—Maria Sgambati, M.D.

DCEG MEMBERS RECOGNIZED AT NCI AWARDS CEREMONY

Several members of DCEG were honored at the NCI Awards Ceremony, held on October 10. The Chornobyl Research Unit won a group NIH Merit award for work on the NCI Collaborative Research Project, which is yielding new insights into the carcinogenic effects of environmental radioiodine exposure to infants and children. **Gilbert Beebe, Ph.D., Andre Bouville, Ph.D., Nickolas Luckyanov, Ph.D., Ihor Masnyk, Ph.D., Kathleen Stine, M.B.A.,** and **Terry Thomas, Ph.D.** (recognized posthumously), were honored for their leadership. Individuals receiving NIH Merit Awards included **Alisa Goldstein, Ph.D.** (for establishing the role of important covariates other than mutation status on the risk of melanoma in melanoma-prone families); **Mindy Kaufman** (for resourceful organization and support of NCI State of the Science workshops and strategy meetings in multiple malignancies); **Richard Hayes, D.D.S., Ph.D.** (for work on the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial), **Elizabeth Maloney, Dr.P.H.** (for research on human T-lymphotropic virus type I infection among children); and **Dilys Parry, Ph.D.** (for developing and directing the DCEG interdisciplinary cancer genetics fellowship program). In addition, **Nathaniel Rothman, M.D., M.P.H.,** was awarded a PHS Commissioned Corps Commendation medal (for work on developing a pilot project to evaluate the ability of commercial laboratories to perform high capacity DNA genotyping for large-scale epidemiologic studies of cancer), and **James Goedert, M.D.,** was honored for being a Mentor of Merit. ■

—Maria Sgambati, M.D.

Chornobyl Research Unit Group Merit Award Recipients: (front row) Drs. Gilbert Beebe, Ihor Masnyk; (back row) Dr. Nickolas Luckyanov, Ms. Kathleen Stine, Dr. Andre Bouville

NIH Merit Award Recipients: Drs. Alisa Goldstein (not shown), Elizabeth Maloney, Dilys Parry, Richard Hayes, and Ms. Mindy Kaufman

NCI SCIENCE WRITERS' SEMINAR SHOWCASES DCEG RESEARCHERS

DCEG scientists helped science writers understand the complexity of epidemiology in a July seminar sponsored by the NCI Press Office. The seminar, titled "Epidemiology in a nutshell," focused on the translation of population-based epidemiologic studies by reporters into cohesive, accurate articles understandable by generally large, diverse readerships. Approximately 65 people attended, including journalists from the *Washington Post, Wall Street Journal, Oncology Times,* and *JAMA,* as well as NIH science writers and local freelance writers.

Over the course of the three-hour seminar, the audience heard four presentations by DCEG researchers. **Patricia Hartge, Sc.D.,** Deputy Director of the Epidemiology and Biostatistics Program (EBP), laid the groundwork, providing a comprehensive overview of epidemiology, study design and considerations, and the translation of findings. She stressed the importance of study methodology and how it plays a critical role in interpreting results. Then **Rashmi Sinha, Ph.D.** (Nutritional Epidemiology Branch), **James Lacey, M.P.H., Ph.D.** (Environmental Epidemiology Branch), and **Aaron Blair, Ph.D.** (Occupational Epidemiology Branch) each presented brief synopses of their work, explaining the science of epidemiology in the context of their fields of expertise.

In her presentation entitled "Western dietary patterns and cancer: role of meat," Dr. Sinha explained how she designs and implements studies to determine links between cancer risk and carcinogens in red meat. Dr. Lacey shared his insights on the cancer risks associated with hormone replacement therapy and how his work specifically addresses methodological problems in pharmacoepidemiology studies. Dr. Blair highlighted the issues and challenges intrinsic to pesticide carcinogenicity research and how such considerations have been handled by careful study design and thorough exposure assessment.

"The evaluations were glowing," said Nancy Nelson, Senior Writer in the NCI Press Office. "The DCEG scientists were largely responsible for the success of the Science Writers' Seminar. Each prepared interesting and easy-to-follow talks with plenty of time for questions from the writers. The writers appreciated the effort that went into making it a stimulating and valuable experience."

Prior to the seminar, Ms. Nelson worked with DCEG staff to prepare a supplementary background document about epidemiology and wrote an interview with DCEG's **Robert Hoover, M.D., Sc.D.,** Director of EBP, which was highlighted in the Press Office's online newsletter, *BenchMarks.* These articles are available online at: *http://www.newscenter.cancer.gov/BenchMarks.* ■

—Alyssa Voss

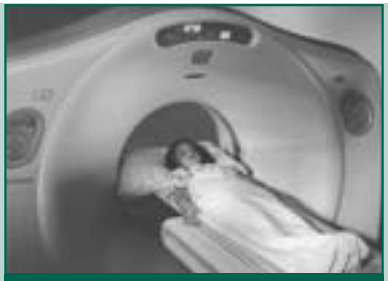
DCEG HELPS PRODUCE GUIDE FOR PEDIATRIC CT SCANS

Approximately 2 to 3 million computed tomography (CT) scans are performed annually on children living in the United States. While these exams provide a valuable imaging tool, their increasing use among the pediatric population has prompted public health concern. To raise awareness of this issue, **Elaine Ron, Ph.D.,** and **Ruth Kleinerman, M.P.H.,** of the Radiation Epidemiology Branch (REB) partnered with the Society for Pediatric Radiology and other professionals to develop a guide for healthcare providers. The guide discusses the use of CT as a diagnostic tool, unique considerations for radiation exposure in children, the radiation risk from CT in the pediatric population, and immediate measures to minimize radiation exposure from CT scans.

Epidemiologic studies of exposed populations reveal that children are considerably more sensitive to radiation than adults. The guide recommends customizing exposure settings for pediatric populations, including adjustments for size and weight, using lower settings for certain organ systems, limiting the region scanned to the smallest possible area, and using lower resolution scans when possible.

Collaborators on the guide included Thomas Slovis, M.D. (Society for Pediatric Radiology), David Brenner, Ph.D. (Columbia University), Donald Frush, M.D. (Duke University Medical Center), Nancy Rosen, M.D. (Memorial Sloan Kettering Cancer Center), and Edward Staab, M.D. (NCI).

The guide was printed in July 2002, and 160,000 copies were distributed to pediatricians, family practitioners, radiologists, and emergency room physicians. The important public health implications of medical radiation exposure underscore the need to evaluate the carcinogenic risks of pediatric CT. Therefore, REB plans to conduct a record-linkage study in collaboration with HMOs belonging to the Cancer Research Network in the United States and the Karolinska Institute in Sweden. Radiology records of all children receiving CT scans, or other diagnostic radiologic examinations, will be linked to medical, hospital, and cancer registry records. The guide is available online at: *http://www.cancer.gov/cancerinfo/causes/radiation-risks-pediatric-CT.*



Pediatric Computed Tomography Scanner

—Ruth Kleinerman, M.P.H.

SCIENTIFIC HIGHLIGHTS

BRAIN TUMORS

Allergies, Autoimmune Diseases, and Risk of Brain Tumors

The role of a history of allergies and autoimmune diseases in the etiology of brain tumors was evaluated in a hospital-based case-control study. There was an inverse association between glioma and history of any allergies (OR = 0.7; CI = 0.5–0.9) or autoimmune diseases (OR = 0.5; CI = 0.4–0.7). No associations were evident for meningioma or acoustic neuroma with history of any allergies. An inverse association was observed between meningioma and history of autoimmune diseases (OR = 0.6; CI = 0.4–0.9). Analyses suggested an interaction between allergies and autoimmune diseases on risk of glioma ($p = 0.06$); subjects having both conditions were at lowest risk (OR = 0.2; CI = 0.1–0.4). Among the specific conditions, asthma and diabetes showed the most consistent associations (OR = 0.6; CI = 0.4–0.9, and OR = 0.4; CI = 0.3–0.7, respectively). **(Brenner AV, Linet MS, Fine HA, Shapiro WR, Selker RG, Black PM, Inskip PD. History of allergies and autoimmune diseases and risk of brain tumors in adults. *Int J Cancer* 2002;99:252–259)**

BREAST CANCER

Second Tumors in Male Breast Cancer Survivors

The risk of second cancers was analyzed among 1,788 men diagnosed with a first primary breast cancer in 1973–1996 who were registered with the Surveillance, Epidemiology, and End Results program. There was no increase in the overall risk of second cancer (standardized incidence ratio = 0.99, CI = 0.86–1.13); however, the risk of contralateral second breast cancer was elevated (standardized incidence ratio = 29.64, CI = 15.48–52.41). The risk was higher for younger men (diagnosed with first breast cancer before age 50 years) than for older men. Type of treatment received for first primary breast cancer did not appear to affect the risk of second contralateral breast cancer. **(Auvinen A, Curtis RE, Ron E. Risk of subsequent cancer following breast cancer in men. *J Natl Cancer Inst* 2002;94: 1330–1332)**

Hormone Levels Vary by Place of Birth in Asian-American Women

Data collected from 1983 to 1987 in a population-based, case-control study of breast cancer among Asian women living in California and Hawaii were used to examine whether endogenous hormones vary with migration history. Plasma levels of estrone (E1), estradiol (E2), estrone sulphate (E1S), and sex hormone-binding globulin did not differ significantly between Asian- and Western-born women, although, among premenopausal women, those least westernized had the lowest levels of E1, E2, and E1S. Androgen levels, particularly dehydroepiandrosterone (DHEA), were lower in women born in the West. Among premenopausal women, age-adjusted geometric mean levels of DHEA were 16.5 and 13.8 nmol/L in Asian- and Western-born women respectively; in postmenopausal women these values were 11.8 and 9.2 nmol/L, ($p < 0.001$) respectively. **(Falk RT, Fears TR, Hoover RN, Pike MC, Wu AH, Nomura AM, Kolonel LN, West DW, Ziegler RG. Does place of birth influence endogenous hormone levels in Asian-American women? *Br J Cancer* 2002;87:54–60)**

Reproductive History and Breast Cancer Risk among *BRCA1/2* Carriers

A community-based study conducted during 1996 in Washington, DC, tested 5,318 Ashkenazi Jews for three *BRCA1/2* founder mutations and identified 120 mutation carriers. A case-case analysis was conducted among 288 participants who had been diagnosed with breast cancer. The estimated relative risk (RR) of breast cancer rose five percent with each five-year increment in age at first birth (RR = 1.05; CI = 0.97–1.15) among noncarriers. By contrast, the estimated risk in mutation carriers fell with each five-year increment in age (RR = 0.65; CI = 0.37–1.16). Among the subjects who were breast cancer survivors, the comparison of carriers with noncarriers showed no protection associated with early birth in the presence of a mutation in *BRCA1* or *BRCA2*. **(Hartge P, Chatterjee N, Wacholder S, Brody LC, Tucker MA, Struewing JP. Breast cancer risk in Ashkenazi *BRCA1/2* mutation carriers: effects of reproductive history. *Epidemiology* 2002;13:255–261)**

Breast Cancer Mortality among Female Radiologic Technologists

Breast cancer mortality among 69,525 female radiologic technologists certified in the United States from 1926 to 1982 was evaluated. Mortality risk was highest among women first employed as radiologic technologists prior to 1940 (relative risk [RR] = 2.92; CI = 1.22–7.00) compared with those first employed in 1960 or later and declined with more recent calendar year of first employment (p for trend = 0.002). Risk increased with number of years employed as a technologist prior to 1950, but was not associated with total years worked as a technologist. Technologists who first performed fluoroscopy (RR = 1.69; CI = 1.02–3.11) and multifilm procedures (RR = 1.87; CI = 1.04–3.34) before 1950 had elevated risks compared with technologists who first performed these procedures in 1960 or later. The high risks of breast cancer mortality and subsequent decline are consistent with the dramatic reduction in recommended radiation exposure limits over time. **(Mohan AK, Hauptmann M, Linet MS, Ron E, Lubin JH, Freedman DM, Alexander BH, Boice JD Jr, Doody MM, Matanoski GM. Breast cancer mortality among female radiologic**

technologists in the United States. *J Natl Cancer Inst* 2002;94:943–948)

CERVICAL CANCER

HLA-I Alleles and Cervical Neoplasia

To explore the relationship between human leukocyte antigen (HLA) class I alleles and cervical neoplasia, a subset of participants from three large U.S. and Costa Rican cervix studies were typed for HLA-I alleles. Study subjects were women with cervical cancer or high-grade squamous epithelial lesions (HSILs; n = 365) or low-grade squamous epithelial lesions (LSILs; n = 275) or who were cytologically normal (control subjects; n = 681). Consistent associations across all studies were observed for HLA-CW*0202 with a combined odds ratio of 0.5 (CI = 0.3–0.9) for cancer or HSILs and 0.6 (CI = 0.4–1.0) for LSILs, compared with control subjects. This finding supports the hypothesis that a single allele may be sufficient to confer protection against cervical neoplasia. Given the relationship between HLA-C and its receptors on natural killer cells, a role is proposed for natural killer cell function in human papillomavirus infection and cervical neoplasia. **(Wang SS, Hildesheim A, Gao X, Schiffman M, Herrero R, Bratti MC, Sherman ME, Barnes WA, Greenberg MD, McGowan L, Mortel R, Schwartz PE, Zaino RJ, Glass AG, Burk RD, Karacki P, Carrington M. Comprehensive analysis of human leukocyte antigen class I alleles and cervical neoplasia in three epidemiologic studies. *J Infect Dis* 2002;186:598–605)**

COLORECTAL CANCER

Metabolism of Heterocyclic Amines Alters Risk of Colorectal Adenoma

High temperature cooking of red meats generates heterocyclic amines (HCAs) that become carcinogenic via metabolization by enzymes including cytochrome P450 1A2 (CYP1A2) and N-acetyltransferase 1 or 2 (NAT1 or NAT2). A clinic-based study of colorectal adenomas focusing on HCA exposures (estimated by use of a HCA database and meat cooking module) and genetic modification of HCA exposures was conducted in 146 cases and 228 frequency-matched controls. The *NAT1*10* allele was associated with a nonsignificant increased risk of colorectal adenomas (OR = 1.4; CI = 0.9–2.4). A six-fold increase in adenoma risk was seen among rapid NAT1 acetylators who consumed more than 27 ng/day of MeIQx (2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline) (OR = 6.5; CI = 2.2–19.7), whereas among slow NAT1 acetylators, the increase in risk was two-fold (OR = 2.3; CI = 1.1–4.8). *NAT2* genotype and CYP1A2 and NAT2 hepatic activity were not associated with adenoma risk **(Ishibe N, Sinha R, Hein DW, Kulldorff M, Strickland P, Fretland AJ, Chow WH, Kadlubar FF, Lang NP, Rothman N. Genetic polymorphisms in heterocyclic amine metabolism and risk of colorectal adenomas. *Pharmacogenetics* 2002;12:145–150)**

INFECTIOUS AGENTS

Factors Contributing to *Helicobacter Pylori* Seropositivity

To investigate possible associations between *Helicobacter pylori* infection and demographic, lifestyle, and environmental factors in a rural Chinese population at very high-risk for stomach cancer, a cross-sectional survey was administered to 3,288 adults (1,994 seropositive, 1,019 seronegative, 275 indeterminate) from 13 villages in Shandong Province, China. *H. pylori* prevalence was elevated for infrequent hand washing before meals (OR = 1.7; CI = 1.0–3.0), crowding (i.e., sharing a bed with more than 2 people [OR = 2.3; CI = 1.3–4.2]), washing/bathing in a pond or ditch (OR = 1.5; CI = 1.0–2.4), and medium (OR = 1.6; CI = 1.3–2.0) and low (OR = 2.3; CI = 1.9–2.9) compared to high village education level. *H. pylori* prevalence was reduced for those never being married or divorced (OR = 0.4; CI = 0.2–1.0). In addition, source of drinking water, especially water from a shallow village well, seemed to be related to *H. pylori* seropositivity. **(Brown LM, Thomas TL, Ma JL, Chang YS, You WC, Liu WD, Zhang L, Pee D, Gail MH. *Helicobacter pylori* infection in rural China: demographic, lifestyle and environmental factors. *Int J Epidemiol* 2002;31:638–645)**

Incidence Changes in Kaposi's Sarcoma and Non-Hodgkin's Lymphoma

The incidence of Kaposi's sarcoma (KS) and non-Hodgkin's lymphoma (NHL) in the general population has markedly increased since the onset of the AIDS epidemic in 1981. To examine the effect of changes in infection rates and introduction of treatments on the incidence of these two neoplasms, age-standardized incidences for KS and NHL from 1973 through 1998 were obtained from nine registries in the Surveillance, Epidemiology, and End Results program. During the mid-1990's, KS incidence declined sharply in all nine registries. Decreases were most evident in San Francisco, where KS rates among white men had risen from 0.5 per 100,000 persons per year in 1973 to between 31.1 and 33.3 from 1987 through 1991, then declined to 2.8 in 1998. In San Francisco, NHL rates among white men rose from 10.7 per 100,000 persons per year in 1973 to a peak of 31.4 in 1995, then declined to 21.6 in 1998. NHL types that were AIDS-associated declined most steeply, whereas the incidence of NHL types not associated with AIDS was either stable or increasing. **(Eltom MA, Jemal A, Mbulaiteye SM, Devesa SS, Biggar RJ. Trends in Kaposi's sarcoma and non-Hodgkin's lymphoma incidence in the United States from 1973 through 1998. *J Natl Cancer Inst* 2002;94:1204–1210)**

SV40 in Human Brain Tumors

Simian virus 40 (SV40), a monkey polyomavirus, was a contaminant of early poliovirus vaccines administered in the

1950's and early 1960's. SV40 causes brain tumors in laboratory animals, and SV40 DNA sequences have been variably identified in human choroid plexus tumors and ependymomas. To study the association between SV40 and human brain tumors in northern India, DNA was extracted from pathologic specimens from 33 ependymomas, 14 choroid plexus tumors, and 18 control brain tissues (contused brain, brain metastases). Real-time PCR was used to detect and quantify SV40 (T antigen) and human (GAPDH) DNA sequences. SV40 DNA was detected in one specimen (an ependymoma). However, few SV40 DNA copies were detected in this sample (<10 copies, equivalent to < 1 copy/per 350 cells) and SV40 was not detected when this sample was retested. These results do not support a role for SV40 in choroid plexus tumors or ependymomas from northern India. **(Engels EA, Sarkar C, Daniel RW, Gravitt PE, Verma K, Quezado M, Shah KV. Absence of simian virus 40 in human brain tumors from northern India. *Int J Cancer* 2002;101:348–352)**

Chemokine Receptor Polymorphisms and Risk of HTLV-I Infection

Subjects from two epidemiologic cohorts in Jamaica were studied to examine the association of polymorphisms in the chemokine receptor gene and the risk of human T lymphotropic virus type 1 (HTLV-I) infection. In the initial analysis of gene frequency, 116 HTLV-I–positive and 126 HTLV-I–negative persons of African descent in Jamaica were evaluated. In this group, the frequencies of *CCR5-Delta 32, CCR2-64I,* and *SDF-1-3′A* genotype were 1.0, 14.9, and 5.4 percent, respectively. The association of HTLV-I infection with the most common variant, *CCR2-64I,* was examined in 532 subjects. Thirteen (5.4 percent) of 241 HTLV-I–negative subjects were homozygous for *CCR2-64I,* versus 3 (1.0 percent) of 291 HTLV-I–positive subjects ($p = 0.005$). Among HTLV-I carriers, provirus load and antibody titer were not significantly different in persons who were heterozygous or homozygous for the *CCR2-64I* allele. *CCR2-64I,* or alleles in linkage disequilibrium with it, may affect the risk of HTLV-I infection in a recessive manner. **(Hisada M, Lal RB, Masciotra S, Rudolph DL, Martin MP, Carrington M, Wilks RJ, Manns A. Chemokine receptor gene polymorphisms and risk of human T lymphotropic virus type I infection in Jamaica. *J Infect Dis* 2002;185:1351–1354)**

Viral Load of HPV and Risk of CIN3 and Cervical Cancer

A cohort of 20,810 women followed for 10 years with cytological screening were studied to assess whether higher viral loads of human papillomavirus (HPV) predict future risk of cervical intraepithelial neoplasia-3 (CIN3) or cancer (CIN3+). Viral loads were measured for 13 types of carcinogenic HPV (relative light units normalized to 1 pg/mL HPV 16 positive controls [RLU/PC]) using Hybrid Capture 2 testing of cervicovaginal lavages obtained at enrollment. Results were stratified into four groups on a logarithmic scale (RLU/PC 1 to <10, 10 to <100, 100 to <1000, > or = 1000). Although presence of HPV strongly increased the risk of CIN3+, high viral load did not further predict the risk. **(Lorincz AT, Castle PE, Sherman ME, Scott DR, Glass AG, Wacholder S, Rush BB, Gravitt PE, Schussler JE, Schiffman M. Viral load of human papillomavirus and risk of CIN3 or cervical cancer. *Lancet* 2002;360:228–229)**

Pleural and Peritoneal Lymphoma in U.S. AIDS Patients

AIDS and cancer registries were used to identify cases of non-Hodgkin's lymphoma (NHL) among 304,439 U.S. adults with AIDS. Among 10,510 cases of NHL, 4 pleural lymphomas and 10 peritoneal lymphomas were identified, representing 0.13 percent of the total NHL cases. Pleural/peritoneal lymphoma cases tended to have a higher prevalence of prior Kaposi sarcoma (KS) (29 percent vs 12 percent; $p = 0.06$), but were otherwise similar to other NHL in age, race, and HIV transmission category. More cases of pleural/peritoneal lymphoma had immunoblastic histology than did other NHL types (43 percent vs 22 percent, $p = 0.06$). Median CD4 counts for pleural/peritoneal lymphomas were also higher than for other NHL (203 vs 65 cells/mm^3, $p = 0.05$), but post-NHL survival was similar (median 7.1 vs 5.1 months, respectively; $p = 0.32$). Pleural and peritoneal lymphomas represent a rare subtype of AIDS-associated NHL and the increased frequency among persons with prior KS suggests a common etiology, presumably infection with KS-associated herpes virus, as found in primary effusion lymphoma. **(Mbulaiteye SM, Biggar RJ, Goedert JJ, Engels EA. Pleural and peritoneal lymphoma among people with AIDS in the United States. *J Acquir Immune Defic Syndr* 2002;29:418–421)**

Hepatitis C Viral Infection and Risk of B-cell Malignancies

A cohort of 48,420 individuals in California was studied to determine whether hepatitis C viral (HCV) infection preceded the development of non-Hodgkin's lymphoma (NHL) and other B-cell lymphoproliferative disorders. Stored sera from 95 subjects with either NHL (n = 57), multiple myeloma (n = 24), or Hodgkin's disease (n = 14) diagnosed a mean of 21 years after phlebotomy were screened for antibodies to HCV as well as viral RNA, based on previous reports of antibody-negative viremia. Sera from 4 cases and 1 of 95 age-, sex-, and race-matched controls were repeatedly reactive by enzyme immunoassay, but none were confirmed by recombinant immunoblot assay; none of the case sera had HCV RNA by reverse transcription-polymerase chain reaction. These prospective data do not support previous reports of a substantial role of chronic HCV infection in the etiology of B-cell neoplasia. **(Rabkin CS, Tess BH, Christianson RE, Wright WE, Waters DJ, Alter HJ, Van Den Berg BJ. Prospective study of hepatitis C viral infection**

as a risk factor for subsequent B-cell neoplasia. *Blood* 2002;99:4240–4242)

KIDNEY CANCER

Kidney Cancer Incidence Increases Worldwide

U.S. and international kidney cancer incidence data for five-year periods from 1973 to 1992 were evaluated for time trends and geographical differences. In the years 1973 to 1977 and 1988 to 1992, incidence rates rose among men and women in all regions and ethnic groups, with a few exceptions—mostly in Scandinavian countries. The largest percentage increases were for men in Japan (171 percent) and for women in Italy (107 percent). In the years 1988 to 1992, kidney cancer incidence rates (age-adjusted to the world-standard population) were highest in France (16.1/100,000 man-years and 7.3/100,000 woman-years) and lowest in India (2.0 and 0.9, respectively). Rates for renal pelvis cancer were less than 1/100,000 person-years in almost all regions in both sexes, and the temporal trends were inconsistent. (Mathew A, Devesa SS, Fraumeni JF Jr, Chow WH. Global increases in kidney cancer incidence, 1973–1992. *Eur J Cancer Prev* 2002;11:171–178)

PANCREATIC CANCER

Dietary Sugar, Glycemic Load, and Risk of Pancreatic Cancer

A cohort of U.S. women (n = 88,802) participating in the Nurses' Health Study was examined to investigate whether diets that increase postprandial glucose levels are associated with pancreatic cancer. During 18 years of follow-up, 180 subjects were diagnosed with pancreatic cancer. Food-frequency questionnaire data from 1980 were used to calculate sucrose, fructose, and carbohydrate intakes; glycemic index; and glycemic load. Carbohydrate and sucrose intake were not associated with pancreatic cancer risk. An increased risk was observed among women with a high glycemic load (relative risk [RR] = 1.53; CI = 0.96–2.45) and fructose intake (RR = 1.57; CI = 0.95–2.57), particularly among women with elevated body mass index (greater than or equal to 25 kg/m^2) or with low physical activity (high glycemic load: RR = 2.67; CI = 1.02–6.99; high fructose intake: RR = 3.17; CI = 1.13–8.91). These findings suggest that impaired glucose metabolism plays a role in pancreatic cancer. (Michaud DS, Liu S, Giovannucci E, Willett WC, Colditz GA, Fuchs CS. Dietary sugar, glycemic load, and pancreatic cancer risk in a prospective study. *J Natl Cancer Inst* 2002;94:1293–1300)

PROSTATE CANCER

Obesity, Insulin, and Insulin-Like Growth Factors and Risk of BPH

The roles of obesity, serum levels of insulin, insulin-like growth factors (IGF) and binding proteins (IGFBP), and leptin in benign prostatic hyperplasia (BPH) were investigated in a case-control study in Shanghai, China among a group of 200 cases and 302 controls. Serum insulin levels, waist-to-hip ratio (WTHR), and IGF-1 were associated with an increased risk of BPH. For serum insulin levels, men in the lowest quartile (less than 5.87 µUnits/mL) relative to those in the highest quartile (greater than 9.76 µUnits/mL) were at increased risk (OR = 2.5; CI = 1.4–4.5; p for trend = 0.009). Relative to men in the lowest WTHR quartile (less than 0.856), those in the highest quartile (greater than 0.923) had an increased risk (OR = 2.4; CI = 1.3–4.4; p for trend = 0.01) for BPH. For IGF-1, relative to the lowest tertile, men in the highest tertile had an elevated risk of BPH (OR = 2.8; CI = 1.6–4.9; p for trend < 0.001). Results for IGF-I were more pronounced after adjustment for serum androgens. In contrast, men in the highest IGFBP-3 tertile had a reduced risk (OR = 0.4; CI = 0.2–0.7; p for trend < 0.001). No associations were observed with body mass index, leptin, IGF-II and IGFBP-1. (Dahle SE, Chokkalingam AP, Gao YT, Deng J, Stanczyk FZ, Hsing AW. Body size and serum levels of insulin and leptin in relation to the risk of benign prostatic hyperplasia. *J Urol* 2002; 168:599–604 and Chokkalingam AP, Gao YT, Deng J, Stanczyk FZ, Sesterhenn IA, Mostofi FK, Fraumeni JF Jr, Hsing AW. Insulin-like growth factors and risk of benign prostatic hyperplasia. *Prostate* 2002;52:98–105)

Polymorphisms in the *AIB1/ SRC-3* Gene and Prostate Cancer Risk

Shorter CAG repeat length in the androgen receptor *(AR)* gene has been related to an increased risk of prostate cancer. To examine the role that coactivating genes may play in prostate cancer risk, the CAG/CAA repeat length polymorphism in the *AIB1/SRC-3* gene (amplified in breast cancer-1/steroid receptor coactivator) was evaluated using genomic DNA obtained from 189 cases and 301 healthy controls recruited for a population-based, case-control study in China. The *AIB1/SRC-3* CAG/CAA repeat length ranged from 24 to 32, with the most common repeat length being 29. Subjects homozygous for 29 CAG/CAA repeats (29/29) and heterozygous (28/29) were the most common genotypes, representing 44 and 30 percent of the controls, respectively. Relative to subjects homozygous for 29 CAG/CAA repeats (29/29 genotype), individuals with the < 29/29 genotype had an OR of 1.31 (CI = 0.87–1.97), whereas those homozygous for the < 29 allele had an OR of 1.81 (CI = 1.00–3.28). Men with both the < 29/ < 29 *AIB1/SRC-3* genotype and a short CAG repeat length in the *AR* gene (< 23) had an OR of 2.78 (CI = 1.24–6.26) relative to men with both the 29/29 genotype of the *AIB1/SRC-3* gene and a long CAG repeat length (23) in the *AR* gene. (Hsing AW, Chokkalingam AP, Gao YT, Wu G, Wang X, Deng J, Cheng J, Sesterhenn IA, Mostofi FK, Chiang T, Chen YL, Stanczyk FZ, Chang C. Polymorphic CAG/CAA repeat length in the *AIB1/SRC-3* gene and prostate cancer risk:

a population-based case-control study. *Cancer Epidemiol Biomarkers Prev* 2002;11:337–341)

Geographic Variation in Prostate Cancer Mortality

Spatial scan statistics were used to determine whether regional rates of prostate cancer mortality vary from the overall U.S. rate. For white men, the primary cluster of elevated mortality was in the northwestern quadrant of the United States, followed by clusters in New England, the eastern part of the north-central area, the mid-Atlantic states, and the South Atlantic area. For black men, the primary cluster was in the South Atlantic area, followed by clusters in Alabama and the eastern part of the north-central area. None of the selected demographic and socioeconomic factors accounted for the primary clusters in the white or black population. The patterns should provide leads for further study of the risk factors and reporting practices that may contribute to geographic variation in mortality from prostate cancer. **(Jemal A, Kulldorff M, Devesa SS, Hayes RB, Fraumeni JF Jr. A geographic analysis of prostate cancer mortality in the United States, 1970–89. *Int J Cancer* 2002;101:168–174)**

RADIATION

Cancer Risk among Korean War Navy Radar Technicians

A cohort of 40,581 Navy veterans with high potential for exposure to high-intensity radar was assembled from Navy records. Deaths from all diseases and all cancers were significantly lower than expected both overall and also for the 20,021 sailors with high radar exposure potential. There was no evidence of increased brain cancer in the entire cohort (standardized mortality ratio [SMR] = 0.9; CI = 0.7–1.1) or in high-exposure occupations (SMR = 0.7; CI = 0.5–.0). Testicular cancer deaths occurred less frequently than expected in the entire cohort and high-exposure occupations. Death rates for several smoking-related diseases were lower in the high-exposure occupations. Non-lymphocytic leukemia was elevated among men in high-exposure occupations but in only one of the three high-exposure occupations, namely, electronics technicians in aviation squadrons (SMR = 2.2; CI = 1.3–3.7). **(Groves FD, Page WF, Gridley G, Lisimaque L, Stewart PA, Tarone RE, Gail MH, Boice JD, Jr., and Beebe GW. Cancer in Korean War Navy Technicians: Mortality survey after 40 years. *Am J Epidemiol* 2002; 155:810–818)**

Cancer Following Treatment for Peptic Ulcer

Cancer mortality data were analyzed on 3,719 subjects following treatment for peptic ulcer disease. Subjects had been treated with either radiotherapy (mean stomach dose 14.8 Gy) and/or surgery and medication for peptic ulcer disease at the University of Chicago during the period 1936 to 1965 and followed through 1997 (average 25 years). Compared to the U.S. rates, stomach cancer mortality was increased for irradiated and nonirradiated patients (observed/expected [O/E] = 3.20 and 1.52, respectively). There was evidence of exposure-related excess mortality for cancers of the stomach (RR = 2.6; CI = 1.3–5.1), pancreas (RR = 2.7; CI = 1.5–5.1), and lung (RR = 1.5; CI = 1.1, 2.1). **(Carr ZA, Kleinerman RA, Stovall M, Weinstock RM, Griem ML, Land CE. Malignant neoplasms after radiation therapy for peptic ulcer. *Radiat Res* 2002; 157:668–677)**

Second Cancers Following Hodgkin's Disease

Data from 32,591 Hodgkin's disease (HD) patients (1,111 25-year survivors) reported to 16 population-based cancer registries in North America and Europe (1935–1994) were analyzed to quantify the relative and absolute excess risks (AER) of site-specific second cancers. A total of 2,153 second cancers (observed-to-expected ratio [O/E] = 2.3; CI = 2.2–2.4) were reported, including 1,726 solid tumors (O/E = 2.0; CI = 1.9–2.0). Cancers of the lung (O/E = 2.9), digestive tract (O/E = 1.7), and female breast (O/E = 2.0) accounted for the largest number of subsequent malignancies. Twenty-five years after HD diagnosis, the actuarial risk of developing a solid tumor was 21.9 percent. The relative risk of solid neoplasms decreased with increasing age at HD diagnosis; however, patients aged 51 to 60 years at HD diagnosis sustained the highest cancer burden (AER = 79.2 per 10,000 patients per year). After a progressive rise in relative risk and AER of all solid tumors over time, there was an apparent downturn in risk at 25 years. Temporal trends and treatment group distribution for certain cancers were suggestive of a radiogenic effect. **(Dores GM, Metayer C, Curtis RE, Lynch CF, Clarke EA, Glimelius B, Storm H, Pukkala E, van Leeuwen FE, Holowaty EJ, Andersson M, Wiklund T, Joensuu T, van't Veer MB, Stovall M, Gospodarowicz M, Travis LB. Second malignant neoplasms among long-term survivors of Hodgkin's disease: a population-based evaluation over 25 years. *J Clin Oncol* 2002;20:3484–3494)**

Cancer Incidence Following Nasopharyngeal Radium Irradiation

A cohort of 4,339 Dutch patients treated with nasopharyngeal radium irradiation (mostly in childhood) and 4,104 frequency-matched controls was studied to determine the risk of subsequent cancer. Average doses to the nasopharynx, pituitary gland, brain, and thyroid gland were 275, 10.9, 1.8, and 1.5 cGy, respectively. During 18–50 years of follow-up, four thyroid malignancies (SIR = 2.8; CI = 0.8–7.2) and five malignant brain tumors (SIR = 1.3; CI = 0.4–3.1) were observed. Increased risks were observed for malignancies of lymphoproliferative and hematopoietic origin (SIR = 1.9; CI = 1.2–2.8) and for breast cancer (SIR = 1.5; CI = 1.1–2.1). **(Ronckers CM, van Leeuwen FE, Hayes RB, Verduijn PG, Stovall M, Land CE. Cancer incidence after nasopharyngeal radium irradiation. *Epidemiology* 2002; 13:552–560)** ■

DCEG PEOPLE IN THE NEWS

Michael Alavanja, Dr.P.H., of the Occupational Epidemiology Branch (OEB) addressed the American Association of Pesticide Control Officials in Kansas City, Missouri, during August. He spoke on "Pesticide exposure and prostate cancer in the Agricultural Health Study."


Dr. Michael Alavanja

Dr. Alavanja also served on the International Agency for Research on Cancer (IARC) monograph committee in June. The committee was tasked with writing on "Tobacco smoke and involuntary smoking."

Blanche Alter, M.D., M.P.H., of the Clinical Genetics Branch (CGB), gave invited presentations on cancer susceptibility and inherited bone marrow syndromes in Baltimore, Bethesda, Chicago, Maine, Manitoba, and Johannesburg.


Dr. Robert Biggar

Robert Biggar, M.D., of the Viral Epidemiology Branch (VEB), gave a presentation titled "Kaposi's sarcoma—infection to cancer" at the 12th Annual Florida Infectious Diseases Society Symposium held in Sarasota, Florida, during June. Dr. Biggar also spoke in June at the Center for Epidemiologic Research in Denmark, on the subject of "KSHV as a cause of Kaposi's sarcoma."


Dr. Aaron Blair

Aaron Blair, Ph.D. (OEB), gave a talk on "Pesticides and cancer," at the Instituto Superiore di Sanita, in Rome, Italy, in April. Dr. Blair also served on a special Environmental Protection Agency Science Advisory Panel, which met in June to evaluate the health effects of trichlorethylene. Dr. Blair was also a co-author on "Physical activity across the cancer continuum," which was published in the September 1 issue of *Cancer* and summarizes the results of a workshop on the role of physical activity in cancer etiology and on directions for future research from basic science to population level studies.

Elizabeth Brown (VEB) addressed the Johns Hopkins School of Medicine Viral Oncology Faculty in March. Her talk was on "Assessing chaos in KS: Peripheral cytokine levels, polymorphisms in cytokine genes and risk for classical Kaposi's sarcoma."


Dr. Linda Morris Brown

Captain Linda M. Brown, Dr.P.H., of the Biostatistics Branch (BB), was appointed by the Acting Surgeon General as Chief Professional Officer for the Health Services Category. As the Chief Health Services Officer (HSO), CAPT. Brown is responsible for providing leadership and coordination of PHS professional affairs for the Office of the Surgeon General and the Department. She also provides guidance and advice to the Surgeon General and the Health Services Professional Advisory Committee on matters such as recruitment, retention, and career development of HSOs. The Health Services Category is comprised of over 700 PHS officers representing clinical, administration, and basic and applied science disciplines. CAPT. Brown and **Lieutenant Junior Grade Claudine Samanic, M.S.P.H.** (OEB), received the Crisis Service Response Award from the Commissioned Corps and a Certificate of Appreciation from the Federal Emergency Management Agency/New York State Emergency Management Office for their service following the September 11, 2001, attacks.


Dr. Kenneth Cantor

Kenneth Cantor, Ph.D. (OEB), was the keynote speaker at the Conference on Arsenic in Health and the Environment held in Manchester, New Hampshire in May. Dr. Cantor spoke on "Arsenic in human history."

Neil Caporaso, M.D., of the Genetic Epidemiology Branch (GEB), was a co-author on the consensus statements from the Second international lung cancer molecular biomarkers workshop, which were published in the August 2002 issue of the *International Journal of Oncology.* The workshop brought together experts in the clinical, epidemiological, and molecular-pathology aspects of lung cancer to address strategies for early lung cancer detection.

OEB scientists **Anneclaire De Roos, Ph.D.,** and **Nathaniel Rothman, M.D., M.P.H.,** plus **Stephen Chanock, M.D.,** of the Core Genotyping Facility, co-authored a chapter on "Toxicological considerations in the application and interpretation of susceptibility biomarkers in epidemiologic studies." The chapter will appear in an IARC monograph on *Mechanistic Considerations in the Design and Interpretation of Molecular Epidemiologic Studies of Cancer.*

Susan Devesa, Ph.D. (BB), spoke on "Changes in the incidence of lymphoma by histologic subtypes in the USA in the last 20 years" at the Eighth International Conference on Malignant Lymphoma held in Lugano, Switzerland, in June. Dr. Devesa also spoke on "International lung cancer incidence patterns by histo-

logic type" at the International Conference on Small Cell Lung Cancer in Lausanne, Switzerland and at IARC in Lyon, France. She also gave a talk at the Leukemia Research Centre, University of Leeds in England.


Dr. Mustafa Dosemeci

Mustafa Dosemeci, Ph.D. (OEB), won the Charles C. Shepard Science Award from the Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry for a manuscript titled "Pooled exposure response analyses and risk assessment for lung cancer in 10 cohorts of silica-exposed workers." Dr. Dosemeci spoke at the June 2002 Reproductive Health Group meeting of the National Institute for Occupational Safety and Health—National Occupational Research Agenda, held in Washington, DC, on "Exposure variability, exposure time windows, and questionnaire design." He also gave a presentation in June at the Lombardi Cancer Center, Georgetown University Medical Center, in Washington, DC, on "Assessing biologically effective dose in epidemiological studies."


Dr. Mitchell Gail

Mitchell Gail, M.D., Ph.D. (BB), spoke on "A comparison of methods to estimate gene penetrance" at the Medical University of South Carolina in Charleston, South Carolina, during April.


Dr. Mark Greene

Mark Greene, M.D. (CGB), gave the Annual Memorial Michael Hammond Lecture at Scottsdale Healthcare Shea in April in Scottsdale, Arizona. His talk was on "Surgical risk reduction options in the management of hereditary cancer." He also addressed the 10th Annual SPORE Investigators Workshop on "GOG 0199: National prospective study of risk-reducing salpingo-oophorectomy and ovarian screening among women at increased genetic risk of ovarian cancer" in July. In May, Dr. Greene gave talks on "Hereditary genodermatoses" for the American Society of Clinical Oncology Comprehensive Review Course in Clinical Cancer Genetics; "Hereditary ovarian cancer: surgical prophylaxis and ongoing studies" for ovarian cancer and high-risk women: workshop on implications of prevention, screening and early detection held in Pittsburgh; and "Genetics of melanoma: Update and implications for clinical management and cancer prevention" at the University of Pittsburgh.

Commander Ruthann Giusti, M.D. (CGB), and **Commander Thomas O'Brien, M.D., M.P.H.** (VEB), received PHS Commissioned Corps Outstanding Service Medals in May. This award is presented to officers who have demonstrated outstanding continuous leadership in carrying out the mission of the PHS.

Michael Hauptmann, Ph.D. (BB), spoke on "The U.S. radiologic technologists cohort: Mortality from diseases of the circulatory system, and design and approaches for studies of the genetic components of breast cancer." The talk was given in July at the Institute of Epidemiology, GSF National Research Center for Environment and Health in Munich, Germany.


Dr. Richard Hayes

Richard Hayes, D.D.S., Ph.D. (OEB), spoke at the Korean National Cancer Institute in June on "Etiologic investigations in a large NCI cohort."

Michie Hisada, M.D., Sc.D., Ph.D. (VEB), gave a talk on "Epidemiology of infectious diseases in the Caribbean: A new perspective from island medicine" at the Symposium for Island Medicine held in Kagoshima, Japan, in July. Dr. Hisada also spoke on "Risk factors of *Helicobacter pylori* infection in the Jamaica Mother-Infant Cohort Study" during a spotlight session on "Infectious disease epidemiology" at the annual meeting of the Society for Epidemiologic Research held during June in Palm Desert, California.


Dr. Michie Hisada

Jennifer Loud, M.S.N., C.R.N.P. (CGB), was an invited faculty member for the Fox Chase Cancer Center's Advanced Course for Nurses in Genetic Cancer Risk Counseling and presented on the "Clinical aspects of hereditary breast-ovarian cancer" at the Summer Genetics Institute of the National Institute of Nursing Research.

Roxana Moslehi, Ph.D., M.S. (CGB), gave an invited talk for the NCI Cancer Prevention Course in July.

Jun-Mo Nam, M.S. (BB), gave a talk on "Inference on intraclass version of Kappa agreement" at the U.S.-Korea Conference on Science and Technology held in July in Seoul.


Dr. Dilys Parry

Dilys Parry, Ph.D. (GEB), has been chosen by Neurofibromatosis (NF) Inc., a national lay support group for patients and families with NF, to be the 2002 NF Scholar. Dr. Parry's research on this disorder began in 1987 and contributed to mapping the gene for neurofibromatosis. She has also played a key role in numerous studies looking for correla-

tions between different types of *NF2* mutations and clinical manifestations. Dr. Parry gave her sponsored talk at the Clinical Cancer Genetics Conference, held at the Karmanos Cancer Institute in Detroit during September.


Dr. Charles Rabkin

Charles Rabkin, M.D. (CGB), spoke on "Cytokine gene polymorphisms in gastric cancer and AIDS-related malignancy" at the Symposium on Molecular Mechanisms Mediating Genetic Susceptibility to Infection. The symposium was part of the 102nd General Meeting of the American Society for Microbiology, held during May in Salt Lake City, Utah.

REB scientists **Elaine Ron, Ph.D.,** and **Jerry Puskin, Ph.D.,** chaired sessions and Drs. Ethel Gilbert, Martha Linet, Kiyo Mabuchi, and Alice Sigurdson presented talks on "Current issues in radiation and health," at the American Statistical Association Conference on Radiation and Health held in June at Deerfield Beach, Florida. Drs. Ron and Gilbert also gave talks at a workshop on radiation risk research in southern Urals, held in Bavaria, Germany. Dr. Gilbert presented "Mayak worker studies: Data improvements and new analyses" and Dr. Ron served on the scientific program committee, chaired a session, and presented a talk, "Health effects from radiation exposure to the Ozyorsk population." Dr. Ron spoke on "Medical radiation and cancer" at the Pediatric Radiology Society meeting held in Philadelphia in April, and on "Cancer risks from medical radiation" at the 38th annual meeting of the National Council on Radiation Protection, held in Arlington, during April.

Patricia Stewart, Ph.D. (OEB), addressed the International Occupational Hygiene Association Conference held in Bergen, Norway, on June 13. Dr. Stewart's talk was on "Performing exposure assessment in practice for use in future epidemiological studies."

Tammy Shields, M.P.H., Ph.D., of the Environmental Epidemiology Branch (EEB), successfully defended her dissertation at the University of Washington in Seattle. Her project was entitled "Endogenous hormones and the risk of cervical cancer" and was based on research she conducted within the Guanacaste, Costa Rica, Natural History Study of Cervical Diseases, under the supervision and mentorship of **Drs. Allan Hildesheim** and **Mark Schiffman.** Dr. Shields will remain in EEB as a postdoctoral fellow and will continue to explore the role of endogenous hormones in the etiology of gynecologic tumors and the effect of these hormones on HPV infections.


Dr. Mary Ward

Mary Ward, Ph.D. (OEB), lectured on "Pesticides and cancer" at the Society for Environmental and Occupational Health international conference held during July in Bethesda, Maryland.

Jim Vaught, Ph.D., of the Office of the Director (OD), spoke on "Specimen processing and preservation for molecular epidemiology studies" at the workshop on clinical specimen procurement, processing, and preservation: now and the future. The workshop, held in July, was sponsored by the NCI Gynecological Malignancies Faculty.


Dr. Roel Vermeulen

Roel Vermeulen, Ph.D. (OEB), spoke on "Diesel exposure: What insights will new technologies provide for assessing the risk of exposure to a complex mixture?" at the Cancer research methods workshop: Applying new biotechnology to the study of occupational cancer held in Washington, DC, during May.

Shelia Hoar Zahm, Sc.D. (OD), presented the keynote address at the Third International Congress on Women's Health: Occupation, Cancer, and Reproduction, held in Barcelona during September. ■

DCEG FELLOW, R. SOWMYA RAO, PRESENTS RESULTS OF NIH MENTORING SURVEY

BB postdoctoral fellow R. Sowmya Rao, Ph.D., a DCEG representative to the NIH Fellows Committee and a member of the mentoring subcommittee, was invited by NCI-Women Scientists Advisors to their June 27, 2002, meeting to present results of a mentoring survey conducted at NIH in the summer of 2001. The survey asked postdoctoral fellows to assess the quality of their mentoring. A sample of 750 fellows (105 from NCI), stratified by Institute, was drawn for this purpose. The survey covered mentor relations, scientific direction and independence, mentor's access and availability, training and career development, recognition, and overall mentoring quality. The response rate was 72 percent. Seventy-two percent of responding fellows reported the overall quality of mentoring to be good/excellent. Based on these results, three documents are being implemented—separate guidelines for mentors and for fellows and an annual form to review progress. The subcommittee plans to publish the results of the survey, which is available on the web site *www.felcom.nih.gov*.

COMINGS … GOINGS

Sally Amundson, Ph.D., has been appointed to the position of Adjunct Investigator in the Radiation Epidemiology Branch (REB). Dr. Amundson, from the Gene Response Section, Basic Research Lab, Center for Cancer Research, is a scientific collaborator in the REB's developing program of research into the molecular mechanisms of ionizing radiation damage and repair. Dr. Amundson has been conducting basic biologic and gene expression studies with cellular and mouse models to elucidate reactions from acute ionizing radiation exposure.


Dr. Erin Bell

Erin Bell, Ph.D., left the Occupational Epidemiology Branch (OEB) in August for a faculty position at the School of Public Health at the State University of New York at Albany. Dr. Bell had been a postdoctoral fellow with OEB since 2000, investigating immune function in 2,4-D appliers, high pesticide exposure events among farmers, and risk factors for non-Hodgkin's lymphoma (NHL) and multiple myeloma, including the role of serum cytokine levels in NHL risk.

Zhanat Carr, M.D. (REB), joined the Program on Radiation and Health World at Health Organization (WHO) in Geneva, Switzerland, in June 2002. Dr. Carr was a postdoctoral fellow in the REB working on the study of thyroid disease following nuclear fallout in Kazakstan and on cancer risk and cardiovascular disease following radiotherapy for peptic ulcer. At the WHO, she is working on issues affecting populations in countries of the former Soviet Union.


Dr. Silvia de Sanjosé

Silvia de Sanjosé, M.D., Ph.D., has joined the Viral Epidemiology Branch (VEB) as a Senior Research Fellow. Dr. de Sanjosé is a leading researcher on studies of cancer-associated infectious diseases. She obtained her M.D. from the Universitat Central de Barcelona in 1974 and a Ph.D. in Epidemiology from the London School of Hygiene and Tropical Medicine in 1989. From 1989 to 1993, she was a research fellow at the International Agency for Research on Cancer (IARC) in Lyon, France. Since 1993, she has worked at the Epidemiology and Cancer Registry Service, Ciutat Sanitaria i Universitaria de Bellvitge in Barcelona, Spain.

Daehee Kang, M.D., Ph.D., a visiting scientist in the OEB, worked on a study of Korean workers exposed to potentially carcinogenic coal tars and on collaborative investigations with Dr. Richard Hayes on prostate diseases in the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial. Dr. Kang returned to Korea, where he is an Associate Professor in the Department of Preventive Medicine, Seoul National University College of Medicine.


Dr. Manolis Kogevinas

Manolis Kogevinas, M.D., Ph.D., will be spending a sabbatical year in the OEB. Dr. Kogevinas is a physician-epidemiologist from the Unit of Respiratory and Environmental Health Research, Institut Municipal d'Investigació Médica (IMIM), Barcelona, Spain. Dr. Kogevinas obtained his M.D. from the Medical School of the University of Athens and a Ph.D. in public health from the University of London. Before taking an appointment at the IMIM, he worked as an epidemiologist at IARC in the Unit of Analytical Epidemiology. He will be analyzing data from the Interdisciplinary Case-Control Study of Bladder Cancer in Spain.


Dr. Nataliya Kuptsova

Nataliya Kuptsova, M.D., returned to the Ukraine after spending three months working in REB on Chornobyl-related research projects. Dr. Kuptsova is a pediatric hematologist-oncologist with specific interests in childhood leukemia and lymphoma and recently received an M.P.H. degree at Emory University, Rollins School of Public Health in Atlanta.


Dr. Michael Leitzmann

Michael Leitzmann, M.D., Dr.P.H., has joined the Nutritional Epidemiology Branch (NEB) as a tenure-track Investigator. Dr. Leitzmann earned his medical degree at the University of Berlin, Germany, in 1986, followed by residency training in internal medicine and a fellowship in exercise physiology. In 1995, he enrolled in the Harvard School of Public Health, where he received an M.P.H. with a concentration in quantitative methods followed by a doctorate in nutrition and epidemiology in 2000. Dr. Leitzmann completed a two-year postdoctoral fellowship in the Department of Nutrition at Harvard, focusing on various dietary and lifestyle risk factors in relation to prostate cancer. Dr. Leitzmann's major activities will involve prostate and breast cancer etiologic research, with a focus on nutritional and molecular factors.

Monica Ter-Minassian, M.S., has joined the Genetic Epidemiology Branch (GEB) as a predoctoral fellow.


Ms. Monica Ter-Minassian

Ms. Ter-Minassian received a B.S. in biology from Massachusetts Institute of Technology in 1991 and an M.S. in biology with emphasis on genetic counseling from Brandeis University in 1999. She worked as a data analyst in the Molecular Neurogenetics Unit at Massachusetts General Hospital, carrying out both parametric and non-parametric linkage analyses on a variety of disorders including late-onset familial Alzheimer's disease, X-linked Charcot-Marie-Tooth disease, multiple sclerosis, late infantile neuronal ceroid lipofuscinosis, and familial spastic paraparesis. She will work with Drs. Maria Teresa Landi and Lynn Goldin on linkage analysis of Italian families with melanoma and with Dr. Alisa Goldstein on linkage analysis of Chinese families with esophageal cancer.


Dr. Tara Vogt

Tara Vogt, Ph.D., left the NEB in June to join the CDC Epidemiology Intelligence Service. Dr. Vogt completed both predoctoral and postdoctoral fellowships in the DCEG, focusing on the nutritional aspects of prostate cancer risk. Dr. Vogt will spend a two-year training assignment at the National Center for Infectious Diseases, focusing on disease surveillance, fieldwork, and outbreaks of hepatitis.


Ms. Margaret Wright

Margaret Wright, M.Phil., has joined the NEB as a predoctoral fellow. She received her B.A. in molecular biology and biochemistry from Wesleyan University in 1996 and an M.Phil. in chronic disease epidemiology from Yale University in 2002. She is currently pursuing a Ph.D. in chronic disease epidemiology at Yale. Her dissertation is concerned with diet and lung cancer risk, focusing on dietary antioxidants and prooxidants, as well as their primary plant food sources in men and women. Ms. Wright will work with Dr. Albanes and others investigating the association between indices of oxidative stress and lung cancer risk in the Alpha-Tocopherol Beta-Carotene Study cohort.


Dr. Shinji Yoshinaga

Shinji Yoshinaga, Ph.D., worked as a special volunteer in the REB this summer. Dr. Yoshinaga received his doctoral degree from the Department of Epidemiology and Biostatistics at the University of Tokyo. He is a researcher at the National Institute of Radiological Sciences in Chiba, Japan, where he studied the health effects among radiological technologists in Japan. While visiting REB, Dr. Yoshinaga evaluated skin cancer risks among U.S. radiological technologists in relation to ionizing and ultraviolet radiation.


Dr. Hongyu Zhao

Hongyu Zhao, Ph.D., of the Department of Epidemiology and Public Health at the Yale University School of Medicine, is visiting the Biostatistics Branch from September through December 2002. Dr. Zhao is well known for his genetic research on cross-over interference and on the design and analysis of linkage and association studies. His current research interests include methods for controlling for population stratification in case-control studies and the use of haplotypes in studies of disease-gene associations. ■


Dr. Elaine Ron


Dr. Martha Linet

RADIATION EPIDEMIOLOGY BRANCH CHANGES LEADERSHIP

In August, **Elaine Ron, Ph.D.,** stepped down as Chief of the Radiation Epidemiology Branch (REB). Dr. Ron led the REB since 1997, overseeing a major expansion of the staff and the science carried out by the Branch. The changes that came about during her tenure include the adoption of the Chornobyl Research Unit, the addition of three health physicists to improve dosimetry in REB projects, the revitalization of the x-ray technologists cohort for use as a general population cohort with biospecimens, and the creation of a radiation epidemiology fellowship program. The vibrant scientific life of REB is a credit to her efforts. Dr. Ron will resume her role as principal investigator within REB. **Martha Linet, M.D., M.P.H.,** will be serving as Acting Branch Chief.

MR. J. MICHAEL STUMP RETIRES AFTER 34 YEAR GOVERNMENT CAREER

On August 2, 2002, **Mr. J. Michael Stump,** known throughout DCEG as "Mike," retired as an Information Technology Specialist after more than 34 years with the Federal government.

Born in Baltimore, Maryland, Mr. Stump stayed in the city to attend Morgan State College, graduating cum laude with a B.S. degree. He continued his studies at American University in the Technology of Management program and started his career at IBM before moving on to a two-year stint as a U. S. Public Health Service Commissioned Officer. Mike then spent what he describes as "thirty-two glorious years of service in DCEG and its predecessor organizations." He worked in a number of technical positions, including computer programmer/analyst, Information Technology (IT) Section Chief, and finally Senior IT Specialist, where he played a key role in formulating policies and management guidelines for complex and changing information technology systems. Most recently, Mr. Stump has served as the Project Officer and Fiscal Agent for the Division's computer support services contracts.

"Mike has brought us from the dark ages of punch cards to the modern age of PCs, from HP programmable calculators to Sun servers, and from small computer operations to multimillion dollar contracts with analysis programming, biospecimen inventory systems, internet, web pages, and global connectivity, and lots of stuff I don't understand," remarked **Dr. Shelia Zahm,** Deputy Director, DCEG, at Mr. Stump's retirement luncheon. "But I want to share my appreciation for the person Mike is and the example he's been in reminding us all that it's the people that count."

Mr. James Michael Stump

Over 75 colleagues and friends gathered at the luncheon to celebrate Mr. Stump's career.

Dr. Robert Hoover, Deputy Director of the Epidemiology and Biostatistics Program in DCEG, praised Mike for his tireless commitment, without fanfare, in helping individuals in need and commended his invaluable contributions to the growth and success of this Division. Mike has been recognized for his effectiveness in national and international consultations on a wide range of studies associated with the application of information technology to scientific problems and the overall management of IT-related resources. In acknowledgment of Mike's many contributions, he has been honored with an NIH Director's Award, an NCI Special Achievement Award, and the NCI-Equal Employment Opportunity Award.

"It was a great experience to work with Mike, he taught me a lot about the internal workings of the Division," remarked **Marianne Henderson,** Chief, Office of Division Operations and Analysis, "He was also a great friend. He will truly be missed." Comments throughout the celebration made it clear that Mike's absence will be felt both in the professional and personal aspects he brought to work. "When I needed a lift, I would stop by Mike's office," commented **Dr. Patricia Hartge,** "and with his inimitable charm, he was able to put a smile on my face and make the day seem so much better."

Mike's immediate plans are to work for Synectics for Management Decisions before ultimately heading off to some beachfront community, overdosing on funky blues and jazz, and enjoying unlimited tennis. ■

—Sandy Rothschild