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Division of Cancer Epidemiology and Genetics

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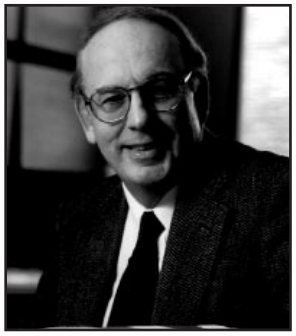
SENIOR ADVISORY GROUP RETREAT, 1999

The third annual DCEG Senior Advisory Group (SAG) Retreat was held July 30 at Kentlands Mansion in Gaithersburg. The retreat included reflections on the highlights and accomplishments of the past year; an in-depth discussion of the Division's scientific review processes; and several short presentations on topics related to recruitment, mentoring, career development, the role of staff scientists, biorepositories, conflict of interest, and information technology.

Dr. Patricia Hartge, Retreat Program Chair, moderated a lively discussion in the morning on the Division's processes for prioritizing research, evaluating concepts and protocols, and planning long-range research goals, particularly in the context of the rapidly increasing costs of large case-control studies aimed at evaluating gene-environment interactions. Drs. Aaron Blair, Martha Linet, Alisa Goldstein, and Mark Schiffman began the discussion with suggestions and ideas for improvements. Dr. Blair thought that SAG members could better evaluate a proposal for a new study if they were more informed about funds available in the DCEG budget and if they knew what other large studies might be proposed in the near future. He believes that the SAG and the Technical Evaluation of Protocols Committee should give as much attention to a project's scientific promise and relevance to cancer as is already given to the rigor of epidemiologic methods. Branch chiefs should also explain how a proposed study complements the branch's and division's existing research program. Dr. Blair recommended that principal investigators be prepared to revise and resubmit proposals to the full SAG membership, instead of assuming approval at the first review.



Joseph F. Fraumeni, Jr., M.D.

Dr. Linet suggested that the review process could be streamlined by using alternative mechanisms for certain types of projects. For example, projects below a certain dollar level could be reviewed by a subcommittee of SAG and submitted directly to Dr. Fraumeni for approval. The concept of seeking broader Division input to evaluate shifts in program direction or large new studies, as was done recently at a Division seminar for a proposed study of lung cancer, was thought to be meritorious. Dr. Schiffman recommended that the leadership take quicker action to terminate poor proposals, recognizing that some projects benefit from a period of "incubation." Dr. Goldstein encouraged more consideration of nontraditional study designs, such as case-case approaches, which may be more efficient and cost-effective. Dr. Fraumeni affirmed the Division's continued commitment to responsible stewardship of government resources, while encouraging relevant high-risk research. A committee was formed to evaluate new approaches to conduct review of research proposals by SAG, taking into consideration the suggestions made during the retreat discussion.

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In the afternoon session, which was moderated by Dr. Shelia Zahm, Dr. Thomas O'Brien, Chair of the Committee of Scientists (COS), expressed strong support for the new DCEG Office of Education, and proposed several services that the Office could provide to enhance the career planning and job placement of fellows, such as job search skill workshops, databases of available positions, formation of an association of former DCEG fellows, and career counseling. Ms. Kristin Kiser, recently hired to establish the Office of Education, described her initiatives to develop these services. Dr. O'Brien also expressed concern regarding the considerable management responsibilities of branch chiefs and other senior staff, and recommended training programs designed to help staff members manage people, time, and resources more effectively. He also recommended an annual anonymous evaluation of each branch's administration, synergy, and morale by all members of the branch to solicit constructive comments and suggestions for improvement. (See the COS column in this issue of *DCEG Linkage* for a more detailed discussion.)

Dr. Louise Brinton led a discussion on the roles and responsibilities of staff scientists and their career development, as compared with principal investigators in the context of the DCEG mission. Both appointments were felt to be critical to the success of the Division.

The bioprocessing and biorepository needs of the Division, and activities under way to meet these requirements, were presented by Dr. Jim Vaught, the DCEG Biorepository Coordinator, and by Dr. Neil Caporaso, Chair of the NCI Biorepository Board. Burgeoning research in molecular epidemiology is producing vast quantities of biospecimens that need to be processed, stored, retrieved, and analyzed. Dr. Vaught projected that 800,000 to 1,200,000 biospecimen vials will be entered into storage annually over the next few years. He described proposals for increasing and improving the physical infrastructure, inventory systems, and bioprocessing capabilities, as well as efforts to improve the responsiveness and quality of support from the Division's contractors. Recognition was given to Drs. Mark Schiffman and Nat Rothman for their significant efforts in managing and planning DCEG's bioprocessing and biorepository activities.

Dr. Arthur Schatzkin, newly appointed as Chief of the Nutritional Epidemiology Branch, challenged SAG members to reconsider conflict of interest issues, their including a heightened awareness of their relevance to outside collaborators. He presented interesting case studies and indicated ways to avoid actual or perceived conflict of interest. One suggestion was to ask scientific collaborators for information on possible conflicts of interest, similar to that required by many NIH advisory groups. Dr. Schiffman wondered if free or discounted reagents, pharmaceuticals, or other study-related materials provided by industry would constitute a conflict of interest.

Mr. Michael Stump updated SAG on information technology activities in the Division, including the Cost Accounting System that tracks expenditures by principal investigator and project, changes in the NCI and DCEG web sites, and the explosive growth in demand on the Division's computer support services contractor.

After a free-for-all session that generated many constructive suggestions for improving the Division's administrative and support systems, the retreat ended with charges for the future. Dr. Alfred Knudson emphasized the tremendous potential of epidemiologic research for identifying causes of cancer with the aim of prevention. He mentioned the additional benefit of understanding mechanisms of carcinogenesis, which could lead to improved treatment. Dr. Knudson encouraged the Division to engage in active scientific debate and discovery aimed at understanding unknown biological processes, and he contrasted science with engineering, which is reductionist and solves problems using known constants. He also encouraged the Division to tackle challenging problems regardless of cost; to discuss ideas freely with colleagues, taking advantage of the considerable breadth of expertise in DCEG and NCI; and to greatly expand training programs. Dr. Knudson said that DCEG should be different than other epidemiology programs by tackling high-risk problems and conducting research in ways that cannot be done elsewhere.

Dr. Robert Hoover indicated that descriptive epidemiologic data continue to be important in providing clues for analytic studies, since most patterns of cancer are determined by environmental factors. He emphasized that the Division needs to use molecular tools in creative ways to identify preventable exposures, and he challenged DCEG to exercise increased leadership in epidemiology, particularly in formulating new paradigms to study gene-environment interactions. Dr. Fraumeni summarized the progress made by the Division since its formation in 1995, the importance of the annual retreats in the planning process, and his commitment to follow-up on all action items emanating from the presentations and discussion. He underscored the importance of high-quality and high-impact epidemiologic research across the Division, and the need to ensure a supportive scientific environment for all staff members. ■

Shelia Hoar Zahm

Shelia Hoar Zahm, Sc.D.

CANCER SURVEILLANCE SERIES: INAUGURAL ISSUE

Measuring national trends in the incidence, morbidity, mortality, and survival of cancer is a vital mission of the National Cancer Institute. A commentary by Fraumeni and Rimer (Cancer surveillance series: inauguration. *J Natl Cancer Inst* 1999; 91:1004) describes a new series of articles on cancer surveillance being launched to elucidate factors contributing to these trends, as well as on health behaviors and services affecting the trends. The patterns will be examined not only for time trends, but also for racial disparities and geographic variations that may suggest new research directions in cancer epidemiology and control. The series is also intended to publicize data sources—such as the population-based cancer registries in the NCI-coordinated Surveillance, Epidemiology, and End Results (SEER) program and other systems—that are available for cancer surveillance research, including methodologic developments in measuring and evaluating various aspects of the cancer burden. Through the collaboration of scientists across the NCI and extramural research community, the series will enhance opportunities to maximize the potential of cancer surveillance programs for

measuring the progress of the National Cancer Program and for providing new epidemiologic leads into the causes and control of cancer. Summarized below are two articles in the inaugural issue involving DCEG investigators.

Trends in Childhood Cancer Incidence and Mortality

Temporal trends in childhood cancers were examined using incidence data reported to nine registries in the SEER program as well as mortality data from the National Center for Health Statistics. Using cancers diagnosed from 1975 through 1995 in 14,540 children under age 15 years, the analysis included a comparison of the new histology-derived International Classification of Childhood Cancer scheme with the primarily anatomic site-based system used by the SEER program. A small rise in the incidence of leukemia, the most common childhood cancer, was found to be largely due to an abrupt increase from 1983 to 1984; the rate has decreased slightly since 1989. For brain and other central nervous system (CNS) cancers, incidence rose modestly, although at a statistically significant rate, mainly from 1983 through 1986. A few rare childhood cancers (e.g., dermatofibrosarcoma, adrenal neuroblastoma, and retinoblastoma) showed upward trends. In contrast, the incidence of Hodgkin's disease decreased modestly but at a statistically significant rate. Mortality rates declined steadily for all major childhood cancer categories. These analyses indicate that there were no substantial changes in incidence for the major childhood cancers over time, and that rates have remained relatively stable since the mid-1980's. The modest increases for brain / CNS cancers, leukemia, and infant neuroblastoma were confined to the mid-1980's, which suggests a role of diagnostic improvements or reporting changes. Dramatic declines in childhood cancer mortality represent treatment-related improvements in survival. (Linet MS, Ries LAG, Smith MA, Tarone RE, Devesa SS. Cancer surveillance series: recent trends in childhood cancer incidence and mortality in the United States. *J Natl Cancer Inst* 1999;91:1051-1058)

Lung Cancer Mortality in the United States: Changing Geographic Patterns

Maps of lung cancer mortality rates across the United States were updated to track changing geographic patterns and to provide clues for epidemiologic studies in high-risk communities. Age-adjusted race- and sex-specific lung cancer mortality rates from 1950 through 1994 were calculated for 9 Census Divisions and 508 State Economic Areas. Pronounced geographic variation in lung cancer rates was evident, with patterns changing substantially over time. Among white males in the 1950's and 1960's, high rates were observed in urban areas of the northeast and north central states and in areas along the southeast and Gulf coasts. By the 1970's, the excess in northern states began to fade, with high rates starting to cover wider areas of the south. By the 1980's to the mid-1990's, clustering of elevated rates was prominent across the southeast and south central areas, with relatively low rates throughout much of the northeast. Among white females, little geographic variation was evident in the 1950's, but thereafter relatively high rates began to appear in clusters along the Atlantic and Pacific coasts. For both sexes, consistently low rates were seen in the mountain states and the plains states. From the 1950's through the mid-1990's, rates among blacks were consistently elevated in northern areas and low across the south. The changes that have occurred in the geographic patterns of lung cancer coincide with regional trends in cigarette smoking, indicating opportunities for public health measures aimed at smoking prevention and cessation. (Devesa SS, Grauman DJ, Blot WJ, Fraumeni JF. Cancer surveillance series: Changing geographic patterns of lung cancer mortality in the United States, 1950 through 1994. *J Natl Cancer Inst* 1999;91:1040-1050) ■

A DCEG SUMMER INTERN'S EXPERIENCE

At the recent annual meeting of the Society for Epidemiologic Research, the award for the outstanding paper by a student went to Ms. Sascha Dublin of the University of Washington. After her presentation at the plenary session of the meeting, Ms. Dublin sent the following note to Linkage.

Starting with my junior year at Brown University, I had the good fortune to spend the summers of 1991, 1992, and 1993 working as an intern in the Division's Viral Epidemiology Branch. It was an eye-opening experience to be able to get a glimpse of many different areas of cancer-related research, from immunology and molecular epidemiology to clinical and behavioral studies. This experience sparked my curiosity and made me more excited about upcoming courses, such as in immunology. In addition, I could not have asked for better mentoring from Dr. Jim Goedert and his colleagues. There was just the right balance of independence and support. I was encouraged to learn and explore, and to pursue my own ideas, yet my mentors gave me lots of feedback and guidance to help me better understand the data generated in various studies. Dr. Phil Rosenberg spent hours teaching me how to interpret the coefficients in my logistic regression analyses. That first summer culminated in the submission of an article that was eventually published in *AIDS Research & Human Retroviruses.*

Looking back, I am amazed at the time and attention that Jim, Phil, and many others were willing to share with a mere college junior who had little previous research experience. I am also amazed by the respect they gave to my ideas and the way that they treated me as a valued member of the group. Jim and Bill Blattner encouraged me to apply to medical school and wrote letters of recommendation on my behalf. I am convinced that their support was one of the most important factors in my admission to the M.D./Ph.D. program at the University of Washington, where I am currently a seventh-year student. (I'm getting my Ph.D. in epidemiology, hopefully within the next few months!) My experience at NCI has shaped my education and my career so much that I simply cannot imagine what my life would be like today without it.

Sascha Dublin

DR. KLAUSNER SPEAKS AT DCEG TOWN MEETING

Dr. Richard Klausner, Director, NCI, addressed the DCEG Town Meeting on April 16. After the presentation of awards, he shared his thoughts about the challenges facing NCI. In particular, he emphasized the need to recognize that scientific progress, like all other endeavors, is never entirely risk free. Science works best when world-class investigators are given both the resources and freedom to pursue research. Dr. Klausner characterized DCEG as the place where investigators are acknowledged as the undisputed leaders in their field, and he challenged the Division to continue to be at the forefront of molecular epidemiologic research.

Dr. Klausner said that he has spent a great deal of time communicating his vision for the NCI to the extramural community, which has received his message with great enthusiasm. He expressed the hope that the intramural program will also share in this excitement. For DCEG, the remarkable advances in cancer genetics provide an unparalleled opportunity to unravel the environmental determinants of cancer. He urged the Division to consider how best to respond to this challenge, and noted that DCEG is uniquely positioned to lead the nation and the world in setting research priorities.

In regard to the NCI Bypass Budget, Dr. Klausner stressed the importance of this mechanism in communicating the extraordinary research opportunities for investment to the U.S. Congress and the nation. Since NCI has met its goal in reducing the proportion of the intramural research budget relative to the extramural program, it is now possible to allocate new investment money to the intramural divisions in high-priority areas of research, such as molecular epidemiology. Dr. Klausner stressed the need for DCEG to continue its collegial partnership with the extramural divisions to promote and maintain scientific excellence throughout the Institute.

Following his talk, Dr. Klausner opened the floor for questions and addressed issues such as technology transfer and the ethical questions related to collaborations with commercial organizations. He

agreed on the need to establish an NCI recruiting office to make the Institute more competitive with the extramural community in recruiting highly talented investigators. Recruitment should be facilitated by the $100 million committed to upgrading the buildings on the main campus in which NCI researchers work. Dr. Klausner mentioned that he has been active in promoting international initiatives, including establishing cancer consortia in the Middle East and Ireland, which are viewed by the State Department as unique opportunities to promote international cooperation as well as scientific discovery.

Dr. Klausner noted that issues surrounding informed consent continue to be formidable potential barriers to molecular epidemiology research, and that their resolution is jeopardized by heated philosophical debate. He favors an approach similar to that used at the Asilomar Conference, in which there can be open discussion about ensuring medical confidentiality in a way that is compatible with the public good. Dr. Klausner stressed that Congress is not attempting to impede molecular epidemiologic research in drafting legislation to safeguard the privacy of patients. He stressed that DCEG is in a unique position to bridge the gap with advocacy groups by explaining common interests in gaining a fuller understanding of environment-gene interactions in cancer etiology. Dr. Klausner noted that we should welcome the interest of these groups and seize the opportunity to form partnerships that benefit all sides. He concluded the Town Meeting by challenging the Division to take what knowledge is already available about environment-gene interactions and communicate it to all interested parties. By promoting the fullest possible understanding of the role of genes and the environment in contributing to the burden of cancer, Dr. Klausner said that we will win the confidence of the American public and Congress, thereby underscoring and justifying the wisdom of their investment in the National Cancer Program. ■

Cathy McClave

DCEG AWARDS

At the April 16 DCEG Town Meeting, Dr. Richard Klausner presented the following awards to members of the Division.

Awards for Exemplary Service

Two scientists received the 1998 DCEG Award for Exemplary Service, which is given for sustained research accomplishments along with outstanding service to the Division and Institute.

Dr. Robert Tarone is an outstanding and dedicated scientist who initiates independent research, works as a collaborator, and serves generously as a consultant and member of various advisory groups. His statistical and epidemiological research has significantly contributed to advances in cancer etiology, while his expertise in service activities has been critical to the success of NCI and NIH research programs.

Dr. Margaret Tucker is renowned for her expertise in genetic cancer epidemiology and as an advisor on issues of critical importance to biomedical research. She has made significant scientific discoveries toward understanding host factors affecting cancer susceptibility, while contributing to service activities having national and international significance.

Outstanding Mentor Awards

Two investigators received the 1998 DCEG Outstanding Mentor Award, which honors scientists who have been selected by the Division's fellows for extraordinary mentoring talents.

Dr. Martha Linet was cited by the fellows as being a remarkably perceptive mentor, with an acute ability to assess the interests of young investigators and provide them with scientific opportunities.

Dr. Catherine Schairer was cited by the fellows for her exceptional ability to demonstrate by example the appropriate approaches for resolving difficult methodologic issues.

Awards for the Outstanding Research Paper by a Fellow

Two DCEG fellows received the 1998 Award for the Outstanding Research Paper by a Fellow, which honors fellows for the impact, innovation, and clarity of thought and language of their reports in the scientific literature.

Dr. Monica Granovsky was recognized for her paper reporting on a case series of children with HIV-associated malignancies. She clearly defined the spectrum of HIV-related malignancies in children, and pointed toward the need for multicenter trials to determine which therapies will be most effective in treating these cancers.

Dr. Susan Sturgeon was recognized for her paper evaluating the relation between exposure to organochlorine compounds and risk of endometrial cancer. Although this tumor is considered estrogen-dependent, it was not associated with these compounds, which have estrogenic properties.

Intramural Research Awards

Two investigators received DCEG Intramural Research Awards in fiscal year 1999. Funding is provided for innovative and interdisciplinary collaborative research projects that cross the usual organizational boundaries and further the mission of the Division and Institute.

Dr. Bu-Tian Ji received an award to examine the relation of organochlorine compounds, cytochrome P4501A1 polymorphisms, and risk of breast cancer.

Dr. Mary Ward received an award to compare carpet dust measurements with remote-sensing data and geographic information systems as methods for estimating residential exposure to crop pesticides.

Customer Service Award

NCI's Office of Management gave the Customer Service Award to **Ms. Lori Henry,** an Administrative Officer, for exceptional efforts in coordinating the DCEG move from Executive Plaza North to Executive Plaza South. Her talents in drafting, design, office storage systems, interior decorating, budgeting, supervising, and other areas contributed greatly to the success of the move. In addition, Ms. Henry received a cash award from DCEG in appreciation of her efforts.

Combined Federal Campaign Awards

The Division received two important awards for its extraordinary support of the 1998 Combined Federal Campaign (CFC). **The President's Award,** which is the highest honor for any federal organization, was given to DCEG in recognition of achieving an average gift of $150 per full-time permanent employee and of exceeding a 75 percent participation rate. The Division also received an award for attaining 100 percent of its goal. **Ms. Catherine Fox,** who served as the DCEG keyworker, received a **Special Service Award** for her outstanding efforts in coordinating the CFC activities for the Division. ■

CHIEFS SELECTED FOR NEWEST DCEG BRANCHES

Congratulations to Dr. Arthur Schatzkin, who has been selected to head the Nutritional Epidemiology Branch. Dr. Schatzkin received a B.A. degree from Yale University, an M.D. degree from the Downstate College of Medicine of the State University of New York, and M.P.H. and Dr.P.H. degrees from Columbia University. He is board certified in internal medicine and in preventive medicine and public health. He began work at NCI in 1984 as a senior staff fellow in the Cancer Prevention Studies Branch of the Division of Cancer Prevention and Control, becoming a senior investigator in 1988. Dr. Schatzkin joined DCEG's Nutritional Epidemiology Branch in 1997. His research focuses on the nutritional causes and prevention of cancer. Dr. Schatzkin's ideas on the role of diet and nutrition in the etiology of cancer and his vision for the Nutritional Epidemiology Branch will be presented in the next issue of *DCEG Linkage*.

Congratulations also to Dr. Mark Greene, who rejoins the Division as the first chief of the Clinical Genetics Branch. Dr. Greene obtained a B.A. degree from Yale University and an M.D. degree from Tufts University School of Medicine, and he is board certified in internal medicine with a subspecialty in medical oncology. He was an investigator at NCI from 1975 through 1985, and deputy chief of the Environmental Epidemiology Branch at the time of his departure. In 1991, Dr. Greene joined the Mayo Clinic in Scottsdale, Arizona, where he was the principal investigator for the Familial Cancer Center. He was also a collaborator on clinical trial cooperative groups and the University of Arizona Cancer Center's Chemoprevention of Skin Cancer Program project. A profile of Dr. Greene will appear in the next issue of *DCEG Linkage*, along with his views on the direction of research in the Clinical Genetics Branch.

ACTIVITIES OF THE DCEG COMMITTEE OF SCIENTISTS

The Committee of Scientists (COS) has been working on a number of issues related to its mandate for improving communications, enhancing the scientific environment, and providing opportunities for career development within DCEG. To more effectively tackle longer term efforts, the length of COS membership was recently increased from 12 to 18 months. Ms. Kristin Kiser, who heads the new DCEG Office of Education, has joined COS as a nonvoting member. Special thanks to Ms. Sam Nhan for her administrative support of the committee.

COS Forum

The COS Forum series was launched with a successful Town Meeting that featured Dr. Joseph Fraumeni's presentation on "The state of DCEG." The COS Forum is intended to promote Division-wide discussion regarding the scientific environment within DCEG. Forums will convene approximately quarterly as part of the Thursday morning DCEG Seminar Series. COS welcomes ideas for future forum topics and speakers.

Career Planning and Mentoring of Fellows

To meet requests from fellows for more assistance with career planning and job placement, COS has begun discussions on how best to proceed. The DCEG Office of Education is one important resource, and COS will work closely with Ms. Kiser in identifying and developing new services (e.g., job search skill workshops, database of job listings, career counseling). In addition, COS is collaborating with the Office of Education and Dr. Shelia Zahm to conduct a fellows follow-up study, which will survey former DCEG fellows about the strengths and weaknesses of the Division's training programs. This effort will also help identify DCEG alumni who may be helpful in job placement and recruitment of fellows.

COS encourages mentors to be actively involved in career counseling of fellows. Beside providing scientific training, mentors should:

- Take the initiative early in the fellowship period to talk with the fellow about career plans;
- Recognize and discuss the potential conflict of interest between the mentor's desire to maximize scientific productivity and the optimal fellowship period for the fellow;
- Encourage the fellow to explore employment opportunities outside of DCEG, when appropriate;
- Help fellows network by introducing them to colleagues at meetings and in other ways; and
- Help fellows write curriculum vitae, cover letters, and other materials to promote their careers.

Branch Administration and Morale

The site visit currently provides the only formal mechanism for DCEG scientists to provide input into branch administration, synergy, and morale. As part of its charge to evaluate branch administration, the site visit team gives each principal investigator the opportunity to address these issues during a private session. COS believes that this approach is inadequate because the 4-year site visit cycle is too long for the timely assessment of branch operations; principal investigators may be reluctant to discuss problems with site visitors; and fellows, staff scientists, and other branch members are excluded from the process.

COS recommends that DCEG institute an annual evaluation of branch administration and morale in which all branch members would have the opportunity to contribute anonymously. Such an evaluation would be consistent with a recent proposal for monitoring mentors (Djerassi. *Nature* 1999;397:291) and with practices employed by many businesses. The evaluation would solicit constructive comments, encourage identification of obstacles to a well-functioning branch, and serve as a means for improving operations. Neither an individual evaluation nor its summary would become part of personnel records.

At any time, DCEG scientists can discuss confidentially their concerns regarding branch administration and morale directly with any member of the Division's senior leadership.

Management Skills

Branch chiefs and many other DCEG scientists have considerable management responsibilities. For example, branch chiefs face the daunting task of creating a synergistic scientific environment among highly educated individuals who themselves are judged on the basis of their independence. Many principal investigators and staff scientists oversee complex studies that require the coordination of many contractors and collaborators. Although DCEG investigators have extensive scientific training, most lack training in managing people and resources.

COS recommends that DCEG develop a training program designed to help branch chiefs and other scientists manage people, time, and resources more effectively. Emphasis should be placed on methods for enhancing effective teamwork. The training should be tailored to the unique situation of DCEG's intramural investigators and based on a careful assessment of the needs of individual scientists.

New COS Members

Drs. Robert Clifford (Laboratory of Population Genetics), James Lacey (Environmental Epidemiology Branch), and Mary Ward (Occupational Epidemiology Branch) have been newly appointed as COS members. The names and terms of the other members, as well as COS's charter, can be accessed on DCEG's intranet site at *http://intranetdceg.ims.nci. nih.gov/scientists.html.* ■

Tom O'Brien

SEARCHING FOR THE ROOTS OF THYROID CANCER

Sometimes you need a little help from your friends. That saying proves especially true when trying to tease out the causes of a relatively rare cancer such as thyroid cancer. For rare cancers, it is a formidable challenge to conduct a single study that will adequately describe the role that hormones, genes, and environment may play in the development of the disease. Instead, Dr. Elaine Ron, Chief of the Radiation Epidemiology Branch, joined forces with colleagues around the world to combine their separate efforts and resources.

"I first became interested in thyroid cancer in graduate school, where I ended up doing my dissertation on thyroid cancer and radiation," Ron said. "I just got interested in the disease itself because it's rare and it's much more common in women than in men, the histologic types are so different, and radiation plays such an important role." Thyroid cancer incidence rates are generally lower than 3 per 100,000 for men and about 5 per 100,000 for women worldwide. The majority of these cancers are well-differentiated, and the 5-year survival rates are extremely high. To date, the only well-defined risk factor for developing thyroid cancer is radiation exposure in childhood.

Dr. Ron and her colleagues in Italy—Dr. Eva Negri at the Instito di Ricerche Farmacologiche Mario Negri in Milan, Dr. Silvia Franceschi at the Centro di Riferimento Oncologico in Aviano, and Dr. Carlo La Vecchia at the Universita degli Studi di Milano—had two choices in trying to pool the results of 14 different research efforts. They could perform a meta-analysis on the results published in the literature, or they could convince the researchers who conducted the original studies to contribute their raw data for a pooled analysis.

The major problem associated with a meta-analysis is that the researchers are limited to the published data from studies using heterogeneous methods and different questionnaires. As a result, the data as published in the literature often do not allow comparisons across studies. In contrast, by analyzing raw data, researchers would be able to at least reformat the data in a uniform manner to allow systematic comparisons. Dr. Ron chose the latter method; she contacted the researchers to get the raw data and, "everybody, luckily, agreed. It is a very, very collegial group and everyone just jumped in."

With raw data in hand from studies conducted in China, Japan, the United States, and Europe, the global team of researchers could examine 2,725 cases of thyroid cancer and 4,776 controls with a variety of environmental exposures. Dr. Ron's colleagues in Italy conducted the bulk of the statistical analysis. The results of the collaboration are currently being published in a series of papers in *Cancer Causes and Control.* (Negri E, Ron E, Franceschi S, Dal Maso L, Mark SD, Preston-Martin S, McTiernan A, Kolonel L, Kleinerman R, Land C, Jin F, Wingren G, Galanti MR, Hallquist A, Glattre E, Lund E, Levi F, Linos D, Braga C, La Vecchia C. A pooled analysis of case-control studies of thyroid cancer. I. Methods. *Cancer Causes Control* 1999;10:131-142; Negri E, Dal Maso L, Ron E, La Vecchia C, Mark SD, Preston-Martin S, McTiernan A, Kolonel L, Yoshimoto Y, Jin F, Wingren G, Rosaria Galanti M, Hardell L, Glattre E, Lund E, Levi F, Linos D, Braga C, Franceschi S. A pooled analysis of case-control studies of thyroid cancer. II. Menstrual and reproductive factors. *Cancer Causes Control* 1999;10:143-155; La Vecchia C, Ron E, Franceschi S, Dal Maso L, Mark SD, Chatenoud L, Braga C, Preston-Martin S, McTiernan A, Kolonel L, Mabuchi K, Jin F, Wingren G, Galanti MR, Hallquist A, Lund E, Levi F, Linos D, Negri E. A pooled analysis of case-control studies of thyroid cancer. III. Oral contraceptives, menopausal replacement therapy and other female hormones. *Cancer Causes Control* 1999;10:157-166) The first three papers were published in April 1999, and subsequent papers have been accepted for publication.

Because women are about three times as likely as men to develop thyroid cancer, many researchers have hypothesized that hormonal differences play an important role in the disease. Thyroid-stimulating hormone secretion is reportedly elevated during puberty, pregnancy, and oral contraceptive use; puberty and the menstrual cycle produce changes in the thyroid gland; and estrogen receptors can be found in thyroid tumors. In addition, the reported association between thyroid cancer and breast cancer suggests a shared etiology; exposure to estrogen is linked to breast cancer. However, individual studies conducted on thyroid cancer have not provided convincing evidence that hormonal and reproductive factors play a role in the development of thyroid cancer.

Dr. Ron and her colleagues focused their first analyses of combined, raw data on examining what role age at menstruation, age at menopause, and factors related to childbirth might have on the risk for thyroid cancer. They also looked at how oral contraceptive use and hormone replacement therapy may be associated with thyroid cancer. Much to the surprise of the collaborators, these factors proved inconsequential to the development of thyroid cancer. "There was some indication that late age at first child birth could be a factor or maybe recent use of oral contraceptives," Ron said. "But, none of the associations was very strong."

Although they failed to prove a clear link between female hormones and thyroid cancer, the collaborators did discover a significant risk for developing thyroid cancer among persons who had benign thyroid disease. Not all benign thyroid disorders are the same, however. Hypothyroidism conferred no increased risk for thyroid cancer, but goiters raised the risk 5-fold among women and almost 40-fold among men. Thyroid cancer was most strongly associated with benign nodules or adenomas: women with such a history had a risk of thyroid cancer 30 times that of women without previous benign nodules or adenomas. Among men, 18 cases had prior benign nodules or adenomas, but none of the controls did. The researchers concluded that, apart from radiation in childhood, goiters and benign nodules or adenomas are the strongest risk factors for thyroid cancer. It is not clear whether the associations are causal. Dr. Ron suggested that some of the benign nodules could have been undetected thyroid cancer in the first place.

The researchers also looked at the risk that height and weight might confer on risk of thyroid cancer, but there were no clear associations. A search will also be made for other possible factors that could affect risk, such as diet, particularly iodine-rich foods and cruciferous vegetables. "Our most challenging area in looking at these data is going to be diet," Ron said. "Only some studies have dietary data, and the quality varies considerably. In a Hawaiian study, a detailed dietary history was collected, but in others only a few food items were studied."

Not all risk factors for thyroid cancer will be clarified by this pooled analysis. It is well established that radiotherapy during childhood confers a higher lifelong risk for thyroid cancer. However, researchers have not been able to determine whether low-dose radiation from diagnostic x-rays increases risk. Furthermore, because the collaborative studies are all case-control studies, the data on diagnostic radiation are subject to recall bias. In addition, most of the studies were not focused on diagnostic radiation, the questionnaires were not designed to collect sufficiently detailed information, and the investigators did not verify the reported diagnostic procedures. "As a result, we had to make the decision that we wouldn't examine diagnostic x-rays. We might, however, look at therapeutic radiation because it is less subject to recall bias and is easier to verify," Ron said.

The collaborative analysis has also offered the researchers a particular opportunity to learn more about medullary carcinoma, a rare histologic type of thyroid cancer with a relatively strong genetic component and little gender difference. Because several studies were restricted to papillary carcinoma, there were only 63 cases of medullary carcinoma in the entire collaborative project. Yet, several interesting risk factors were identified. The researchers are now trying to retrieve medical records for these cases to look for unique pathologic features and to identify cases with a high probability of a genetic cause. ■

Lisa Seachrist

RISE IN KIDNEY CANCER FUELS NEW STUDY

From personal computers to cell phones to the internet, the world has experienced a dizzying profusion of new technologies since 1973 when the Surveillance, Epidemiology, and End Results (SEER) program began tracking the rates at which Americans fall victim to cancer. Among the most significant technological advances in medicine have been those that allow physicians to image the human body with remarkable precision.

Magnetic resonance imaging, ultrasound, and computer-assisted tomography scans have dramatically increased physicians' abilities to detect a number of presymptomatic tumors, yet the very use of these technologies can result in temporary surges in cancer incidence. Dr. Wong-Ho Chow and her colleagues described the rising incidence of kidney cancer in a recent issue of the *Journal of the American Medical Association*. (Chow WH, Devesa SS, Warren JL, Fraumeni JF Jr. Rising incidence of renal cell cancer in the United States. *JAMA* 1999;281:1628-1631)

Looking at nine population-based registries in the SEER program, Dr. Chow and her co-workers found a rapid increase in the incidence of both early and late-stage renal cell cancers. Although use of new technologies may have caused some detection bias, the increases in the incidence of renal cell cancer could not be explained entirely by earlier diagnosis of the cancers. The researchers found that mortality from kidney cancer increased as well in all races and genders. Like many cancers, the prognosis for kidney cancer is much better when the cancer is caught early. Thus, the researchers concluded that increases in renal cell cancer incidence could not be attributed entirely to imaging technology catching the cancers earlier, when they are most treatable. "The increased incidence is probably not artifactual," Dr. Chow said. "We really need to have a better understanding of risk factors for this cancer and reasons for the increase."

Even more startling, this work showed great divergence between the increase in renal cell carcinoma incidence among blacks and whites. Blacks experienced a 4-percent annual increase in the age-adjusted renal cell cancer incidence rate, and whites experienced a 2-percent annual increase. "Among blacks, the increase in renal cell cancer incidence generally outpaces that of any other cancer site," Dr. Chow said. "This is a rapid increase, for reasons that we still don't understand, because none of the previous studies has included enough African Americans to examine their risk factors separately. Probably, blacks will have similar risk factors as . . . whites, but the extent of contribution from each risk factor is unclear."

The risk factors for this cancer include cigarette smoking, obesity, and hypertension or the use of medications to control hypertension. Some studies have associated an increase in renal cell cancer risk with high blood pressure, while others have linked this risk to the use of medications to control high blood pressure. It's not clear whether hypertension or the medications used to control it play the predominant role in conferring risk for this cancer.

To evaluate risk factors for renal cell cancer among blacks and whites in the United States, Dr. Chow and her colleagues are designing a population-based, case-control study to include a large number of blacks. Dr. Chow noted that other studies have indicated that blacks are known to have a higher prevalence of hypertension, and perhaps less control over their blood pressure. She intends to explore other risk factors as well (e.g., diet and reproductive history), genetic polymorphisms, and gene-environment interactions. ■

Lisa Seachrist

MAGNETIC FIELD EXPOSURE AND RISK OF LEUKEMIA IN CHILDREN

Two decades ago, researchers reported that children who died from leukemia were two to three times more likely to have lived within 40 meters of a high-current power line. A series of studies followed in an attempt by researchers to clarify the relation between exposure to the 60-cycle-per-second (60-Hz) magnetic fields produced by alternating current from residentially proximate power lines and the development of acute lymphoblastic leukemia (ALL) in children. However, the results of these studies were conflicting.

The difficulties in evaluating the relation between residential magnetic field exposure and risk of childhood leukemia are multifold: It is difficult to establish accurately the exposure a child received to magnetic fields after the fact; there is no biological model or mechanism to establish which exposures, exposure metrics, or time periods are relevant; and many potential biases can affect the results. Ten years

of conflicting reports led investigators from the NCI, led by Dr. Martha Linet of the Radiation Epidemiology Branch (REB), to collaborate with those from the Children's Cancer Group (CCG) in a comprehensive case-control study of the various postulated risk factors for childhood leukemia. This study included a residential magnetic field measurement component and an interview with the mothers to evaluate risks to their offspring from electrical appliance exposures during the prenatal and postnatal periods.

The ability to estimate cancer risks associated with magnetic fields, an ever-present exposure, requires a large-scale study with accurate and reproducible exposure assessment. Furthermore, to have confidence that there is truly no relation (i.e., null effect) between the exposure and risk of cancer, the most rigorous methods for data collection, exposure assessment, and statistical analysis in more than a single study are required.

The magnetic field exposure of ALL cases was measured as soon as possible after diagnosis and compared with that of healthy control children. Beginning in 1991, data collectors for the NCI/CCG study visited study participants' current and former homes to measure 24-hour exposure to magnetic fields in the children's bedrooms and 30-second exposure in the center of those bedrooms, the family room, the kitchen, the room in which the mother slept during her pregnancy, and within 3-foot radius outside the front door. A "wire code," which does not require an in-home measurement, was assigned as a surrogate measure for magnetic fields.

The exposure measurements covered current and former homes in which each child had lived for at least 70 percent of his or her life, or for older children, for 70 percent of the 5 years immediately before diagnosis. The NCI/CCG study ended up comparing the magnetic field exposures of 638 children with leukemia and 620 control children. About 58 percent of the children were under age 5.

In the July 3, 1997, issue of the *New England Journal of Medicine* (*NEJM*), Dr. Linet and her colleagues reported that they found little evidence that risk of ALL was increased among children residing in residences with summary high measured time-weighted average magnetic fields or high wire code levels. (Linet MS, Hatch EE, Kleinerman RA, Robison LL, Kaune ET, Friedman DR, Severson RK, Haines CM, Hartsock CT, Niwa S, Wacholder S, Tarone RE. Residential exposure to magnetic fields and acute lymphoblastic leukemia in children. *N Engl J Med* 1997;337:1-7)

"Most members of the public were greatly relieved when our paper was published," Linet said. "There was just a small fraction of the public and scientists who disagreed with our conclusions. Even those persons generally praised the quality and meticulousness of the study."

An editorial accompanying the report praised the study and suggested that no additional research resources be committed to further investigations into the relationship of childhood cancer and residential magnetic field exposures. The editor cited the absence of any laboratory or animal model or a body of convincing epidemiologic research linking residential electromagnetic field exposure and childhood cancer as a main reason for the suggestion. However, several scientists wrote letters to the *NEJM* criticizing the editorial's conclusions and urging further epidemiologic research.

Following their report in the *NEJM*, Dr. Linet and her colleagues have continued to examine other aspects of the data from the case-control study. They have considered the effects on risk of measuring magnetic fields in fewer homes per subject, evaluated alternative metrics, and searched for potential biases that may have affected the outcome of their original study.

A possible reason for a lack of a relation between exposure and risk was a misclassification of wire code designations that attenuated the risk estimates. To evaluate this possibility, Dr. Robert Tarone, a statistician in the Biostatistics Branch, led a detailed analysis of the wire code data. Excellent reproducibility between two wire coders was found for each of the three classifications of codes. The different wire codes were found to serve as proxy measurements for magnetic field exposure to similar degrees, as was observed in earlier studies. Although previous studies had used wire code classifications to establish the association between magnetic field exposure and risk of ALL, Dr. Tarone and his

colleagues concluded that there was little support for the hypothesis that Dr. Linet's study results had been affected by misclassification of wire code designations. (Tarone RE, Kaune WT, Linet MS, Hatch EE, Kleinerman RA, Robison LL, Boice Jr JD, Wacholder S. Residential wire codes: reproducibility and relation with measured magnetic fields. *Occup Environ Med* 1998;55:333-339)

Dr. Elizabeth Hatch, an epidemiologist in REB, led an effort to evaluate the risk of ALL in relation to use of electrical appliances during pregnancy and in childhood. The investigators focused on appliances most likely to produce high exposure to magnetic fields: electric blankets and mattress pads, heating pads, waterbeds, television sets, video games, computers, microwave ovens, sewing machines, hair dryers, curling irons, humidifiers, and electric clocks. An increased risk was observed among children whose mothers used an electric blanket or mattress pad during pregnancy and among children exposed postnatally to electric blankets and mattress pads, hair dryers, arcade video machines, and television-connected video games. However, no dose-response was found for years of use or frequency of use for most of the appliances. As a result, Dr. Hatch and her colleagues concluded that it was unlikely that the use of electrical appliances was associated with risk of ALL. (Hatch EE, Linet MS, Kleinerman RA, Tarone RE, Severson RK, Hartsock CT, Haines C, Kaune WT, Friedman D, Robison LL, Wacholder S. Association between childhood acute lymphoblastic leukemia and use of electrical appliances during pregnancy and childhood. *Epidemiology* 1998;9:234-245)

Because their analyses found increasing risk of ALL associated with increasing hours of television viewing by children, Dr. Hatch and her colleagues carried out a small measurement study to examine a broad range of magnetic field exposures at different distances from a television set, including extremely low frequency (ELF range, 0 to 3,000 Hz), very low frequency (VLF, 3,000 to 30,000 Hz), and low frequency (LF, 30,000 to 300,000 Hz). Taking into account the distance that children typically sit away from a television set, their exposure to ELF was no different than background, but to VLF and LF it was slightly higher. (Kaune WT, Miller MC, Linet MS, Hatch EE, Kleinerman RA, Wacholder S, Mohr AH, Tarone RE, Haines C. Children's exposure to magnetic fields produced by television sets used for viewing programs and playing video games. *Bioelectromagnetics,* in press) Dr. Linet noted that televisions "do not appear to contribute much to children's overall exposure to [ELF] residential magnetic fields, but exposures from VLF and LF should be considered in any future epidemiologic studies of electrical appliances that may incorporate magnetic field measurements." She added that "we don't know if there is any risk associated with VLF and LF exposure because this has not been investigated in an epidemiologic study."

To further evaluate risk associated with living near power lines, the NCI team analyzed in depth the wire code data for 408 case-control pairs. The team, led by Ms. Ruth Kleinerman, an epidemiologist in REB, did not find any association between ALL with distance from the nearest power line within 40 meters of a house, or with an exposure index that accounted for the contribution of all nearby power lines. (Kleinerman RA, Linet MS, Hatch EE, Wacholder S, Tarone RE, Severson RK, Kaune WT, Friedman DR, Haines CM, Muirhead CR, Boice Jr JD, Robison LL. Magnetic field exposure assessment in a case-control study of childhood leukemia. *Epidemiology* 1997;8:575-583)

Dr. Dalsu Baris, an epidemiologist in the Occupational Epidemiology Branch, led an analysis to investigate the impact of measuring only a single home, then imputing estimates for a second home when relevant to exposure measurement. She found some correlation between the measured values for the two homes, indicating a lack of independence between the them. Differences in average exposure occurred between current and former homes of control subjects, and between homes lived in longer versus those lived in for shorter periods of time. All methods using measurements from one home in conjunction with imputed values for the second home led to marked attenuation of risk estimates associated with exposures in the highest category, particularly when actual measurements were used from homes resided in at diagnosis. These findings argue against attempting to estimate lifetime magnetic field exposure by using imputed values derived from homes resided in at the time of diagnosis to fill in gaps from unmeasured homes lived in previously. (Baris D, Linet MS, Tarone RE, Kleinerman RA, Hatch EE, Kaune WT, Robison LL, Lubin J, Wacholder S. Residential exposure to magnetic fields: an empirical examination of alternative measurement strategies. *Occup Envrion Med* 1999;56:562-566)

Without a biological or laboratory model to explain how magnetic fields might cause ALL, no single exposure metric can be considered *a priori* the most appropriate. Consequently, a variety of exposure metrics was examined to tease out those that may be most relevant to establishing an association between magnetic field exposure and risk of ALL. In an analysis led by Dr. Ansi Auvinen, a visiting associate in REB, the 24-hour measures of central tendency (such as time-weighted average or median measurements), and particularly the 10 pm to 6 am interval (nighttime) 8-hour measurements (the latter showing a slightly higher association with ALL), were found to give the highest odds ratio estimates. Other measures such as peak exposure, threshold values, measures of short-term variability, and spot measurements showed little association with risk of childhood ALL. (Auvinen A, Linet AA, Hatch EE, Kleinerman RA, Robison LL, Kaune WT, Misakian M, Niwa S, Wacholder S, Tarone RE. Extremely low frequency magnetic fields and childhood acute lymphoblastic leukemia: an exploratory analysis of alternative exposure metrics. Unpublished paper)

In an analysis of selection bias and confounding, Dr. Hatch and colleagues compared risk of ALL for study subjects who participated in part of the data collection versus those who had participated in only some parts. Risk of ALL among persons living in homes with high wire codes increased by 23 percent when partial participants were excluded. Partial participants tended to be characterized by lower socioeconomic status than those who participated fully, suggesting a potential for selection bias. Control subjects were more likely than case subjects to be partial participants. Although Dr. Hatch and her co-workers suggested that selection bias may be a more important issue than confounding, they could not evaluate this issue conclusively because of the lack of exposure data for nonparticipants. Future studies, they advise, should strive to increase the participation rate of control subjects to overcome this study weakness. (Hatch EE, Kleinerman RA, Linet MS, Tarone RE, Kaune WT, Auvinen A, Baris D, Wacholder S. Residential wiring codes and magnetic fields: do confounding or selection factors distort findings of EMF studies? Unpublished paper)

NCI researchers point out that the controversy about magnetic field exposure and risk of cancer arose exclusively from epidemiologic investigations. Dr. Tarone noted that "Although 20 years have passed since the first epidemiologic study linking magnetic field exposure and cancer, there is still no credible laboratory or animal evidence to support a role for magnetic fields in the etiology of cancer. All comprehensive reviews of the field have come to a similar conclusion—there is no compelling evidence of adverse health effects due to magnetic field exposures, except for a few epidemiologic findings that can not be completely ignored." He added that "the field of epidemiology has a lot at stake in this controversy." ■

Lisa Seachrist

INTERNATIONAL CONFERENCE ON OCCUPATIONAL CANCER AMONG WOMEN

The Women's Health: Occupation, Cancer, and Reproduction Conference was held in Reykjavik, Iceland, in May 1998 to assess cancer and reproductive risks among working women, discuss methodological challenges in occupational studies of women, and stimulate and enhance future research related to these and other aspects of women's health and occupation. Proceedings of the conference have been recently published, as a supplement of the *American Journal of Industrial Medicine* (1999;36:1-222).

The conference, formally opened by Mr. Olafur Ragnar Grimsson, President of Iceland, expanded on themes presented at an earlier conference, Women's Health: Occupation and Cancer, organized by DCEG and held in Baltimore in 1993. The international meeting was held at the initiative of the Icelandic Medical Department of the Administration of Occupational Safety and Health in close collaboration with the NCI, the International Agency for Research on Cancer, and other cosponsors from Europe, Iceland, Scandinavia, and

the United States. Seven DCEG scientists gave presentations: keynote speaker Dr. Aaron Blair, Dr. Mustafa Dosemeci, Dr. Capri-Mara Fillmore, Ms. Gloria Gridley, Dr. Ellen Heineman, Dr. Sandra Petralia, and organizing committee member Dr. Shelia Zahm.

Occupational exposures are thought to account for about 5 percent of human cancer in developed countries. This estimate, however, is derived from research that has focused almost entirely on men and on exposures sustained in the 1950's and 1960's. Since that time, there have been dramatic changes in the employment patterns of women, which may have increased the burden of occupational cancers among women. Many more women are in the workforce, the number of years they spend working outside the home has increased, and more women are employed in jobs that may involve hazardous exposures. These changes underscore the need for a more thorough evaluation of cancer risk among working women and a reassessment of the proportion of their cancer burden that may be attributable to occupational exposures.

In her opening remarks, Dr. Zahm, who cochaired the Baltimore conference 5 years earlier, noted a significant expansion of research in the field since that time. She cited the nearly twofold increase in the number of presentations and fourfold increase in exposure-specific studies at the Icelandic conference as evidence of advances in the study of occupational health among women.

Dr. Blair emphasized the need for studies focusing on women. In addition to female breast and gynecologic cancers, which cannot be studied in men, he noted that targeted research efforts may uncover gender differences in exposures, metabolism, susceptibility, and interactions. Dr. Blair also described methodologic issues related to study size, disease classification, exposure assessment, vital status determination, and confounding factors, all of which pose challenges and may require innovative approaches in studies of occupational cancer among women.

Several of the presentations at the conference evaluated the role of occupational exposures in the development of breast and ovarian cancers. Interesting findings were presented on exposures to solvents and risks of breast, kidney, and ovarian cancers; silica and esophageal cancer; lead and meningiomas; and other associations. A sizable fraction of lung cancer among nonsmoking women in Europe was linked to occupational exposures, as were leukemia and other lymphatic and hematopoietic malignancies.

Other speakers addressed recent developments and methodologic issues related to women's reproductive health and occupation; the use of administrative databases to evaluate economic activity, education, and socioeconomic and family status in relation to women's health; and the plight of working women in developing countries, where occupational health and safety lags far behind that of developed nations.

The conference demonstrated that the field of women's occupational health has made important strides. Where once the only data available were those generated as secondary analyses from studies primarily focused on men, studies are now designed and conducted specifically to address occupational risks among women. Although much has been accomplished, further methodologic improvements, larger studies, and better exposure assessment tools are needed for further advances in this field of research. ■

Cathy McClave

RECENT SCIENTIFIC REPORTS

Biostatistics Branch

Cancer in First-degree Relatives of Women with Early-onset Breast Cancer

A population-based incidence study was undertaken in Denmark to quantify the extent of familial risk of cancers of the breast, ovary, and other sites of first-degree relatives of women in whom breast cancer was diagnosed before age 40. From the 2,860 eligible cases, 14,973 parents, siblings, and offspring were identified from population registers and parish records. Women with early-onset breast cancer were at a nearly fourfold increased risk of developing a new cancer later in life, with the excess greatest for second cancer of the breast and for ovarian cancer. For mothers and sisters of women with early-onset breast cancer, risk of cancers of the breast and ovary was increased two- to threefold. Bilateral breast cancer and breast/ovarian cancer were very strong predictors of familial risks, with one in four female relatives predicted to develop breast or ovarian cancer by age 75. Mothers had a slightly increased risk of colon cancer, but not endometrial cancer. Although based on small numbers, the risk of breast cancer was also increased among fathers and brothers. These findings indicate that first-degree relatives of women with early-onset breast cancer are prone to ovarian cancer and to male and female breast cancer, but not to other tumor types that may share susceptibility genes with breast cancer. (Olsen JH, Seersholm N, Boice JD, Kjaer SK, Fraumeni JF. Cancer risk in close relatives of women with early-onset breast cancer—a population-based incidence study. *Br J Cancer* 1999;79:673-679)

Multiple Myeloma and Family History of Cancer among U.S. Blacks and Whites

A population-based case-control interview study was conducted in three areas of the United States to investigate whether family history of cancer contributes to risk of multiple myeloma and explains why blacks are at more than twice the risk than whites of developing disease. For blacks (cases=204; controls=954) and whites (cases=361; controls=1,150) combined, the risk of multiple myeloma was significantly elevated for subjects who reported a first-degree relative with multiple myeloma (odds ratio [OR]=3.7). Increased risk was also associated with a family history of any hematolympho-proliferative (HLP) cancer (OR=1.7), especially in a sibling (OR=2.3). The risk associated with familial occurrence of HLP cancers was higher among blacks than whites, but the difference was not statistically significant. These findings are consistent with previous studies indicating increased risk of multiple myeloma associated with a family history of HLP cancers; however, they do not explain the racial disparity in incidence rates. (Brown LM, Linet MS, Greenberg RS, Silverman DT, Hayes RB, Swanson GM, Schwartz AG, Schoenberg JB, Pottern LM, Fraumeni JF. Multiple myeloma and family history of cancer among blacks and whites in the U.S. *Cancer* 1999;85:2385-2390)

Cancer Risks among Hip and Knee Replacement Patients

With use of the Danish hospital discharge and cancer registries, a record linkage study of 22,997 osteoarthritis hip and 4,771 knee replacement patients was carried out to assess cancer risks associated with these implant procedures. No overall excess was found for cancer in either the hip cohort (average follow-up=6.9 years; standardized incidence ratio [SIR]=0.94) or the knee cohort (average follow-up=5.3 years; SIR=0.97). The SIRs below unity reflect mainly lower risk of cancers of the respiratory system and digestive tract, particularly stomach cancer (SIR=0.69 for hip; SIR=0.46 for knee). The low risk of gastric cancer may be due to the eradication of *Helicobacter pylori* infection by the frequent use of antibiotics in these patients. Neither implant group showed a significant excess risk of lymphohematopoietic cancers or tumors of the bone or connective tissue, but both groups had elevated risk of melanoma of the skin. (Olsen JH, McLaughlin JK, Nyren O, Mellemkjaer L, Lipworth L, Blot WJ, Fraumeni JF. Hip and knee implantations among patients with osteoarthritis and risk of cancer: A record-linkage study from Denmark. *Int J Cancer* 1999;81:719-722)

Analysis of Abrupt Changes in U.S. Cancer Mortality Trends

Statistical methods were used to evaluate cancer mortality trends from 1973 to 1995 for more than 15 anatomic sites for white and black males and females. The analysis used existing methods and a new weighted, piecewise linear regression with a stepwise forward selection procedure. For black males, the overall cancer mortality rate declined in the 1990's because of decreases in lung, esophageal, oral cavity, and prostate cancer mortality rates. No significant

declines were seen for cancer of the colon / rectum. For white males, the overall cancer mortality rate declined in the 1990's because of decreases in mortality rate of cancers of the lung and colon / rectum since the mid-1980's and decreases in prostate cancer mortality rate in the 1990's. Cancer mortality rates for all sites except the lung declined significantly in the 1990's for white females because of decreasing trends for cancers of the colon / rectum since the mid-1980's and of the breast in the 1990's. Similar declines were not observed for black females. These results demonstrate the value of these analytic procedures for identifying major changes in cancer mortality trends, and show a widening gap between blacks and whites in mortality trends for cancers of the breast and colon / rectum. (Chu KC, Baker SG, Tarone RE. A method for identifying abrupt changes in U.S. cancer mortality trends. *Cancer* 1999;86:157-169) ■

Environmental Epidemiology Branch

Accuracy and Distinctiveness of Cervical Lesion Diagnoses

A review of cervical smears was conducted to evaluate the accuracy and distinctiveness of the original diagnosis of *atypical squamous cells of undetermined significance, rule out high-grade squamous intraepithelial lesion* (ASCUS-rule-out-HSIL) among women participating in a 5-year prospective study of human papillomavirus (HPV) infection and squamous intraepithelial lesions. Women with ASCUS-rule-out-HSIL were compared with cases of *ASCUS, not otherwise specified* (ASCUS-NOS) and HSIL in the same cohort. On the basis of the review, 11 of 46 ASCUS-rule-out-HSIL diagnoses (24 percent) and 1 of 80 ASCUS-NOS diagnoses (1 percent) were reclassified as HSIL. With use of test results at enrollment in the cohort (1 to 4 years before diagnosis), HPV detection in women with ASCUS-rule-out-HSIL was intermediate in frequency between ASCUS-NOS and HSIL. These findings indicate that ASCUS-rule-out-HSIL is a distinct and more serious diagnosis than ASCUS-NOS, and suggest that women in this diagnostic group should be considered for colposcopic examination. (Sherman ME, Tabbara SO, Scott DR, Kurman RJ, Glass AG, Manos MM, Burk RD, Rush BB, Schiffman M. ASCUS-rule-out-HSIL: Cytologic features, histologic correlates, and human papillomavirus detection. *Modern Pathol* 1999;12:335-342)

HPV Infection and Risk of Squamous Intraepithelial Lesions

A prospective, nested case-control study was carried out within a large cohort of women to assess the risk of developing squamous intraepithelial lesions (SIL), cytologic precursors of cervical carcinoma, in relation to infection by a wide range of human papillomavirus (HPV) types. HPV-positive women who were cytologically normal at enrollment were 3.8 times as likely to subsequently develop low-grade SIL and 12.7 times as likely to develop high-grade SIL as women who were initially HPV-negative. Among the virus types, HPV16 was the most predictive of SIL. These findings support the hypothesis that HPV infection is the primary cause of cervical neoplasia. (Liaw KL, Glass AG, Manos MM, Greer CE, Scott DR, Sherman M, Burk RD, Kurman RJ, Wacholder S, Rush BB, Cadell DM, Lawler P, Tabor D, Schiffman M. Detection of human papillomavirus DNA in cytologically normal women and subsequent cervical squamous intraepithelial lesions. *J Natl Cancer Inst* 1999;91:954-960)

Risk Factors for Rapid-onset Cervical Cancer

A study was conducted to elucidate risk factors associated with rapid-onset cervical cancer among 483 women diagnosed with cervical cancer between 1985 and 1990 in Connecticut. On the basis of screening history information, slide review, and questionnaire data, 43 women were classified as having rapid-onset cervical cancer, 111 as possible rapid-onset cervical cancer, and 329 as normal-onset cervical cancer. Compared with normal-onset cases, rapid-onset cases tended to be younger and white, be diagnosed with adenocarcinomas or adenosquamous carcinomas, and have early-stage disease. Cases diagnosed as possible rapid-onset disease were likely to have a profile between those observed for rapid-onset and normal-onset cases. No excess risk of rapid-onset disease was associated with human papillomavirus infection among the 278 cases that had test results for the virus. In addition, no association was found with oral contraceptive use, cigarette smoking, number of pregnancies, or a maternal history of cervical cancer. These results suggest that the risk factors associated with the development of rapid-onset cervical cancer are similar to those for normal-onset disease. (Hildesheim A, Hadjimichael O, Schwartz PE, Wheeler CM, Barnes W, Lowell DM, Willett J, Schiffman M. Risk factors for rapid-onset cervical cancer. *Am J Obstet Gynecol* 1999;180:571-577)

*Oral Contraceptive Use in Relation to HER-2/*neu *Overexpression in Breast Cancer*

A population-based case-control study of breast cancer among women under age 45 examined the relation between oral contraceptive (OC) use and *HER-2/neu* protein expression status. Among the 371 incident cases of in situ or invasive breast cancer, 159 (43 percent) were immunochemically determined to be HER-2/neu-positive. With use of the ratio of the odds ratios of HER-2/neu status (HER-2/neu$^+$: HER-2/neu$^-$), little difference was found in risk of breast cancer for OC use of 6 months or more by expression status (age-adjusted odds ratio [OR]=1.29). Among women who started OC use at age 18 or younger, the difference in HER-2/neu status was significant (OR=2.39), but was attenuated in a multivariate model (OR=1.99). In analyses by estrogen receptor status, women starting use of OC at a young age were five times as likely to overexpress HER-2/neu protein if their tumors were estrogen receptor-negative. These findings confirm an earlier report of a relation between breast cancer risk and OC use when cases are stratified by *HER-2/neu* status, and suggest that early use of OCs may be a risk factor. (Gammon MD, Hibshoosh H, Terry MB, Bose S, Schoenberg JB, Brinton LA, Bernstein JL, Thompson WD. Oral contraceptive use and other risk factors in relation to HER-2/*neu* over-expression in breast cancer among young women. *Cancer Epidemiol Biomark Prev* 1999;8:413-419)

Power and Sample Size in Gene-environment Interactions

Appropriate power and sample size calculations are critical in designing epidemiologic studies of gene-environment interactions. Comparisons were made of approaches published for case-control studies and for general multivariate regression models for odds ratios. (Lubin JH, Gail MH. On power and sample-size for studying features of the relative odds of disease. *Am J Epidemiol* 1990;131:552-566) Under some circumstances, the comparisons of approaches for case-control studies revealed substantial differences that resulted from the highly restrictive characterization of the null hypothesis by Hwang et al. (*Am J Epidemiol* 1994;140:1029) and Foppa and Spiegelman, (*Am J Epidemiol* 1997;146:596) causing an underestimation of sample size and overestimation of power for testing gene-environment interactions. (Garcia-Closas M, Lubin JH. Power and sample size calculations in case-control studies of gene-environment interactions: Comments on different approaches. *Am J Epidemiol* 1999;149:689-692) Using the approach by Lubin and Gail, DCEG scientists are developing a computer program to perform sample size and power calculations for detecting additive or multiplicative scenarios of gene-environment interactions. The program will be available free of charge from NCI in early fall. ■

Genetic Epidemiology Branch

Melanoma Susceptibility Genes

In a consortium study, families at high risk of melanoma were screened for germline mutations in the predisposing *INK4A* and *CDK4* genes, as well as in the candidate susceptibility gene *p19 INK4D*, a cyclin-dependent inhibitor. Of the nine families with *INK4A* mutations, 8 of 22 cases (35 percent) were in families with three or more cases of melanoma and 1 of 20 cases (5 percent) was in a family with two cases. One family had a novel single Gly67Arg base pair substitution occurring at a site predicted to be critical to function. None of the multiple-case families had the rarer *CDK4* exon 2 mutation. *p19 INK4D* mutations were not found in any of the 48 melanoma-prone families screened, although its chromosomal location at a translocation site suggests that it may occur as a rare susceptibility gene. (Bishop JAN, Harland M, Bennett DC, Bataille V, Goldstein AM, Tucker MA, Ponder BAJ, Cuzick J, Selby P, Bishop DT. Mutation testing in melanoma families: INK4A, CDK4 and INK4D. *Br J Cancer* 1999;80:295-300)

Anticipation in Familial Chronic Lymphocytic Leukemia

Analyses were undertaken of clinical data on 27 families with two or more confirmed cases of chronic lymphocytic leukemia (CLL) to determine whether anticipation (i.e., earlier age-of-onset and/or increased severity of a genetic disease in successive generations) occurred between generations. Age-of-onset data were analyzed for 32 affected individuals in 13 families with cases of CLL in two generations. A highly significant difference was found in the average age-of-onset in the first generation (66.7 years) and that in the second generation (50.7 years). Further analyses revealed that the difference was not due to gender or diagnostic stage, and that preferential ascertainment of families with simultaneous onset of illness did not affect the results. These findings indicate significant anticipation in familial CLL. (Goldin LR, Sgambati M, Marti GE, Fontaine L, Ishibe N,

Caporaso N. Anticipation in familial chronic lymphocytic leukemia. *Am J Hum Genet* 1999;65:265-269)

Thyroid Carcinomas in Japanese Patients with Werner Syndrome

A study was undertaken to describe the peculiarities associated with thyroid carcinomas among Japanese patients with Werner syndrome (WS), an autosomal recessive disease characterized by premature aging and an excess of certain rare neoplasms. In a comparison of cell types from 23 WS patients (average age=39 years; male:female=1:2.3) and 19,446 patients with thyroid tumors (average age=49 years; male:female=1:6.6) in the Japanese national registry, 35 vs. 78 percent were papillary, 48 vs. 14 percent were follicular, and 13 vs. 2 percent were anaplastic. Among five patients whose peripheral blood was examined for germline mutations, the four cases of follicular carcinoma had mutations in the C-terminal region of the WS gene, and the one papillary carcinoma had a mutation in the N-terminal region. These findings suggest two WS genotype-phenotype relations, one involving thyroid carcinoma histology, and the other mutations in the C-terminal region. The latter may account for the higher frequency of WS in Japanese than Caucasians, resulting from the greater occurrence of marriage in Japan among cousins. (Ishikawa Y, Sugano H, Matsumoto T, Furuichi Y, Miller RW, Goto M. Unusual features of thyroid carcinomas in Japanese patients with Werner syndrome and possible genotype-phenotype relations to cell type and race. *Cancer* 1999;15:1345-1352)

Genetic Basis of Rothmund-Thomson Syndrome

Rothmund-Thomson syndrome (RTS) is a rare, recessively inherited disorder characterized by abnormalities in skin and skeleton, juvenile cataracts, premature aging, and predisposition to neoplasia. Three of seven patients were found to carry two types of compound heterozygous mutations in the *RECQL4* gene, a helicase that may be involved in unwinding double-stranded DNA into single-stranded DNA. The fact that the mutated alleles were inherited from the parents in one affected family and were not found in ethnically matched controls suggests that a mutation in the *RECQL4* gene is responsible for at least some cases of RTS. (Kitao S, Shimamoto A, Goto M, Miller RW, Smithson WA, Lindor NM, Furuichi Y. Mutations in *RECQL4* cause a subset of cases of Rothmund-Thomson syndrome. *Nat Genet* 1999;22:82-84) ■

Nutritional Epidemiology Branch

Alcohol Consumption and Risk of Prostate Cancer

With use of data collected in the Epidemiologic Followup Study of the first National Health and Nutrition Examination Survey (NHANES I), the association between alcohol consumption and risk of prostate cancer was investigated prospectively in two cohorts, one with 5,766 men (average follow-up=17 years) and one with 3,868 mean (average follow-up=9 years). No significant association was found between total alcohol consumption and prostate cancer risk among 252 incident cases in the two cohorts. However, in the smaller cohort, significant inverse associations were observed at the heaviest level of drinking (>25 drinks / week; relative risk [RR]=0.23) and at age 25 (RR=0.20), 35 (RR=0.30), 45 (RR=0.39), and 55 (RR=0.43) among these heavy drinkers. Although these results are based on a small number of cases, they suggest that distant past alcohol consumption may be an important factor in evaluating risk of prostate cancer. (Breslow RA, Wideroff L, Graubard BI, Erwin D, Reichman ME, Ziegler RG, Ballard-Barbash R. Alcohol and prostate cancer in the NHANES I epidemiologic follow-up study. *Ann Epidemiol* 1999;9:254-261)

Stage of Breast Cancer in Relation to Body Mass Index and Breast Size

By using data from a population-based case-control study of 1,361 women under age 45, analyses were undertaken to assess the association between stage of breast cancer and body mass index (BMI) and breast size, as measured by bra cup. Risk of late-stage disease increased with higher BMI (odds ratio for highest vs. lowest tertile=1.46) and with larger bra cup size (odds ratio for D cup vs. A cup=1.61). These associations were not modified by method of breast cancer detection. These findings indicate that among young women with breast cancer, BMI and breast size are positively associated with disease stage, and suggest that etiologic effects rather than detection methods explain the association with stage. (Hall HI, Coates RJ, Uhler RJ, Brinton LA, Gammon MD, Brogan D, Potischman N, Malone KE, Swanson CA. Stage of breast cancer in relation to body mass index and bra cup size. *Int J Cancer* 1999;82:23-27)

Diet and Risk of Early-stage Breast Cancer

A population-based case-control study was undertaken to evaluate the association between consumption of foods from a variety of nutrient groups and risk of early-stage breast cancer among women under age 45 with *in situ* and localized disease. In a comparison of highest and lowest intake quartiles, reduced risks were observed for high intake of cereals and grains (odds ratio [OR]=0.84), vegetables (OR=0.86), beans (OR=0.87), and fiber from beans (OR=0.88). However, trends of an inverse relation between risk and intake were not seen across quartiles. Risk was not associated any food group's dietary constituents (including fiber, carotenoids, vitamins A, C, and E, and folate) nor with vitamin supplements. These findings suggest that consumption of cereals and grains, vegetables, and beans may be only minimally related to reduction in risk of early-stage breast cancer among young women. (Potischman N, Swanson CA, Coates RJ, Gammon MD, Brogan DR, Curtin J, Brinton LA. Intake of food groups and associated micronutrients in relation to risk of early-stage breast cancer. *Int J Cancer* 1999;82:315-321)

Validation of Assay for Urinary Steroid Hormones in Postmenopausal Women

Two laboratories participated in a methodologic study to evaluate the reproducibility and validity of urinary assays for estrone, estradiol, estriol, pregnanediol glucuronide, and estrone glucuronide. Specimens were from postmenopausal women who were part of a case-control study of breast cancer among Asian Americans. All the analytes were measured by radioimmunoassay; estrone, estradiol, and estriol were measured gas chromatography-mass spectroscopy as well. The findings suggest that urinary hormones and their metabolites can be reliably measured by radioimmunoassay, thereby providing an alternative matrix to serum, where assays of estrone and estradiol are problematic because of their low levels in postmenopausal women. (Falk RT, Gail MH, Fears TR, Rossi SC, Stanczyk F, Adlercreutz H, Kiura P, Wahala K, Donaldson JL, Vaught JB, Fillmore CM, Hoover RN, Ziegler RG. Reproducibility and validity of radioimmunoassays for urinary hormones and metabolites in pre- and post-menopausal women. *Cancer Epidemiol Biomark Prev* 1999;8:567-577) ■

Occupational Epidemiology Branch

Alcohol and Tobacco Use and Risk of Oral Cancer in Puerto Rico

A case-control study of oral cancer was carried out in Puerto Rico, a high-rate area, to assess risk associated with use of alcohol and tobacco. Both products were strong independent risk factors among men and women, and their combination had a multiplicative effect. Risk did not vary systematically by use of filtered vs. nonfiltered cigarettes. Other forms of smoked tobacco were associated with about a sevenfold increased risk among both men and women. Tobacco use (but not alcohol) was linked to cancers of the salivary glands as well. The burden of oral cancer related to alcohol and tobacco use in Puerto Rico was about 76 percent for men and 52 percent for women; these percentages agree closely with estimates for the mainland U.S. population. (Blot WJ et al. *Cancer Res* 1988;48:3282) About 72 percent of salivary gland cancer (men and women combined) was associated with tobacco use. These findings indicate that the elevated incidence of oral cancer in Puerto Rico is largely explained by patterns of alcohol and tobacco use. (Hayes RB, Bravo-Otero E, Kleinman DV, Brown LM, Fraumeni JF, Harty LC, Winn DM. Tobacco and alcohol use and oral cancer in Puerto Rico. *Cancer Causes Control* 1999;10:27-33)

Smoking and Stomach Cancer in Poland

A population-based case-control study was carried out in Warsaw to identify reasons for the high incidence of stomach cancer in Poland. Interviews were conducted with 464 incident cases and 480 matched controls. Among men, the risk of stomach cancer was significantly elevated among current smokers (odds ratio=1.7), with the excess largely confined to long-term and heavy smokers. Among women, a similar increased risk occurred in both current and former smokers (odds ratio=1.8). These findings support the growing consensus that cigarette smoking is a risk factor for stomach cancer; it accounted for about 20 percent of the cases in this study population. (Chow WH, Swanson CA, Lissowska J, Groves FD, Sobin LH, Nasierowska-Guttmejer A, Radziszewski J, Regula J, Hsing AW, Jagannatha S, Zatonski W, Blot WJ. Risk of stomach cancer in relation to consumption of cigarettes, alcohol, tea and coffee in Warsaw, Poland. *Int J Cancer* 1999;81:871-876)

Dietary Factors and the Risk of Gastric Cancer in Mexico

A population-based case-control study was carried out in the Mexico City to investigate the relation of dietary factors to risk of gastric cancer. Compared with controls (n=752), cases (n=220) had a threefold increased risk of gastric cancer for frequent consumption (highest quartile) of both fresh (odds ratio [OR]=3.1) and processed meat (OR=3.2). Odds ratios were also elevated for frequent consumption of dairy products (OR=2.7) and fish (OR=2.2). A decreasing gradient of risk with increasing frequency of vegetable consumption was observed, mainly because of a significant inverse trend associated with intake of yellow and orange vegetables. High consumption of citrus fruits showed a slight inverse association with risk. Consumption of salty snacks more than twice per month was associated with an 80-percent increased risk. These findings are consistent with other studies implicating salt, processed meats, and vegetable consumption in risk of gastric cancer. (Ward MH, Lopez-Carrillo L. Dietary factors and the risk of gastric cancer in Mexico City. *Am J Epidemiol* 1999;149:925-932)

Residential Radon Exposure and Risk of Lung Cancer

A population-based case-control study was conducted to investigate the risk of lung cancer associated with residential radon exposure among women living in Missouri. Radon levels were measured using standard indoor air detectors and with newer CR-39 alpha-particle surface dosimeters, which may provide better estimates of cumulative exposure. A significant trend in lung cancer odds ratios was observed for 20-year time-weighted average radon concentrations when exposure data were used from surface monitoring, but not from standard air dosimetry. These findings suggest that air measurements may underestimate health risks associated with residential radon exposure. (Alavanja MCR, Lubin JH, Mahaffey JA, Brownson RC. Residential radon exposure and risk of lung cancer in Missouri. *Am J Public Health* 1999;89:1042-1048)

Measurement of Insecticide Exposure among Farmers

Because exposure assessment is an important component of epidemiologic investigations, studies were carried out to evaluate exposures among farmers applying insecticides to animals. With a fluorescent dye as a surrogate for the active insecticide ingredient, assessments were made of four methods of application. Exposure levels of dye were nondetectable with use of a backpack sprayer, nondetectable among most but not all farmers using the pour-on method, and consistently detectable with use of low- and high-pressure sprayers. Multiple layers of clothing, gloves, and boots were associated with a low mean exposure concentration, whereas poor work practices were related to high levels of exposure. (Stewart P, Fears T, Nicholson HF, Kross BC, Ogilvie LK, Zahm SH, Ward MH, Blair A. Exposure received from application of animal insecticides. *Am Ind Hyg Assoc J* 1999;60:208-212) Another project measured dermal and inhalation exposures to phosmet during its application to animals. Farmers had measurable exposures to this insecticide, but the levels were lower than what has been observed for other pesticide applications. Inhalation exposure was insignificant compared with dermal exposure, which was primarily associated with the hands. Clothing, particularly gloves, provided substantial protection. (Stewart PA, Fears T, Kross Burton, Ogilvie L, Blair A. Exposure of farmers to phosmet, a swine insecticide. *Scand J Work Environ Health* 1999;25:33-38) ■

Viral Epidemiology Branch

Chemokine Variants and Risk of HIV-related Non-Hodgkin's Lymphoma

Because genetic polymorphisms may affect a person's infectivity, HIV-1-infected persons were examined for associations between risk of B-cell non-Hodgkin's lymphoma and gene variants of stromal cell-derived factor 1 (SDF-1) chemokine and CCR5 and CCR2 chemokine receptors. Median follow-up was 11.7 years. The SDF1-3'A chemokine variant (carried by about 37 percent of whites and 11 percent of blacks) was associated with a doubling of risk among heterozygotes and a roughly fourfold increase in risk among homozygotes. The AIDS-protective chemokine receptor variant CCR5- 32 was highly protective, whereas the AIDS-protective variant CCR2-641 had no significant effect. Racial differences in SDF1-3'A frequency may contribute to the lower risk of HIV-1-associated non-Hodgkin's lymphoma among blacks than whites. These findings indicate that SDF-1 genotyping of HIV-1-infected individuals may identify subgroups warranting enhanced monitoring and targeted interventions to reduce the risk of non-Hodgkin's lymphoma. (Rabkin CS, Yang Q,

Goedert JJ, Nguyen G, Mitsuya H, Sei S. Chemokine and chemokine receptor gene variants and risk of non-Hodgkin's lymphoma in human immunodeficiency virus-1-infected individuals. *Blood* 1999;93:1838-1842)

HERV-K10 Antibodies Associated with Testicular Cancer but Not with HIV Infection

A seroprevalence study was carried out to determine whether human endogenous retrovirus K10 (HERV-K10) antibodies, which have been reported in patients with testicular cancer, are elevated in persons with HIV infection or AIDS. Immunofluorescence assays revealed HERV-K10 env or gag expression in 17 of 27 testicular cancer patients (63 percent) but only 4 of 77 controls (5 percent). Antibody levels were similar (50 to 60 percent) for seminoma, teratocarcinoma, and embryonal carcinoma; however, seroprevalence was not increased in cases or controls with HIV infection. HERV-K10 antibodies were detected in 12 of 19 cases (63 percent) more than 6 months before seminoma diagnosis, and in 4 of 6 cases (67 percent) with residual or recurrent malignancy more than 1 month after initial diagnosis. These findings confirm that HERV-K10 antibodies are detectable in patients with testicular cancer, but leave unexplained the increased risk of this malignancy among persons with HIV infection or AIDS. (Goedert JJ, Sauter ME, Jacobson LP, Vessella RL, Hilgartner MW, Leitman SF, Fraser MC, Mueller-Lantzsch NG. High prevalence of antibodies against HERV-K10 in patients with testicular cancer but not with AIDS. *Cancer Epidemiol Biomark Prev* 1999;8:293-296)

Smoking and Risk of Anal Cancer Among Women

Data from a population-based case-control study in Denmark and Sweden were analyzed to evaluate whether smoking influenced the risk of anal cancer among premenopausal and postmenopausal women. Compared with lifelong nonsmokers, the risk of anal cancer was significantly elevated among premenopausal women who were current smokers (odds ratio=5.6) and increased linearly by 6.7 percent per pack-year smoked. Smoking was not significantly associated with risk among postmenopausal women. Women whose menstrual periods started at a later age (17 vs. 12 years) were at higher risk of anal cancer (odds ratio=3.6), and body mass index was inversely associated with this risk. These findings suggest that female sex hormones may be a cofactor in anal carcinogenesis, since increased risk was associated with smoking only among premenopausal women, later age at menarche, and lean body composition. (Frisch M, Glimelius B, Wohlfahrt J, Adami HO, Melbye M. Tobacco smoking as a risk factor in anal carcinoma: An antiestrogenic mechanism? *J Natl Cancer Inst* 1999;91:708-715)

Diseases Associated with Infection by HTLV-I

Human T-cell lymphotropic virus type I (HTLV-I) was the first human retrovirus to be associated with a malignant disease (i.e., adult T-cell leukemia / lymphoma). This review article summarizes the nonmalignant conditions associated with this virus, notably chronic neurodegenerative disorder, HTLV-I associated myelopathy (also known as tropical spastic paraparesis), infective dermatitis of children, and uveitis. Recent evidence points to disease associations not previously linked to HTLV-I, indicating that its full disease spectrum still needs to be elucidated. The distribution of HTLV-I is worldwide; major endemic foci are in the Caribbean and southern Japan. The public health importance of the virus is evident from its major routes of transmission, which include blood transfusion, sexual activity, and mother-to-infant. No vaccine is currently available, and there is no proven treatment for advanced HTLV-I-related disease. (Manns A, Hisada M, La Grenade L. Human T-lymphotropic virus type I infection. *Lancet* 1999;353:1951-1958)

Bowen's Disease and Risk of Cancer

A study was undertaken to investigate whether persons with Bowen's disease, a condition characterized by squamous cell carcinoma *in situ* and usually occurring on sun-exposed surfaces, are at increased risk of internal malignant neoplasms. A cohort of 1,147 Danish patients with Bowen's disease at nongenital sites were followed for cancer occurrence up to 16 years after initial diagnosis. Excesses were found of nonmelanoma skin cancer (standardized incidence ratio [SIR]=4.3), lip cancer (SIR=8.2), and among men, leukemia (SIR=3.2). No excess was observed for noncutaneous cancers. These findings suggest that persons with Bowen's disease are not genetically predisposed to an unusually high risk of cancer in general. (Jaeger AB, Gramkow A, Hjalgrim H, Melbye M, Frisch M. Bowen disease and risk of subsequent malignant neoplasms: A population-based cohort study of 1147 patients. *Arch Dermatol* 1999;135:790-793) ■

IDENTIFICATION OF GENE VARIATIONS FROM EXISTING DATA RESOURCES

Part of the NCI's Cancer Genome Anatomy Project (CGAP) is the Genetic Annotation Initiative (GAI), whose aim is to compile a comprehensive catalog of single nucleotide polymorphisms (SNPs) that occur in cancer-related genes. Identifying and evaluating SNPs may lead to an understanding of the genetic basis that governs differences between individuals in cancer susceptibility and the growth of tumors, thereby leading to more effective prevention and treatment strategies.

Headed by the Chief of DCEG's Laboratory of Population Genetics, Dr. Kenneth Buetow, the GAI team consists of Dr. Robert Clifford, Dr. Cu Nguyen, Dr. Ying Hu, Ms. Titia Scherpbier, and Mr. Michael Edmonson. Using existing databases of human gene sequences, Dr. Buetow's team recently reported the discovery of 10,435 possible new variations (as defined by SNPs) among the 22,000 genes analyzed. Although the variations still must be validated, each of the candidate SNPs met a statistical confidence level of 0.99 percent. The effort required three computer software programs specially designed to examine existing sequence data.

Information about GAI, recent findings, and the special SNP software package is internet accessible (*http://lpg.nci.nih.gov/GAI/*), as is a description of CGAP (*http://www.ncbi.nlm.nih.gov/CGAP/*). In addition, the approach for identifying candidate SNPs from expressed sequence tag (EST) data in the public domain has been published recently. (Buetow KH, Edmonson MN, Cassidy AB. Reliable identification of large numbers of candidate SNPs from public EST data. *Nat Genet* 1999;21:323-325)

A BOOK REVIEW: CATALOG OF HUMAN CANCER GENES

Mulvihill JJ. *Catalog of Human Cancer Genes: McKusick's Mendelian Inheritance in Man for Clinical and Research Oncologists (Onco-MIM).* Baltimore: Johns Hopkins University Press, 1999, 646 pp.

Dr. John J. Mulvihill was a member of NCI's Clinical Epidemiology Branch from 1970 to 1990, when he retired from the Commissioned Corps of the U.S. Public Health Service. In 1975, Dr. Joseph Fraumeni, the scientific organizer of an American Cancer Society–National Cancer Institute meeting on risk factors for human cancer, asked Dr. Mulvihill to speak on the genetics of cancer in advance of papers on environmental causes of cancer, which was the main topic. For his presentation, Dr. Mulvihill culled 161 gene-related cancers from the third edition of McKusick's *Mendelian Inheritance in Man: A Catalog of Human Genes and Genetic Disorders.* Since that time, the number of cancer-related genes has increased with each update of McKusick's catalog (now in its 12th edition) and its internet OMIM version (*http://www3.ncbi.nlm.nih.gov/Omim*).

Dr. Mulvihill's new book is devoted to genes and disorders that are associated with cancer. *Onco-MIM's* 635 entries (6.2 percent of all OMIM entries) represents 424 clinical disorders and 211 other genes or proteins that are cancer-related. Each entry, which runs up to several pages in length, opens with a note from the author giving an overview or personal insight into the disease. The note for ataxia telangiectasia, for example, states that "This condition is rightly considered a Rosetta stone of modern biology [with] manifestations that represent immunology, neurosciences, DNA repair, altered gene expression, chromosome breakage and translocation, clonal progression, cancer predisposition . . . ." The text provides a wealth of details. The grouping of the conditions is at times arguable, but it and the author's notes stimulate new thinking about cancer genetics. ■

Robert W. Miller

RESEARCH CONTRACTS & ACQUISITION BRANCH

Submission of Research Contract Abstracts by Project Officers

The Research Contracts & Acquisition Branch (RCAB) will no longer submit the Project Objectives form (NIH-1688) for new research contracts for entry into the NIH Computer Retrieval of Information on Scientific Projects (CRISP) database. NIH policy now requires project officers to complete and submit the form electronically to the CRISP database. This policy streamlines the process by eliminating RCAB's involvement and automating project submission. It should also improve the accuracy and timeliness of data submission. Contact Ms. Cathy McClave, DCEG's Extramural Program Management Committee representative, for additional information about this new requirement for project officers.

NIH-1688 summarizes (in 250 words or fewer) the general objectives of a research contract, and is used by NIH in various management and reporting activities. Promptly on award of an N01-type research contract, project officers should e-mail the completed form to Ms. Dorrette Finch (dw33v@nih.gov) in the NIH Office of Extramural Research. She may be contacted at 435-0656 about questions and related issues concerning submission of the form. NIH-1688 and guidance on its completion are accessible at *http://odoerdb2.od.nih.gov/oer/committees/popof/popof.htm.* ■

Sharon A. Miller

ARC NEWS

Changes in ARC Personnel

Mr. Roberto Minutillo, who has been working as an Administrative Officer while in NCI's Administrative Career Development program, has accepted a permanent appointment within the Administrative Resource Center (ARC). **Ms. Sara Sutphin** joined the ARC in June as a senior Personnel Management Specialist. She has 10 years of personnel experience at NIH and the Food and Drug Administration, and is located in EPS/8052.

The ARC welcomed **Ms. Candice Coles** and **Mr. Gyasi Ross** as summer interns. Ms. Coles is an NCI Human Resources/Personnel Intern who is training to become a Personnel Management Specialist. Mr. Ross is sponsored by the Washington Internships for Native Students Program. He has been involved in various activities aimed at promoting his professional development.

Ms. Lori Henry has accepted a position with the Food and Drug Administration as a budget analyst. **Mr. Tim Sakemiller,** a Presidential Management Intern, has joined the ARC to fill her position, and is located in EPS/8078. **Ms. Karen Webb,** a personnel management specialist, has accepted a position at NINDS, and **Ms. Vivian Walton,** a purchasing agent, has taken a position with another ARC within NCI. ■

Mary Jude Jacobs

Integrated Time and Attendance System

As NCI embarks on a new era of timekeeping under the Integrated Time and Attendance System (ITAS), civil service employees (ITAS does not apply to Commissioned Corps Officers or fellows) must be aware of their personal obligation for maintaining time and attendance records. Under the previous system (TAIMS), timekeepers and supervisors bore the major responsibility for ensuring that employee time and attendance data were accurately recorded. ITAS shifts this responsibility to employees and allows them much greater access to their time and attendance information.

Civil service employees are strongly encouraged to submit leave requests on-line in ITAS to their supervisor for approval during the relevant pay period. Approved leave requests are automatically posted to the employee's timecard, so that leave balances are always current. Supervisors retain the same level of responsibility under ITAS as they had under TAIMS for ensuring that their employees' time and attendance information is accurate. Under ITAS, supervisors must also approve timecards in addition to leave requests for their employees. An ITAS web-based tutorial is available at *http://itasinfo.nih.gov/itas_wbt/.* If you have any questions, contact Ms. Linda Littlejohn at 496-1282. ■

Linda Littlejohn

DCEG PEOPLE IN THE NEWS

Dr. Louise Brinton and **Dr. Montserrat Garcia-Closas** received a $120,000 award from the NIH Office of Research on Minority Health to support research into genetic predictors of disease risk among African American women in a collaborative effort with investigators at Boston University.

In July, **Dr. Neil Caporaso** received an exceptional capability promotion to the rank of Captain in the Commissioned Corps of the U.S. Public Health Service. In another achievement, Dr. Caporaso and his wife, Nan, took part in AIDS Ride 4, a 323-mile, 4-day bike ride in June from Raleigh, North Carolina, to Washington, DC. The event raised $4.8 million to support medical care at the Whitman-Walker Clinic and daily food deliveries by Food & Friends to persons with AIDS.

At its annual meeting in June, the Commissioned Officers Association of the U.S. Public Health Service honored **Ms. Michele Doody** with the J.D. Lane Clinical Society Award for her paper entitled "Breast cancer mortality following diagnostic x-rays: U.S. scoliosis cohort study."

Dr. Montserrat Garcia-Closas has been appointed as a tenure-track investigator in the Environmental Epidemiology Branch. She received an M.D. degree from the University of Barcelona, and M.P.H. and Dr.P.H. degrees in epidemiology from the Harvard School of Public Health. Dr. Garcia-Closas is particularly interested in genetic susceptibility factors in cancer, with particular emphasis on breast and bladder cancers. She is also involved in methods research to define samples sizes for effectively assessing gene-environment interactions and determining the impact of misclassification in such studies.

Dr. Lynn Goldin has been appointed to a 2-year term as a member of the Genome Study Section, Center for Scientific Review, NIH. Study section members are selected for their competence and achievement in their scientific discipline, as evidenced by the quality of research accomplishments, publications in scientific journals, and other significant scientific activities. Members are also selected for their mature judgment and objectivity, and their ability to work effectively as a group member.

Dr. Robert Hoover was presented the Distinguished Service Award by the DES ACTION USA, a national, nonprofit consumer organization dedicated to informing the public about diethylstilbestrol (DES) and helping persons exposed to the drug. Dr. Hoover was honored for his tireless dedication to research benefitting the lives of DES-exposed persons.

Dr. Ann Hsing received a $250,000 award from the NIH Office for Research on Minority Health to carry out a study entitled "Intraprostatic androgenicity in relation to circulating levels of hormones and polymorphisms of hormone-related genes: Racial differences and epidemiologic implications."

Dr. Bu-Tian Ji has been appointed to a staff scientist position in the Occupational Epidemiology Branch. He will participate in several epidemiologic investigations in China, including the coordination of a Shanghai women's cohort study, a benzene cohort study, and case-control studies of digestive and childhood cancers.

Dr. Maria Teresa Landi has been appointed to a tenure-track position in the Genetic Epidemiology Branch. She received an M.D. degree from the University of Milan and a Dr.P.H. degree from the Italian Universities Consortium in occupational medicine and industrial hygiene. Dr. Landi also completed advanced clinical training in medical oncology at the San Raffaele Hospital in Milan. In Italy, she is conducting the first family study of melanoma with biospecimens from over 35 well-characterized multiplex families. Her research interests focus on the genetic contribution to common malignancies, particularly melanoma and lung cancer. Dr. Landi is currently participating in the design of a large interdisciplinary study of lung cancer.

In June, **Dr. Martha Linet** received the NIH Director's Award for her achievements in initiating and directing a comprehensive study to evaluate the relation between exposure to electromagnetic fields and risk of childhood lymphoblastic leukemia.

Dr. Thomas O'Brien and his collaborators at the Centers for Disease Control and Prevention (CDC) received the 1998 Charles C. Shepard Science Award. This annual honor is given to the authors of the most outstanding peer-reviewed research paper published

by CDC scientists. The paper, "New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes" (*J Am Med Assoc* 1998;280:42-48) used specimens and data from DCEG's study of acute HIV-1 seroconverters in Trinidad.

Ms. Tammy Shields has been appointed as the DCEG representative to the NIH Pre-IRTA Committee. She replaces Ms. Rebecca Schiller, who has returned to graduate school. Ms. Shields, who is enrolled in a doctoral program at the University of Washington, is doing her thesis work in the Environmental Epidemiology Branch. She is located in EPS/7055, and can be reached at 435-3975 or by e-mail at shieldst@epndce.nci.nih.gov.

In June, **Dr. Rashmi Sinha** received the NIH Merit Award for her work on the relation between meat cooking practices, formation of heterocyclic amines, and risk of cancer. She and Dr. Jo Freudenheim of State University of New York at Buffalo served as guest editors for the *Journal of Nutrition* supplement (1999;129:550S-565S) on interactions of diet and nutrition with genetic susceptibility in cancer.

Dr. Mary Ward has been appointed to a tenure-track position in the Occupational Epidemiology Branch. She received a Ph.D. degree in epidemiology from Johns Hopkins University and became a postdoctoral fellow in the Branch in 1994, focusing on the etiology of non-Hodgkin's lymphoma and stomach cancer. Among her research findings are the first reports linking nitrate in drinking water and increased risk of non-Hodgkin's lymphoma, consumption of well-done meat and increased risk of stomach cancer, and fruit and vegetable intake and decreased risk of non-Hodgkin's lymphoma. Dr. Ward is now developing procedures for using satellite sensing and other remote techniques to study nonoccupational exposure to pesticides.

Dr. Stephanie Weinstein was selected to attend the Nutrition Leadership Institute, which is sponsored by the Dannon Institute to provide doctoral graduates in nutrition with the global perspective and skills to become effective leaders in academia, government, and industry. The program was held in June at the Wye Woods Conference Center in Maryland. ■

NEWS FROM THE TRENCHES

Biostatistics Branch

At the April meeting of the American Association for Cancer Research in Philadelphia, **Dr. Mitchell Gail** gave a presentation on weighing the risks and benefits of tamoxifen for preventing breast cancer.

At the invitation of the Korean Federation of Science and Technology Societies, **Mr. Jun-Mo Nam** presented a paper in Seoul at the 1999 World Congress of Korean Scientists and Engineers on significance testing to establish equivalence between two treatments in matched pairs design. He also gave a seminar to the Korean branch of the International Biometric Society on the importance of a reliable and efficient statistical method in equivalence trials.

At the invitation of the University of Bologna, **Dr. Wei-Cheng** You presented a paper entitled "*H. pylori* and gastric cancer: Prevention/regression of gastric lesions in Shandong Province" at a workshop in June in Sardinia, Italy. The workshop brought together scientists from around the world to discuss the latest research on *Helicobacter pylori.* ■

Environmental Epidemiology Branch

In April, **Dr. Louise Brinton** gave talks on cancer prevention and screening at the annual Southeastern Wisconsin Cancer Conference on Women's Cancer, and on the epidemiology of breast cancer at the American Society for Nutritional Sciences Symposia on Physical Activity and Cancer Risk in Washington, DC. In May, she gave a presentation on behavioral and lifestyle risk factors for breast cancer at the Komen Foundation National Race for the Cure Conference on Critical Issues in Breast Health, held in Washington, DC. In July, Dr. Brinton presented a paper on the epidemiology of endometrial cancer at the Gynecologic Oncology Group meeting in Phoenix.

In May, **Dr. Ann Hsing** gave a seminar at the UCSF School of Medicine on her population-based case-control study of prostate cancer in China. In June, she was a featured speaker at the International

Conference on Prostate Cancer Research at the University of Iowa College of Medicine, presenting a talk entitled "International trends and patterns of prostate cancer rates: Clues to etiology and prevention."

In June, **Dr. James Lacey** presented a paper entitled "Prostate cancer, benign prostatic hyperplasia, and physical activity in Shanghai, China" at the Spotlight session on "Running for Your Life: Measurement and Effects of Physical Activity," which was held at the annual meeting of the Society for Epidemiologic Research in Baltimore. ■

Genetic Epidemiology Branch

In April, **Dr. Neil Caporaso** chaired the "Molecular Epidemiology of Lung Cancer" session at the annual meeting of the American Association of Cancer Research (AACR) in Philadelphia.

Also at the AACR meeting, **Dr. Margaret Tucker** presented a paper on the origins of melanoma at a Meet-the-Expert sunrise session. In May, she chaired an educational session on pediatric second malignancies at the annual meeting of the American Society of Clinical Oncology in Atlanta. ■

Nutritional Epidemiology Branch

In May, at the invitation of the Japan National Cancer Institute and Foundation for the Promotion of Cancer Research, **Dr. Regina Ziegler** spoke in Tokyo on migration patterns, lifestyle, and breast cancer risk in Asian American women. Earlier in the spring, she presented a paper on vegetable and fruit consumption and risk of cancer at a Harvard Medical Area conference on nutrition and cancer. At the annual meeting of the Federation of American Societies for Experimental Biology, Dr. Ziegler completed her year as the elected chair of the Nutritional Epidemiology Section of the American Society for Nutritional Sciences, and resumed a position on the nutritional epidemiology steering committee. ■

Occupational Epidemiology Branch

The Board of Scientific Counselors site visit was held at the end of June, after a period of intense preparation by members of the branch. Preparation included a successful retreat in May to discuss activities over the last year, future research directions, and administrative issues.

At a June meeting in Philadelphia, **Dr. Dalsu Baris** and **Dr. Shelia Zahm** presented the results of their mortality study of Philadelphia firefighters, one of the largest studies to examine risk of cancer and other diseases among firefighters, to officials of Local No. 22 of the International Association of Fire Fighters and representatives of the City of Philadelphia Fire Department.

In July, **Dr. Ken Cantor** organized a 5-day workshop in Krakow, Poland, on water-related health risks, which was part of the epidemiology in public health program of the eastern European summer school run by the London School of Hygiene and Tropical Medicine for students from former soviet bloc countries.

In May, **Dr. Richard Hayes** presented a poster on biomarkers of 1,3-butadiene exposure at the Health Effects Institute's annual conference in San Diego. In September, he spoke on the compound's genotoxic effects at the International Society for Environmental Epidemiology in Athens, Greece.

Dr. Bu-Tian Ji presented a paper in June on the case-control study of pancreatic cancer in Shanghai at the National Conference on Cancer Epidemiology and Prevention in China.

In April, **Dr. Mary Ward** spoke on the health effects of nitrate in drinking water at the annual meeting of the Iowa Groundwater Association in Des Moines. ■

Radiation Epidemiology Branch

In July, the Chornobyl Oversight Panel conducted a 2-day scientific review of the Chornobyl thyroid and leukemia projects, which are overseen by the Branch's Chornobyl Research Unit, headed by **Dr. Gilbert Beebe**.

At the June meeting of the Health Physics Society in Philadelphia, **Dr. Andre Bouville** and **Dr. Ethel Gilbert** gave a joint lecture on estimating thyroid doses and risks from iodine-131 fallout following the Nevada atmospheric nuclear bomb tests. Dr. Gilbert also spoke on the risk of cancer from occupational exposures to radiation at the Mayak Nuclear Facility in Ozyorsk, Russia. Her presentation was part of a special session on U.S.-Russian Joint Radiation Health Effects Studies in the Southern Urals.

In July, **Dr. Elizabeth Hatch** led a breakout session on epidemiology at an NIH workshop to update research on diethylstilbestrol.

In July, **Dr. Charles Land** and **Dr. Andre Bouville** held the third in a series of workshops aimed at developing a consensus on reconstructing the thyroid radiation dose among villagers exposed to fallout from weapons testing at the Semipalatinsk test site in Kazakstan. The dose reconstruction data will be used in a collaborative epidemiologic screening study to evaluate risk of thyroid cancer associated with exposure. The workshop, held in Rockville, was attended by five experts from Russia and five from the United States.

In May, **Dr. Martha Linet** presented a paper entitled "Do electromagnetic fields cause cancer?" at the annual Carroll W. Feist Symposium on Cancer in a Toxic Environment, which was held at Louisiana State University School of Medicine in Shreveport. In June, she reviewed the epidemiology research agenda related to non-Hodgkin's lymphoma during an invited talk at the International Conference on Malignant Lymphoma in Lugano, Switzerland.

Ms. Ruth Kleinerman and **Dr. Martha Linet** presented papers in the educational session on pediatric second malignancies at the May meeting of the American Society of Clinical Oncology in Atlanta. Ms. Kleinerman spoke about cancer incidence and mortality in long-term survivors of retinoblastoma, and Dr. Linet spoke about cohort studies of survivors of childhood cancer. In addition, **Dr. Lois Travis** delivered a talk on the risk of leukemia following radiotherapy and chemotherapy for testicular cancer. ■

Viral Epidemiology Branch

In April, **Dr. Angela Manns, Dr. Michie Hisada,** and **Ms. Beth Maloney** presented papers at the International Conference on Human Retrovirology in Kagoshima, Japan. In a plenary session on genetic and environmental effects, Dr. Manns spoke on the familial aggregation of adult T-cell leukemia/lymphoma (ATL)-associated and human T-lymphocyte virus type I (HTLV-I)-associated myelopathy/tropical spastic paraparesis. Dr. Hisada spoke on sex-specific mortality from ATL among HTLV-I carriers. She also presented two posters, one on HLA antigens associated with HTLV-I antibody and proviral load, and one on gender differences in purified protein derivative anergy among HTLV-I carriers in Japan. Ms. Maloney spoke on disease risk in a cohort of Jamaican children infected with HTLV-I. ■

COMINGS . . . GOINGS . . .

Dr. Nilanjan Chatterjee has joined the Biostatistics Branch as a research fellow under the Visiting Scientist Program. He holds undergraduate and masters degrees from the Indian Statistical Institute and a Ph.D. degree in statistics from the University of Washington. For research related to his doctoral thesis, Dr. Chatterjee received the Z. W. Birnbaum Prize, given by the Department of Statistics of the University of Washington for outstanding performance, and the International Biometrics Society's 1998 Western North American Region award for best paper presented at its annual meeting. His research interests include two-phased sampling and missing data problems. Dr. Chatterjee's office is EPS/8038, and he can be called at 402-7933.

Dr. Michal Freedman has transferred from the Occupational Epidemiology Branch to the Radiation Epidemiology Branch as a staff scientist. Among Dr. Freedman's research interests are studies of cancer risks associated with exposures to ultraviolet and ionizing radiation. Her office is in EPS/7087, and she can be phoned at 594-7163.

Dr. Morton Frisch has joined the Viral Epidemiology Branch as a visiting scientist from the Institute of Epidemiologic Research in Copenhagen, Denmark. Using the AIDS Cancer Linkage Registry and other resources, he is investigating the relation between human papillomavirus infection and risk of oral cancers, particularly of the tonsils. Dr. Frisch's office is in EPS/8009, and he can be called at 594-7825.

Dr. Joseph Gastwirth, Professor of Statistics and Economics at George Washington University, has joined the Biostatistics Branch for the 1999–2000 academic year. Dr. Gastwirth is an expert on nonparametric methods, diagnostic screening, and statistical aspects of confidentiality. He received a Guggenheim Fellowship for his research on problems arising in law and public policy. Dr. Gastwirth will be conducting research on statistical genetics and on using robust methods to analyze cancer-related data. He will also be exploring applications of statistical methods to problems posed by the need to protect confidentiality. Dr. Gastwirth is located in EPS/8105, and he can be reached at 594-7833.

After receiving a Ph.D. degree in statistics from the University of Dortmund in Germany, **Dr. Michael Hauptmann** joined the Biostatistics Branch as a visiting fellow. His research interests include exposure–time-response relationships and statistical problems in radiation epidemiology. Dr. Haupmann's office is in EPS/7089, and he can be called at 594-7906.

Ms. Marianne Henderson has been selected as the new Chief of the Office of Division Operations and Analysis. She has been at NCI since 1988, and for the past 4 years she has worked in the Division of Basic Sciences as a scientific program specialist in the Office of the Director. Ms. Henderson has an M.S. degree in zoology with an emphasis in marine biology, as well as extensive laboratory and science administrative experience. Her office is located in EPS/8060, and she can be reached at 496-8672.

Mr. Hormuzd Katki has joined the Biostatistics Branch as a mathematical statistician. He received a masters degree in statistics from Carnegie Mellon, and has experience in statistical computing, time series, and related areas. Mr. Katki is located in EPS/8044, and he can be reached at 594-7818.

In July, **Dr. Qing Lan** joined the Occupational Epidemiology Branch as a visiting fellow. Dr. Lan has an M.D. degree and comes from the Environmental Protection Agency, where she conducted studies to evaluate lung cancer risks associated with occupational exposures and genetic factors. She will be involved in a cross-sectional study of early biomarkers among workers exposed to benzene in China and in a case-control study of stomach cancer in Poland focusing on susceptibility markers.

Dr. Elizabeth McNeil has joined the Genetic Epidemiology Branch as a clinical fellow in the Cancer Genetics and Epidemiology Training Program. Dr. McNeil received an M.D. degree from Columbia University College of Physicians and Surgeons, and completed residencies in pediatrics at Texas Children's Hospital and in pediatric neurology at Children's Hospital of Philadelphia. She also completed a clinical fellowship in neuro-oncology in Philadelphia. Dr. McNeil is board-certified in neurology and board-eligible in pediatrics. Her major research interest is the epidemiology of pediatric tumors, particularly brain tumors. Dr. McNeil's office is in EPS/7110, and she can be reached at 402-9529.

Ms. Katie Miller, a graduate student in the School of Public Health at Emory University, has joined the Occupational Epidemiology Branch. She is working on case-control studies of brain cancer in Nebraska farmers and breast cancer among women in Alabama exposed to DDT.

Professor Emad El-Omar has joined the Viral Epidemiology Branch as a visiting scientist. He was recently appointed Chair of Gastroenterology at the University of Aberdeen, Scotland. Professor El-Omar received a 2-year award from the British Digestive Foundation to study the role of immune response and inflammatory mechanisms in gastric cancer at Vanderbilt University and NCI. As a Branch member, Professor El-Omar is investigating genetic determinants of inflammation on risk of gastric cancer. He is located in EPS/8015, and can be reached at 435-4721.

In August, **Ms. Claudine Samanic** joined the Occupational Epidemiology Branch as a predoctoral fellow in the Cancer Epidemiology and Biostatistics Training Program. She has an M.S.P.H. in epidemiology and biostatistics from the University of South Florida and an M.A. in medical anthropology from Case Western Reserve College. Ms. Samanic's research experience includes studies on migrant farm workers and on the risk of seconds cancers following nonmelanoma skin cancer in a cohort of veterans. She is located in EPS/8109, and can be reached at 402-7824.

Ms. Rebecca Schiller, a predoctoral fellow in the Nutritional Epidemiology Branch, is returning to graduate school at the University of Washington to begin work on a doctoral degree in nutritional science. She will continue to collaborate with Branch scientists on a study evaluating the role of individual fatty acids in the etiology of prostate cancer, and on analyses of plasma samples from a case-control study of tumors that occur in excess among blacks.

Ms. Stacy Young, a graduate student at the University of Michigan School of Public Health, is working for the summer in the Occupational Epidemiology Branch. She is providing support for case-control studies of non-Hodgkin's lymphoma and prostate cancer and a follow-up questionnaire of the etiology component of the prostate, lung, colon, and ovary screening trial. ■

DCEG ESTABLISHES OFFICE OF EDUCATION

Ms. Kristin Kiser recently joined the Office of the Director to establish a new DCEG Office of Education. Ms. Kiser came to NIH in 1983, after receiving an M.H.A. degree from Ohio State University, and has worked in a number of areas relevant to the Division. Her experience includes positions as an NIH legislative analyst and administrator in Clinical Center's Facility Management, as well as in the offices of the NIH Ombudsman and Loan Repayment and Scholarship. Most recently, Ms. Kiser worked in the NIH Office of Intramural Research, where she helped develop the Intramural Research Sourcebook, a comprehensive web-based manual *(http://www1.od.nih.gov/oir/ sourcebook)* of topics related to the intramural research program. Ms. Kiser is located in EPS/8057, and can be reached by phone at (301) 594-3005 and by e-mail at kiserk@mail.nih.gov.

CALENDAR OF EVENTS

Date	Event
September 16	DCEG Seminar: Program of Second Cancer Studies of the Radiation Epidemiology Branch Drs. R. Curtis, C. Metayer, and L. Travis and Ms. R. Kleinerman 10:30 am–12:00 pm, EPN / H
September 23	DCEG Seminar: Plans and Status of the DCEG Study of Non-Hodgkin's Lymphoma Dr. P. Hartge 10:30 am–12:00 pm, EPN / J
September 23–24	National Cancer Advisory Board Meeting Conference Rm. 10, Bldg. 31
September 30	DCEG Seminar: Incidence and Risk Factors of Central Nervous System Relapse in Non-Hodgkin's Lymphoma Dr. C. Besson 10:30 am–12:00 pm, EPN / G
October 2–4	American College of Epidemiology Annual Meeting Hyatt Regency, Bethesda, MD
October 7	DCEG Seminar: Meat Cooking Methods, Heterocyclic Amines and Cancer Dr. R. Sinha 10:30 am–12:00 pm, EPN / H
October 7	DCEG Senior Advisory Group Meeting 1:00–4:00 pm, EPN / G
November 4–5	NCI Executive Committee Retreat Wye River, MD
November 8	DCEG Senior Advisory Group Meeting 1:00–4:00 pm, EPN / G
November 15	Board of Scientific Counselors Meeting 8:30 am–5:00 pm, Bldg. 31 / CR6
December 2	DCEG Senior Advisory Group Meeting 1:00–4:00 pm, EPN / G
December 7–8	National Cancer Advisory Board Meeting Conference Rm. 10, Bldg. 31
December 9	Brain Tumor / EMF Study Advisory Panel Meeting 9:00 am–5:00 pm