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Division of Cancer Epidemiology and Genetics

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Second Cancers Research Helps Define Risks for Survivors

Along with their health care providers, cancer survivors who remain cancer-free after 5 or 10 years need to be aware of their risk of developing a new cancer. Estimates show that of the 1.8 million new cancers diagnosed each year, more than 159,000 occur in people previously treated for cancer. "There are 8.9 million cancer survivors in the United States, and second cancers represent one of the most serious late effects of cancer treatment," noted **Lois B. Travis, M.D., Sc.D.,** one of the lead DCEG investigators in the field of second cancers. "Research will help to better define these late effects." She also noted that second cancers may reflect other etiologic factors shared with the initial cancer, such as tobacco smoking, genetic susceptibility, or gene-environment interactions.

DCEG researchers have been particularly interested in studying Hodgkin's disease (HD) survivors because second cancers are the leading cause of death in those who are cured of HD. **Graça M. Dores, M.D., M.P.H., Ethel Gilbert, Ph.D., Catherine Metayer, M.D., Ph.D.** (now at University of California, Berkeley), **Rochelle Curtis, M.A.,** and Dr. Travis worked with investigators in Europe and Canada to compile a cohort of over 32,000 HD patients from 16 registries in Europe and North America. In a study published in the *Journal of Clinical Oncology* (2002;20:3484–3494), Dr. Dores and her collaborators observed a nearly twofold increase in solid tumors among HD survivors. Cancers of the breast, lung, and digestive tract accounted for most of these excess risks. While some of the risks decreased over time, others—notably those for cancers of the breast, esophagus, stomach, and uterine cervix—persisted for 25 years after completion of treatment.

Second Cancers Research Team: (front row) Lois Travis and Rochelle Curtis, (back row) Deirdre Hill, Ethel Gilbert, and Graça Dores

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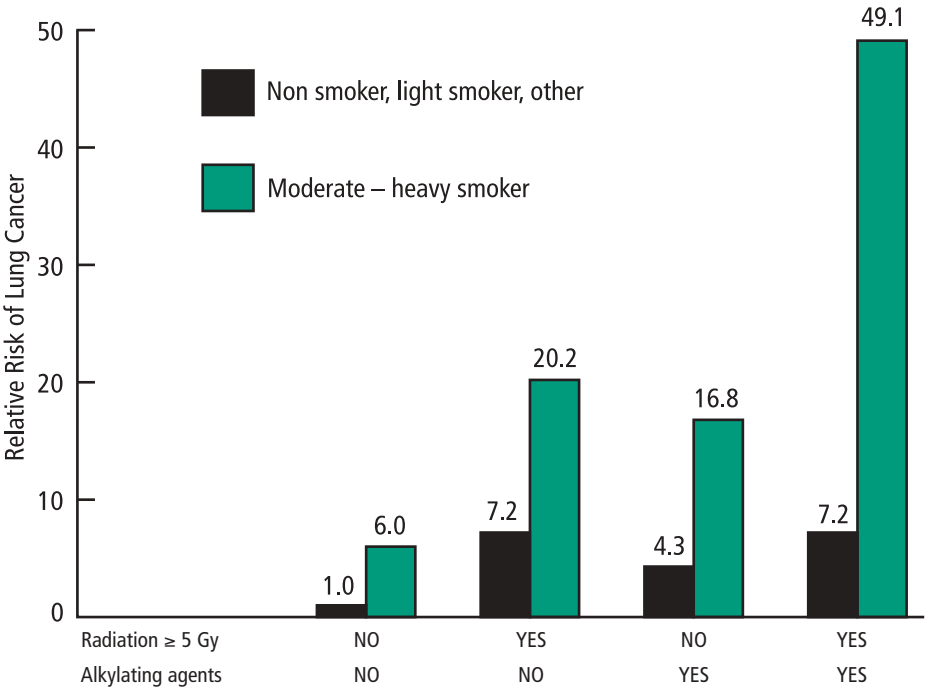
Following up on these findings, Dr. Travis and colleagues decided to dig deeper into the breast cancer risk in this cohort. In a study that appeared as the lead article in the *Journal of the American Medical Association* (2003;290:465–475), they reported that among more than 3,800 young women with HD, the higher the dose of chest radiation, the greater the risk of breast cancer. A dose higher than 40 Gy raised the risk eightfold and the increased risks persisted for years. "The high radiation-related risk, which did not diminish over 25 years after radiotherapy, strongly suggests the need for lifetime surveillance in this population," noted co-author **Deirdre Hill, Ph.D.** In contrast, alkylating-agent chemotherapy and radiotherapy to the ovaries decreased the risk of breast cancer, probably due to a reduction of ovarian function, which led to lower hormonal stimulation of breast tissue. "There is a general paucity of data on the hormone receptor status of breast tumors following HD, observed Dr. Travis. "Future studies should make a concerted effort to include data on this and other hormonal factors."

"This research will help determine how long and what kind of follow-up care these patients should receive, as well as potential life-style changes that survivors can make to help lower their risk of second cancers."

At the same time, DCEG investigators delved into the increased risk of lung cancer, which is the most common malignancy following HD treatment. Similar to the breast cancer findings, lung cancer risk rose with increasing radiation dose to the lung, however, lung cancer risk also rose with an increasing number of alkylating agent chemotherapy cycles (*Journal of the National Cancer Institute*, 2002; 94:182–192). A further look at the data revealed that smoking multiplied all treatment-associated risks. Dr. Gilbert, the senior author, estimated that treatment alone accounted for 10 percent of the lung cancers, smoking alone for 24 percent, and the combined effects of treatment and smoking accounted for about 65 percent.

"These are critical pieces of information for HD survivors and health care providers," remarked Dr. Dores. "This research will help determine how long and what kind of follow-up care these patients should receive, as well as potential lifestyle changes that survivors can make to help lower their risk of second cancers." Dr. Dores also noted that HD treatment regimens have undergone appreciable modification over the past 35 years and that evaluation of second cancer risk among long-term survivors often reflects the effects of earlier, more aggressive protocols. Quantifying long-term risks is crucial to maximizing HD cure rates while minimizing adverse treatment effects.

Ms. Curtis and other DCEG scientists have also examined the cancer risks associated with bone marrow transplantation (BMT). This relatively new therapeutic approach—often used for leukemia and lymphoma and still under study for other solid tumors—combines high doses of chemotherapy and radiation with the re-infusion of either the patient's or a donor's bone marrow cells. In a recent study, Dr. Metayer, Ms. Curtis, and Dr. Travis evaluated more than 2,700 patients who received autologous BMT as treatment for either HD or



Risk of lung cancer in patients with Hodgkin's disease according to type of treatment and smoking category (graph adapted from Table 5, *JNCI* 2002;94:182–192).

non-Hodgkin's lymphoma. The findings, reported in *Blood* (2003;101:2015–2023), showed that the risk of myelodysplastic syndrome and acute myelogenous leukemia increased with the intensity of pre-BMT chemotherapy. This elevated risk was particularly associated with higher doses of two chemotherapy drugs: mechlorethamine (nitrogen mustard) and chlorambucil. Earlier DCEG research in the 1990's showed that BMT recipients of a donor's bone marrow cells have elevated risks for solid tumors, including malignant melanoma and cancers of the oral cavity, liver, brain, thyroid, bone, and connective tissue. Higher doses of radiation contributed to this increased risk, although other factors such as immunologic alterations appeared involved as well.

Looking for links between specific chemotherapeutic agents and second cancers helped Dr. Travis and colleagues demonstrate a connection between platinum-based chemotherapy for ovarian cancer (*New England Journal of Medicine,* 1999;340:351–357) and testicular cancer (*Journal of the National Cancer Institute,* 2000;92:1165–1171) and subsequent leukemia. Among women with ovarian cancer, the risks of leukemia reached eightfold following a cumulative dose of 1,000 mg or more of cisplatin. The findings have implications for many other tumors as well, since platinum compounds are now one of the most commonly used cancer chemotherapeutic agents.

The research by DCEG investigators and others has not only raised the level of awareness about second cancers but has also contributed to changes in treatments, such as lowering doses of chemotherapy or radiation. Because of these treatment modifications, second cancers and other late effects should have less impact on the lives of cancer survivors. In addition, these studies by DCEG researchers are providing new insights into cancer biology and are helping to shift attention to epidemiology studies using molecular biomarkers to identify pharmacogenetic susceptibility and gene expression in second tumors, which may help determine therapeutic options and delineate carcinogenic pathways.

DCEG is currently involved in several new international research initiatives, including studies of second cancers of the gastrointestinal tract among patients with testicular cancer, HD, and breast cancer. The study team, led by Dr. Travis, also includes Ms. Curtis, Dr. Dores, **Linda Morris Brown, Dr.P.H., Michael Hauptman, Ph.D., Mary Lou McMaster, M.D., Kiyohiko Mabuchi, M.D., Dr.P.H., Ankur Saini, B.S.,** and many colleagues outside DCEG and NCI. ■

—Cathy Kristiansen

SECOND CANCERS MONOGRAPH AND WEB SITE COMING SOON

To help disseminate information about second cancers to patients, clinicians, researchers, and others, NCI is preparing a monograph describing the risk of second cancers following each major cancer site based on population-based data from the Surveillance, Epidemiology, and End Results program. A collaborative effort between DCEG and the Division of Cancer Control and Population Sciences, the report will contain information on more than 1.8 million cancer survivors diagnosed between 1973 and 1998, of which nearly 9 percent so far have developed a new malignant tumor. The monograph will be published in late 2004; however, in November 2003, NCI will release a user-friendly interactive software module that will enable scientists to perform their own analyses of multiple primary cancers.

MATERIALS ON I-131 EXPOSURE FROM FALLOUT AVAILABLE ON NCI WEB SITE

Extensive materials developed on exposure to radioactive iodine (I-131) in fallout from nuclear weapons testing in the United States are now available on the NCI web site *(http://cancer.gov/i131)*. Designed for effective communication with the public, the web site includes background information on the Nevada atmospheric nuclear bomb tests conducted in the 1950's and 1960's and explains how Americans were subsequently exposed to I-131. Radiation Epidemiology Branch members **Elaine Ron, Ph.D., Charles Land, Ph.D., Andre Bouville, Ph.D., Steven Simon, Ph.D., Bob Weinstock M.S.,** and **Mark Buckley** were responsible for the technical content of the dose and risk calculator and worked closely with **Alyssa Voss, M.P.H.,** and **Betsy Duane,** in DCEG's Office of the Director, as well as with the NCI Office of Communications to develop the materials for the web site.

The web site also provides information on the risk of thyroid cancer, the most common tumor attributable to I-131 exposure, and displays maps showing exposure levels by state and county. The full scientific report on this subject can also be found on the web site; it contains results from NCI's decade-long study to assess exposures of the U.S. population to I-131 fallout from the Nevada Test Site. Estimates of radiation dose, as explained on the web site, are derived from several key factors: sex, date of birth, place of residence at the times fallout occurred, source of milk, and rate of milk consumption. An interactive dose and risk calculator helps web users approximate the doses of I-131 received from nuclear weapons testing in Nevada, computes estimated risk of developing thyroid cancer as a consequence of exposure, and explains the meaning of radiation dose and risk. The current dose and risk calculator is a highly improved, more sophisticated version of an earlier dose calculator and is a unique resource for the public and the scientific community.

The development of the educational materials relied on input from advocacy groups, community representatives, and health officials, as well as recommendations from a 1999 Institute of Medicine report. In January 2000, NCI and the Centers for Disease Control and Prevention held a workshop to gather feedback from public representatives, medical professionals, experts on science and Federal policy, and state health departments about the best ways to communicate information on I-131 exposure and related risks.

Focus groups were conducted to test the effectiveness of key messages about I-131 and web site usability of the dose calculator. Community health clinic staff, physicians, state health department officials, and Native American leaders, whose communities live in western parts of the United States mainly affected by fallout, were also consulted when developing these materials. ■

HPV Monograph Working Group

HPV MONOGRAPH IDENTIFIES PROMISING RESEARCH DIRECTIONS

Mark Schiffman, M.D., M.P.H. (Hormonal and Reproductive Epidemiology Branch), Dr. Diane Solomon (Division of Cancer Prevention), and DCEG visiting scientist **Xavier Bosch, M.D.** edited a *Journal of the National Cancer Institute Monograph* entitled "Future directions in epidemiologic and preventive research on human papillomaviruses and cancer," published in June. Comprised of 18 chapters, the monograph reviews the etiologic and preventive aspects related to human papillomavirus (HPV) infection and cancer risk, and focuses on defining the most promising areas for future research.

The process for developing and writing the monograph had some unique features. While one or two epidemiologists wrote each chapter, more than 30 cooperated in an informal review process of each other's chapters by e-mail and during a workshop held at NCI in June 2002. At the workshop, approximately 10 scientists were invited as "animators" who sparked freewheeling discussion of controversial topics. The meeting attempted to replicate the spirit of productive give-and-take that often occurs informally outside of workshops. This critical interaction led to quick publication of very up-to-date coverage of a wide range of topics including descriptive epidemiology, natural history, etiologic co-factors that promote HPV carcinogenesis, immunosuppression, screening by visual and cytologic methods, HPV DNA testing, public health policy, vaccinology, therapy, and special statistical issues. Early reviews of the monograph have suggested that it will be a useful research summary and teaching tool.

—Mark Schiffman, M.D., M.P.H.

NOTES FROM NEW CHAIR OF DCEG COMMITTEE OF SCIENTISTS

After two years of service on the DCEG Committee of Scientists (COS), I was both delighted and a little awed when **Dr. Joseph Fraumeni, Jr.,** invited me to serve as Chair. Delighted because over the past two years I have come to see COS as an effective vehicle devoted to enhancing the overall scientific environment of DCEG. Several factors contribute to this success. Most importantly, committee members have served with enthusiasm, creativity, and thoughtful care for the concerns of their colleagues. They demonstrate a committed effort to consider the needs of DCEG as a whole, reserving exploration of individual- or branch-specific issues only within the greater context of the Division. Candid discussions take place among DCEG members, who are valued for their unique perspective, experience, and leadership, irrespective of their title or status within DCEG. Moreover, the response by the Office of the Director to issues and recommendations voiced by COS has been gratifying. Division Director Dr. Fraumeni and Deputy Director **Dr. Shelia Zahm** have fully supported COS by listening to us, challenging us, and acting to implement our recommendations within the limits of their authority.

My awe arises from having to follow in the wake of three stellar previous COS Chairs: **Dr. Sholom Wacholder, Dr. Tom O'Brien,** and most recently, **Dr. Lois Travis.** All have provided strong leadership, vision, thoughtful guidance, and careful attention to detail, cementing COS's reputation for impartial, thorough consideration of issues important to all DCEG scientists. Each has left an indelible mark on COS and DCEG and we are indebted to them.

COS is committed to continuing valuable existing initiatives and proposing new endeavors consistent with its four-fold mandate: (1) improving communication, (2) reducing obstacles to productive research, (3) enhancing the scientific environment, and (4) promoting career development opportunities. Some of our recent efforts are summarized here.

Contractor Procurement Issues

To address concerns expressed by DCEG scientists, COS initiated a general review of issues affecting satisfaction with the performance of our major support service contractors. Discussions with Ms. Sharon Miller, of the Research Contracts Branch, reinforced the need for active, ongoing communication between Project and Contract Officers, between Branch members and contractors, and for critical performance review of contractor activities. At the recommendation of COS, a special seminar on contract management was presented to DCEG staff.

In response to concerns regarding aspects of the procurement process, COS recommended that instructions and guidance regarding procurements be maintained on the Intranet as a resource for DCEG staff. In addition, the DCEG Administrative Resource Center has developed standardized statements of work to assist staff.

DCEG Fellows

Following the first Town Meeting with Fellows in 2001, COS identified several issues of importance to DCEG fellows, including ambiguity of employment

DCEG LAUNCHES NEW WEB SITE

Hunting for the latest research at NCI in cancer epidemiology? Want to find out about fellowships in DCEG? Need to know what resources are available to conduct genetic research projects?

Then visit the DCEG web site, *http://dceg.cancer.gov,* which launched in July with a new look and feel. The site highlights key research areas pursued by DCEG staff and includes areas such as statistics and survey sampling, molecular epidemiology, genetics, and much more. Geared for prospective fellows, epidemiologists, statisticians, and clinicians involved in cancer epidemiology, the site also has a database of 4,440 publications from the Division. The "Areas of Research" section helps users identify staff members working in specific areas of epidemiology. Information and an online application for prospective fellows interested in training in cancer epidemiology and related areas are also available.

Since the debut of the new site, an average of 8,000 hits per day have been recorded. Ten percent come from overseas visitors. Research and fellowship pages have received the most frequent visits. During development, DCEG staff members provided critical content and feedback. Comments are welcome and can be emailed to Ms. Chitra Mohla *(mohlac@mail.nih.gov)*.

status, desire for consistent high-quality mentoring, and the need for a resource that provides consistent responses to commonly asked questions. COS investigated these matters at the DCEG, NCI, and NIH levels. Recommendations included introduction of a mentoring module in the COS Annual Survey of Branch Management (see below) and addition of information of general interest to fellows to the DCEG Intranet. This year, COS invited three former DCEG fellows to host a roundtable discussing their perspectives and recommendations for enhancing the DCEG fellowship experience.

DCEG Town Meetings

A series of town meetings with specific groups of DCEG scientists (principal investigators, staff scientists, fellows) has been sponsored by COS, providing opportunities for direct communication with Dr. Fraumeni and the Division leadership. The first cycle of town meetings was productive and identified several important issues for each group. Because of the transitory nature of the fellowship period, town meetings for DCEG fellows have been conducted annually with Dr. Fraumeni, Dr. Zahm, and **Dr. Demetrius Albanes,** Chief of the DCEG Office of Education. These meetings have evolved into a format that promotes a small-group atmosphere conducive to interactive exchange. All issues raised at these meetings have been addressed to the fullest extent possible. We anticipate repeating the town meetings for all groups at one- to three-year intervals.

Annual Survey of Branch Management

COS developed an anonymous, web-based survey asking DCEG members to evaluate how well their Branches function. Results are summarized by COS in a fashion to preserve anonymity and presented to Dr. Fraumeni and Dr. Zahm, who in turn share the results with each Branch Chief. The summary results are also made available to all DCEG scientists on the Intranet. Past survey results have indicated a high degree of satisfaction overall as well as areas that need attention, such as management skills training for DCEG scientists, which COS subsequently worked to implement. Comments from the survey have been particularly illuminating and have prompted corrective actions when appropriate. COS continually modifies the content of the survey to reflect evolving issues within the Division. New in 2003, for example, were expanded sections addressing mentoring and authorship issues, plus an evaluation of activities in the Office of the Division Director.

Mary Lou McMaster

Future Directions

In 2002, COS began a comprehensive assessment of the role of Staff Scientists within the Division, with particular emphasis on clarifying the performance review and promotion process for a group notable for its heterogeneity of function, skill sets, and appointment mechanisms. This complicated effort has been ably led by **Dr. Elizabeth Maloney** of the Viral Epidemiology Branch, assisted by **Ms. Kris Kiser** of the Office of Education. We are also considering other issues, such as promoting equitable access to research resources.

In summary, COS exists to serve the needs of all DCEG scientists, and its agenda is determined by the issues and concerns identified by our colleagues around the Division. I strongly encourage each of you to talk with your COS representative and/or me. I maintain COS office hours in Room 7010 on the second Friday of every month, from 2:00 to 4:00 pm. We always welcome your comments and suggestions on how to continue to cultivate a strong, positive working environment in DCEG. ■

—Mary L. McMaster, M.D.

James Lacey and Lifang Hou

DCEG SCIENTISTS WIN RESEARCH AWARDS

Lifang Hou, M.D., Ph.D., of the Occupational and Environmental Epidemiology Branch and **James Lacey, Ph.D., M.P.H.,** of the Hormonal and Reproductive Epidemiology Branch won top awards for their research at the 2003 American College of Epidemiology Annual Meeting, held in Chicago during September. Out of the 104 posters presented at the meeting, Dr. Hou received second prize for her poster on "Body mass index, physical activity, and risk of colon cancer in Shanghai," and Dr. Lacey received third prize for his poster on "Menopausal estrogen therapy and endometrial cancer in a U.S. cohort: Recency and potential interactions with other risk factors."

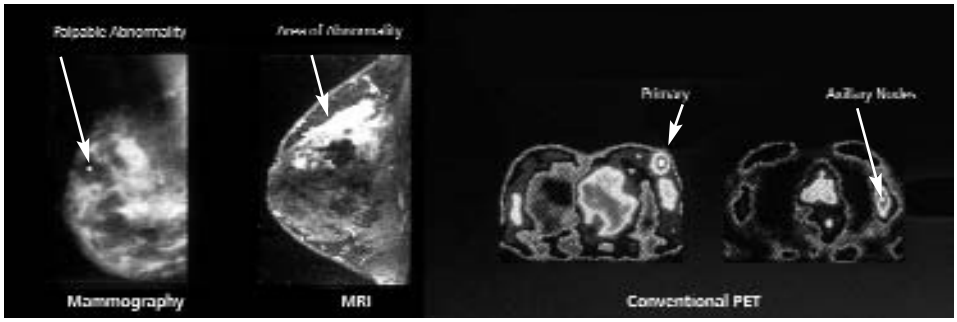
BREAST IMAGING STUDY

Seeking To Improve Cancer Detection in High-Risk Women

The Clinical Genetics Branch (CGB) is conducting the Breast Imaging Study, which will evaluate the use of several new and promising breast cancer screening techniques in women at high genetic risk of breast cancer. Reducing the burden of cancer is critical to women who have mutations in the breast cancer susceptibility genes *BRCA1* or *BRCA2*. Estimates show that 50 to 85 percent of these women will develop breast cancer by age 70 years; many will develop breast cancer before age 50 years. Although mammography plays a key role in early detection, it may miss breast cancers in young women. New techniques being evaluated include breast scanning using magnetic resonance imaging (MRI), positron emission tomography (PET), and breast duct lavage (BDL). The latter technique is used to obtain epithelial cell samples from breast ducts for cytologic evaluation.

Women who carry a *BRCA1* or *BRCA2* mutation are eligible to join the study, as are women who have a first- or second-degree relative with a breast/ovarian cancer related to *BRCA* mutations. All participants will receive a mammogram, an MRI, and BDL; women with abnormal mammograms or MRIs will be asked to undergo a PET scan. Screening is repeated at three-year intervals and involves evaluations for ovarian tumors as well. The study aims to recruit 200 women between 25 to 56 years.

To facilitate subject recruitment and to accelerate the completion of this study, **Sheila Prindiville, M.D., M.P.H.,** of the Genetics Branch in the Center for Cancer Research (CCR), has joined CGB as an Adjunct Investigator. Dr. Prindiville has become the Principal Investigator for the Breast Imaging Study and will work closely with **Mark H. Greene, M.D.,** Chief of CGB. In addition, **Lanny Kirsch, M.D.,** Chief of the CCR Genetics Branch, has joined the CGB as an Adjunct Investigator and will be collaborating on future laboratory-based research projects. Drs. Prindiville, Greene, and Kirsch were brought together by their mutual interests in hereditary breast cancer and in cancer prevention and early detection as they relate to high-risk populations.



Breast imaging technology comparing mammography, and MRI and PET scans

To enhance enrollment in the study, the group launched a media and educational campaign in the Washington, DC, metropolitan region in September 2003. More information about the Breast Imaging Study can be found at *http://breastimaging.cancer.gov.* ■

CERVICAL CANCER SCREENING STUDY RESULTS

In a series of articles appearing in the June 2003 issue of the *American Journal of Obstetrics and Gynecology* (volume 188; pages 1381–1412), Diane Solomon, M.D. (Division of Cancer Prevention), **Mark Schiffman, M.D., M.P.H.** (Hormonal and Reproductive Epidemiology Branch), and their colleagues published the major findings of a multiyear randomized clinical trial addressing the optimal management of minor cytological abnormalities found during screening for cervical cancer (Pap smear).

More commonly known as ALTS—**A**typical Squamous Cells of Undetermined Significance (ASCUS)/ **L**ow Grade Squamous Intraepithelial Lesion **T**riage **S**tudy (LSIL)—the trial built on the discovery that persistent infection with oncogenic types of human papillomavirus (HPV) causes virtually all cases of cervical cancer worldwide. ALTS concentrated on the evaluation of HPV DNA testing to clarify as ASCUS and LSIL the two categories of common cytologic abnormalities, which affect millions of women each year in the United States. The trial found that HPV testing is a useful method for determining which women with equivocal cytologic interpretations (ASCUS) have potentially precancerous lesions and which women can be safely reassured that their abnormalities are not threatening.

Because of the potential clinical impact of the findings, ALTS investigators decided to release the data a year before publication to a consensus meeting of more than 25 professional organizations. The consensus group relied heavily on the information to draft practice recommendations, which appeared in the April 24, 2002, issue of the *Journal of the American Medical Association.* The manuscripts outlining the detailed analyses were published as a quartet of papers, with many more ancillary analyses still under way.

—Mark Schiffman, M.D., M.P.H.

SAG RETREAT IDENTIFIES RESEARCH PRIORITIES

The DCEG Senior Advisory Group (SAG) held its sixth annual retreat on July 18 at Rockwood Manor in Potomac, Maryland. This year, the retreat focused on strategic planning for the Division at a time of budget constraints as the Institute embarks on a broad effort to contribute to NCI Director Dr. Andrew von Eschenbach's 2015 challenge goal to end suffering and death from cancer.

Senior Advisory Group

In his opening remarks, DCEG Director **Joseph Fraumeni, Jr., M.D.,** highlighted the importance of careful budgetary planning while developing research initiatives that build on the strengths and mission of the Division; have high potential for affecting scientific, clinical, or public health; and are aligned with the plans and goals of NCI, NIH, or the U.S. Department of Health and Human Services. He stressed that investigators should strive to incorporate multidisciplinary partnerships across the Division, NCI, and NIH, as well as to develop interagency and extramural collaborations that may leverage available resources. Investigators were also encouraged to seek ways to conduct research that are aligned with Congressional priorities and mandates, to identify gaps and unattended opportunities that are best addressed by the Division, and to optimize resources through good management and by ensuring equitable access to resources for both junior and senior researchers.

As part of a strategic training exercise, each Branch Chief presented an overview of the Branch research portfolio and identified key research opportunities to be pursued over the next four years under varying budget scenarios. At the conclusion of the presentations, SAG members were asked to identify the Division's highest research priorities. **Patricia Hartge, Sc.D.,** the Retreat Program Chair, summarized the results of the straw poll and led a discussion of ways to coordinate research activities across the Division to maximize data-mining opportunities.

The afternoon session, moderated by **Shelia Zahm, Sc.D.,** was devoted to a discussion of DCEG standing committees and working groups. **Aaron Blair, Ph.D.,** presented a summary of the Data Sharing Working Group's efforts to devise a formal Division-wide policy on sharing research data. **Andrew Bergen, Ph.D.,** described the efforts of the Epi-Informatics Working Group to develop recommendations for managing the impending data avalanche from molecular epidemiology studies. **Marianne Henderson, M.S.,** and **Chitra Mohla, M.S.,** provided an update on the activities of the Information Technology Oversight Committee to address the need for a research information system that will integrate data from studies across the Division into an accessible database with common elements. The Committee is also intensifying efforts to review and oversee the use of the contract that supports Division-wide computing activities.

Over the course of the day, a number of action items were identified, including approaches to leverage Division resources, to carefully track expenditures and implement cost control measures, to foster strategic scientific planning, and to deploy standing committees and working groups to devise measures to improve DCEG operations.

In the final session, **Robert Hoover, M.D., Sc.D.,** and Dr. Fraumeni led a wide-ranging discussion of strategic planning activities involving the Division, NCI, and NIH. Emphasis was placed on mechanisms to ensure careful deliberations in setting research priorities, developing budget proposals, deploying resources, and coordinating the research enterprise in the most cost-efficient manner. ■

—Cathy McClave, M.S.

CANCER AND NUTRITION EXPERT ELIO RIBOLI VISITS DCEG

One of the leading international experts in the area of diet and cancer spent six months in the Nutritional Epidemiology Branch as a Visiting Scientist. Elio Riboli, M.D., Sc.M., M.P.H., of the International Agency for Research on Cancer (IARC) in Lyon, France, worked in DCEG on methodologic issues related to measurement of dietary exposures and on the recently funded Cohort Consortium project on hormone metabolizing gene variants, gene-environment interactions, and breast and prostate cancer risk. Dr. Riboli, who heads the Unit of Nutrition and Cancer at IARC, is well known for his key role in initiating and coordinating EPIC—the European Prospective Investigation into Cancer and Nutrition. This large project, which began in 1989, involves some 500,000 subjects enrolled in multicenter prospective studies across nine European countries and aims at investigating the role of nutrition and other lifestyle factors in the etiology of cancer. EPIC plays a critical part in the Consortium project on breast and prostate cancer risk, of which Dr. Riboli serves as the project co-leader.

Dr. Riboli's interest in public health and disease prevention began in the early 1970's during his medical school years at the Institute of Hygiene in Milan. While working on a thesis on environmental disease, he observed that the epidemiology of common diseases was dramatically changing. Riboli recalls, "Cancer and cardiovascular disease were increasing in Italy and most of Europe. Treatment for these diseases could certainly be improved but was and still is of limited efficacy. Prevention seemed to me one complementary approach to reduce suffering and premature death."

His path into nutrition research happened "almost by chance," according to Dr. Riboli. During the early part of his career, while working on some projects involving diseases of the upper gastrointestinal tract, he became curious about the role of nutrition in disease etiology. "Eating and moving [physical activity] are, with breathing, the most universal ways by which our bodies interact with what we call the environment," he remembers thinking at the time. "Just imagine that a medium-sized person may consume as much as 4 kg of food and drinks per day—that's more than 1,500 kg per year—more than 20 times a person's body weight! Quite a lot of exogenous compounds come into our body through diet and end up being metabolized. So whatever is good or bad in nutrition could potentially be of universal relevance for public health."

Elio Riboli visits from the International Agency for Research on Cancer

Since moving to IARC in 1983, Dr. Riboli's main task has been developing new research projects in the area of nutrition and cancer. In addition to the EPIC study, he has collaborated in the planning and analysis of case-control studies on diet and cancers of the esophagus, stomach, colorectum, and bladder conducted in several European countries. In 1995, Dr. Riboli was appointed Chief of the Unit of Nutrition and Cancer where his foremost goal is the follow-up of the EPIC project over the next decade, involving an investigation into the role of nutrition and related metabolic, hormonal, and genetic factors in the etiology of cancers of the reproductive, respiratory, and digestive organs. He is also highly interested in improving the measurement of dietary exposures.

"The biggest challenge facing the field of nutrition and cancer research," notes Dr. Riboli, "is how to best investigate if there is a 'dose-effect' relationship between a factor A and a disease B. If the levels of exposure to factor A vary by small amounts in a given population and our measurement of A is imprecise, we may incorrectly conclude that A is not related to B. In nutrition we are often in the situation of studying a modest variation with a lot of imprecision."

These difficulties can be overcome by conducting multicenter prospective cohort studies (more populations, more heterogeneity of exposure) and by using combined methods for measuring diet, including calibration of dietary measurements and de-attenuation of relative risk estimates. Finding better and scientifically more informative ways of using biomarkers in epidemiological studies will also be vital in moving the field forward.

"There is much we can learn by introducing the dimension of 'genetic susceptibility,' which is expected to increase the power of detecting associations in subgroups defined by common genetic traits," concludes Dr. Riboli. "By deciphering these pieces, we hope to greatly enhance our understanding of the relationship between nutrition in health and various disease states, including cancer." ■

—Tanuja Rastogi, Ph.D., and
Maria Sgambati, M.D.

SUMMER PROGRAM

Record Number of Posters Mark a Successful 2003 Summer Program

Summer 2003 marked another highly successful summer student program at DCEG. The application process begins as early as November; this year DCEG received nearly 200 applications at all academic levels and accepted 17 students. The demographics broke out as follows: four high school students, three undergraduates, seven M.P.H. students, two M.S. students, and one doctoral student. Two students from last summer returned and two plan to continue work on research projects in the coming year, either at a master's level or in conjunction with their graduate work. "Spending the summer working at DCEG was amazing. In addition to gaining valuable work experience, I was able to put what I learned in class into practical use," remarked **Lindsay Hannan,** a student from Emory University.

"It is the sense of acceptance and respect by those we have looked up to for their achievements in the field, the free exchange of ideas that occurs on a daily basis, and the willingness of the mentors to unselfishly pass on their knowledge that make the summer experience so memorable."

This year was a landmark year for student poster presentations. Inspired by the example of **James Goedert, M.D.,** Chief, Viral Epidemiology Branch (VEB), who has long encouraged student presentations at the NIH summer poster session, DCEG had a record number of 13 posters for both the NIH and DCEG summer poster sessions. [See side bar for list of posters.] Many of the students were at first apprehensive about the task of putting together a coherent poster representing their summer's work, but they were pleasantly surprised at how much fun it was to discuss their research with senior scientists as well as other students. **Michael Pan** of Winston Churchill High School, described how his experience culminated in a poster: "I learned enough information to follow along in discussions, develop my own ideas, and complete a poster within a few months. It has been truly exciting, and I would recommend the experience to anybody."

The summer program aims to inspire and help students define their academic and career goals. "My experience in VEB was very fulfilling," commented **Bonnie Pederson,** of Tulane University. "I learned statistical, technical, and writing skills in a challenging and dynamic atmosphere. I was able to work independently on a

SUMMER STUDENTS AND MENTORS

BIOSTATISTICS BRANCH

- **Anney Che, M.S.,** mentor: **Philip Rosenberg, Ph.D.** Poster: *Power of SNP-by-SNP versus haplotype-based analysis of case-control studies.*
- **Samiran Sinha,** mentors: **Sholom Wacholder, Ph.D.** and **Nilanjan Chatterjee, Ph.D.** Poster: *Estimating joint effects of two exposures in the presence of model uncertainty: Bayesian, frequentist, and model-selection approaches.*

CLINICAL GENETICS BRANCH

- **John Mission,** mentor: **Mark H. Greene, M.D.** Poster: *Colorectal cancer in first degree relatives of BRCA1/2 mutation carriers: A case-control study of ovarian cancer patients in Israel.*
- **Stephanie Ashley,** mentor: **June Peters, M.S., C.G.C.**

NUTRITIONAL EPIDEMIOLOGY BRANCH

- **Lindsay Hannan,** mentor: **Michael Leitzmann, M.D., Dr. P.H.** Poster: *Physical activity and ovarian cancer.*
- **Daniel Koralek, M.A.,** mentor: **Michael Leitzmann, M.D., Dr.P.H.** Poster: *Specific sources of alpha-linolenic acid and the risk of prostate cancer.*
- **Katherine Hohman,** mentor: **Ulrike Peters, Ph.D.**
- **Katherine Roberts,** mentor: **Rachel Stoltzenberg-Solomon, Ph.D., M.P.H.** Poster: *Folate metabolism polymorphisms and risk for colorectal adenoma.*

DCEG summer students gain research experience

specific project along with good guidance from my mentor and other people working at DCEG. This experience has greatly contributed to my career direction following completion of my master's degree." **Katherine Roberts,** of George Washington University, intends to continue working on nutritional epidemiology projects through the coming school year and observed, "My mentor went out of her way to make sure I was getting a valuable experience. The summer also further reinforced my interest in epidemiology and helped shape my decision to continue in research. It was refreshing to be around so many people with a high intellectual curiosity and love of what they are doing."

All of this wouldn't be possible without DCEG mentors, who provide the guidance to make the program truly remarkable. "It is the sense of acceptance and respect by those we have looked up to for their achievements in the field, the free exchange of ideas that occurs on a daily basis, and the willingness of the mentors to unselfishly pass on their knowledge that make the summer experience so memorable," commented **Kate Hohman,** of Boston University.

Laura Gold, of Emory University, summed it up beautifully, "One of the best things about NCI is its friendly, intelligent atmosphere. Whenever I've needed advice about anything at all, I know I can get help not only from my mentors but also from anyone else at NCI. Everyone is very enthusiastic about the work they're doing, and that attitude rubs off on the summer students….We are constantly encouraged to think independently and be creative in solving problems."

More information about the summer program can be found at the DCEG web site: *http://dceg.cancer.gov.* ■

—Kris Kiser, M.H.A.

OCCUPATIONAL AND ENVIRONMENTAL EPIDEMIOLOGY BRANCH

- **Laura Gold,** mentor: **Roel Vermeulen, Ph.D.** Poster: *Parental occupational exposures and Ewing's sarcoma.*
- **Chuankai 'Michael' Pan,** mentors: **Bu-Tian Ji, M.D., Dr.P.H., Joseph Coble, Sc.D.,** and **Mustafa Dosemeci, Ph.D.** Poster: *An analysis of benzene measurements by industry, occupation, time period, and job exposure matrix rating.*

RADIATION EPIDEMIOLOGY BRANCH

- **Meredith Foster**, mentor: **Ruth Kleinerman, M.P.H.**

VIRAL EPIDEMIOLOGY BRANCH

- **Eric Nawar,** mentor: **Charles Rabkin, M.D.** Poster: *Risk factors for Kaposi's sarcoma among HHV-8 positive individuals with AIDS.*
- **Bonnie Pedersen,** mentor: **Greg Kirk, M.D., Ph.D., M.P.H.** Poster: *CYP3A5 haplotypes and serum aflatoxin-albumin adduct levels in West Africans.*
- **Len Rodman,** mentor: **Eric Engels, M.D., M.P.H.**
- **Danielle Rufo,** mentor: **James Goedert, M.D.** Poster: *Use of alcohol among HCV infected people with hemophilia.*
- **Nina Rustgi,** mentors: **Thomas O'Brien, M.D., M.P.H., Denise Whitby, Ph.D., Betty Conde, Ph.D.,** and **Rachel Bagni, M.S.** Poster: *Creating a HCV genotype archive for use in phylogenetic analyses.*
- **Tian Yang,** mentor: **James Goedert, M.D.** Poster: *Effects of acetaminophen and NSAID use among hemophiliacs.*

SCIENTIFIC HIGHLIGHTS

CERVICAL CANCER

Obesity and Body Fat Linked to Cervical Adenocarcinoma

Subjects with either adenocarcinoma (n = 124) or squamous cell carcinoma (n = 139) of the cervix and controls (n = 307) were studied to evaluate whether obesity, which can influence hormone levels, plays a role in cervical cancer. For adenocarcinoma, positive associations were found for height, weight, body mass index (BMI) ≥ 30 kg/m^2 versus BMI < 25 kg/m^2 (OR = 2.1; CI = 1.1–3.8), and waist-to-hip ratio ([WHR]; highest versus lowest tertile (OR = 1.8; CI = 1.0–3.3). For squamous cell carcinoma, associations for BMI and WHR were weaker and no association was found for height or weight. Analyses using only human papillomavirus positive controls showed similar associations. Higher BMI and WHR were associated with more advanced disease stage at diagnosis, even among recently and frequently screened patients with adenocarcinoma. **(Lacey JV Jr, Swanson CA, Brinton LA, Altekruse SF, Barnes WA, Gravitt PE, Greenberg MD, Hadjimichael OC, McGowan L, Mortel R, Schwartz PE, Kurman RJ, Hildesheim A. Obesity as a potential risk factor for adenocarcinomas and squamous cell carcinomas of the uterine cervix. *Cancer* 2003;98:814–821)**

HPV Identifies High-Grade Cervical Neoplasia

Data from the cervical cancer screening trial, ALTS—**A**typical Squamous Cells of Undetermined Significance (ASCUS)/**L**ow-Grade Squamous Intraepithelial Lesions (LSIL) **T**riage **S**tudy—were analyzed to compare post-colposcopy management strategies among women referred for LSIL or oncogenic human papillomavirus (HPV) DNA-positive ASCUS with cervical intraepithelial neoplasia (CIN) grade 1 or less found at initial colposcopy. Among 1,539 women followed for two years, HPV testing at 12 months showed 92 percent sensitivity for detection of CIN grade 2 or 3 with a referral rate to repeat colposcopy of 55 percent. Repeat semiannual cytology with referral to colposcopy at an ASCUS threshold demonstrated similar sensitivity (88 percent) but with a higher rate of referral to colposcopy (64 percent). Combining cytology and HPV testing did not increase sensitivity and impaired specificity. The most efficient test for identifying women with CIN grade 2 or 3 after colposcopy might be an HPV test alone at 12 months. Within the same study, 897 cases of LSIL and 1,193 cases of HPV-DNA positive ASCUS were followed for two years to determine the cumulative risk of CIN grade 2 or 3 according to initial colposcopy and directed biopsy results. The cumulative risk of CIN grade 2 or 3 was equivalent for LSIL (28 percent) and for HPV-DNA positive ASCUS (27 percent). After excluding women with a diagnosis of CIN grade 2 or 3 at initial colposcopy and directed biopsy (18 percent), the remaining women were at nearly identical risk for subsequent CIN grade 2 or 3 regardless of initial colposcopy result. LSIL and HPV DNA-positive ASCUS are clinically equivalent. Initial colposcopic detection of obviously prevalent CIN grade 2 or 3 reduces risk. For the remaining women who have CIN grade 1 or less on colposcopy and directed biopsy, however, the risk for subsequent CIN grade 2 or 3 (whether missed, prevalent, or truly incident) is approximately 12 percent over two years. This risk does not vary meaningfully by initial distinction of histologic CIN grade 1 from negative colposcopy and biopsy. **(Guido R, Schiffman M, Solomon D, Burke L, and the ALTS Group. Post-colposcopy management strategies for women referred with low-grade squamous intraepithelial lesions or human papillomavirus DNA-positive atypical squamous cells of undetermined significance: a two-year prospective study** and **Cox JT, Schiffman M, Solomon D, and the ALTS Group. Prospective follow-up suggests similar risk of subsequent cervical intraepithelial neoplasia grade 2 or 3 among women with cervical intraepithelial neoplasia grade 1 or negative colposcopy and directed biopsy. *Am J Obstet Gynecol* 2003;188:1401–1405** and **1406–1412)**

ESOPHAGEAL AND GASTRIC CANCER

Population Attributable Risks of Esophageal and Gastric Cancers

Population attributable risks (PARs) for various risk factors were estimated using 293 patients with esophageal adenocarcinoma, 261 with gastric cardia adenocarcinoma, 221 with esophageal squamous cell carcinoma, 368 with noncardia gastric adenocarcinoma, and 695 control subjects from a population-based case-control study. Smoking was included for all four tumor types and *Helicobacter pylori* infection was included for noncardia gastric adenocarcinoma. Ever smoking, BMI above the lowest quartile, history of gastroesophageal reflux, and low fruit and vegetable consumption accounted for 40, 42, 30, and 15 percent of esophageal adenocarcinomas, respectively, with a combined PAR of 79 percent. Ever smoking and BMI above the lowest quartile were responsible for 45 and 19 percent of gastric cardia adenocarcinomas, respectively, with a combined PAR of 56 percent. Ever smoking, alcohol consumption, and low fruit and vegetable consumption accounted for 57, 72, and 29 percent of esophageal squamous cell carcinomas, respectively, with a combined PAR of 89 percent. Ever smoking, history of gastric ulcers, nitrite intake above the lowest quartile, and *H. pylori* infection were responsible for 18, 10, 41, and 10 percent of noncardia gastric adenocarcinomas,

respectively, with a combined PAR of 59 percent. The incidence of these cancers would be lowered by reducing the prevalence of smoking, gastroesophageal reflux, and obesity, and by increasing fruit and vegetable consumption. **(Engel LS, Chow WH, Vaughan TL, Gammon MD, Risch HA, Stanford JL, Schoenberg JB, Mayne ST, Dubrow R, Rotterdam H, West AB, Blaser M, Blot WJ, Gail MH, Fraumeni JF Jr. Population attributable risks of esophageal and gastric cancers. *J Natl Cancer Inst* 2003;95:1404–1413)**

Serum Vitamin E and Risk of Upper Gastrointestinal Cancers

Participants in the Linxian, China General Population Trial, a randomized nutrition intervention study, who received a combination of selenium, beta-carotene, and vitamin E supplements, had lower cancer mortality rates than those who did not receive the supplements. Within this trial, a case-cohort design was used to examine the association between pretrial serum vitamin E levels and the risks of developing esophageal and gastric cancers. Serum alpha- and gamma-tocopherol and cholesterol levels were measured in 1,072 cases with incident esophageal squamous cell carcinoma (ESCC), gastric cardia cancer (GCC), or gastric noncardia cancer (GNCC) and in 1,053 control subjects. The relative risks for comparisons of the highest to the lowest quartiles of serum alpha-tocopherol were 0.63 (CI = 0.44–0.91) for ESCC, 0.84 (CI = 0.55–1.26) for GCC, and 2.05 (CI = 0.89–4.75) for GNCC. Serum gamma-tocopherol levels were not associated with the incidence of any of these cancers. In this endemic area for ESCC and GCC, these findings provide support for the role of alpha-tocopherol in the etiology of upper gastrointestinal cancers. **(Taylor PR, Qiao YL, Abnet CC, Dawsey SM, Yang CS, Gunter EW, Wang W, Blot WJ, Dong ZW, Mark SD. Prospective study of serum vitamin E levels and esophageal and gastric cancers. *J Natl Cancer Inst* 2003;95:1414–1416)**

GENETICS

Gynecologic Surgery Reduces Risk of Ovarian Cancer in *BRCA* Mutation Carriers

Women with *BRCA1* and *BRCA2* mutations are reported to have a low risk of peritoneal carcinoma in the first years after bilateral oophorectomy (BO). To assess the level and persistence of reduction of ovarian and peritoneal cancer risk after gynecologic surgeries, 847 Israeli women with incident ovarian cancer or primary peritoneal cancer were tested for the three Ashkenazi founder mutations. A comparison of gynecologic surgery history among all case patients, *BRCA1* (n = 187) and *BRCA2* (n = 64) carrier case patients, and non-carrier case patients (n = 598) to control subjects drawn from a population registry (n = 2,396) found that 8 women with primary peritoneal cancer and 128 control subjects reported a previous BO (OR = 0.1, CI = 0.1–0.2). Other gynecologic surgeries were associated with a 30 to 50 percent reduced risk of ovarian cancer. Removal of some ovarian tissue was associated with the most risk reduction (OR = 0.3, CI = 0.2–0.7). Reduced risks were seen in *BRCA1/2* carriers and non-carriers. Age at surgery and years since surgery did not affect risk reductions but type and extent of surgery did. **(Rutter JL, Wacholder S, Chetrit A, Lubin F, Menczer J, Ebbers S, Tucker MA, Struewing JP, Hartge P. Gynecologic surgeries and risk of ovarian cancer in women with *BRCA1* and *BRCA2* Ashkenazi founder mutations: An Israeli population-based case-control study. *J Natl Cancer Inst* 2003;95:1072–1078)**

Clues to Familial CLL Susceptibility Genes

Chronic lymphocytic leukemia (CLL) shows significant familial aggregation, but the mode of inheritance is unknown. To search for susceptibility genes, DNA from 94 individuals (38 affected patients) in 18 families was used for a genome scan using medium density linkage mapping set (average spacing of 10 cM and average heterozygosity of 80 percent). Genotypes for 359 markers were scored. Multipoint limit of detection scores of 1.0 or greater were found on regions of chromosomes 1, 3, 6, 12, 13, and 17, but none of these loci achieved statistical significance. Four of these six regions (6q, 13q, 12, and 17p) coincide with areas where cytogenetic abnormalities are frequently observed in CLL tumor cells and are, therefore, strong candidate regions for containing germ line changes. In a separate study of the same population, lymphocytes and DNA from 35 of 37 affected patients and from all 46 unaffected relatives revealed normal ATM (ataxia-telangiectasia mutated) protein expression and no mutations in the ATM gene region (11q23). Two CLL cases had impaired ATM protein expression. These results do not support a role for the ATM gene in familial CLL susceptibility. **(Goldin LR, Ishibe N, Sgambati M, Marti GE, Fontaine L, Lee MP, Kelley JM, Scherpbier T, Buetow KH, Caporaso NE. A genome scan of 18 families with chronic lymphocytic leukaemia. *Br J Haematol* 2003;121:866–873)** and **Ishibe N, Goldin LR, Caporaso NE, Sgambati MT, Dean M, Albitar M, Manshouri T, Gerrard B, Marti GE. ATM mutations and protein expression are not associated with familial B-CLL cases. *Leuk Res* 2003;27:973–975)**

Mitochondrial Enzyme Linked to High-Grade Prostate Tumors

Manganese superoxide dismutase (MnSOD) is a mitochondrial enzyme that plays a key role in protecting the cell from oxidative damage. A polymorphism in the mitochondrial targeting sequence (a valine [*val*] to alanine [*ala*] substitution) has been associated with increased risk for breast cancer. The role of MnSOD in the development of prostate cancer was examined in 197 cases and 190 controls from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study conducted among male smokers. Men homozygous for the MnSOD *ala* allele had an increased risk

over men homozygous for the *val* allele (OR = 1.7; CI = 1.0–3.1). Alpha-tocopherol supplementation had no impact on the MnSOD-prostate cancer association. Although there was no difference in the association with disease stage, men homozygous for MnSOD *ala* (compared to *val/val* or *val/ala*) showed a threefold increase in risk of high-grade tumors (OR = 2.7; CI = 1.2–6.4). These data suggest an effect of the MnSOD *ala/ala* genotype on the development of prostate cancer; the stronger association with high-grade tumors may have prognostic implications. **(Woodson K, Tangrea JA, Lehman TA, Modali R, Taylor KM, Snyder K, Taylor PR, Virtamo J, Albanes D. Manganese superoxide dismutase (MnSOD) polymorphism, alpha-tocopherol supplementation and prostate cancer risk in the alpha-tocopherol, beta-carotene cancer prevention study (Finland).** ***Cancer Causes Control*** **2003;14:513–518)**

HORMONE-RELATED CANCERS

Maternal Hormone Levels in Preeclamptic and Uncomplicated Pregnancies

Epidemiological studies show a substantially reduced risk of breast cancer in adult daughters of preeclamptic pregnancies; modest risk reductions have also been demonstrated for the mothers. Alterations in pregnancy hormone concentrations are hypothesized to mediate this association. Pregnancy hormone concentrations were measured in maternal sera collected at hospital admission for labor and delivery from 86 preeclamptic and 86 uncomplicated, singleton pregnancies. Case and control pregnancies had similar levels of serum unconjugated estradiol, estrone, and estriol concentrations. Serum unconjugated androstenedione (506 versus 316 ng/dL; $p = 0.0007$) and testosterone concentrations (214 versus 142 ng/dL; $p = 0.004$), however, were significantly higher in preeclamptic compared with control pregnancies, whereas dehydroepiandrosterone and dehydroepiandrosterone sulphate did not differ. These findings do not support a role for maternal blood estrogen concentrations in breast cancer risk among mothers and offspring of preeclamptic pregnancies, but they do raise the possibility that androgens play a role. **(Troisi R, Potischman N, Roberts JM, Ness R, Crombleholme W, Lykins D, Siiteri P, Hoover RN. Maternal serum estrogen and androgen concentrations in preeclamptic and uncomplicated pregnancies.** ***Int J Epidemiol*** **2003;32:455–460)**

INFECTIOUS AGENTS

No Link Between Simian Virus 40 and Lymphoid Neoplasms

Some recent studies have implicated simian virus 40 (SV40) in non-Hodgkin's lymphoma based on detection of SV40 DNA sequences in tumors. A virus-like-particle (VLP)-based enzyme immunoassay for antibodies to SV40 was used to test sera from 520 cases with lymphoid neoplasms and 587 controls in Spain. The SV40 seroprevalence was 9.5 percent in controls and 5.9 percent in cases, with low antibody levels detected in the positive sera. There was no association of SV40 seropositivity with any subtype of lymphoma, and VLPs of the human BK virus substantially inhibited the SV40 reactivity of human sera. **(de Sanjose S, Shah KV, Domingo-Domenech E, Engels EA, Fernandez de Sevilla A, Alvaro T, Garcia-Villanueva M, Romagosa V, Gonzalez-Barca E, Viscidi RP. Lack of serological evidence for an association between simian virus 40 and lymphoma.** ***Int J Cancer*** **2003;104:522–524)**

Predictors of AIDS-Associated Kaposi's Sarcoma

A nested case-control analysis was conducted to identify immunologic and virologic predictors of AIDS-associated Kaposi's sarcoma (KS) among a cohort of 132 HIV-infected homosexual men in New York and Washington, DC. Thirty-one men developed AIDS-associated KS (incidence 3.1 per 100 person years). KS incidence was higher among those with K8.1 seropositivity (5.0 versus 1.4 per 100 person years; $p = 0.004$), low CD4 cell count (hazard ratio [HR] = 1.49; CI = 1.24–1.79 per 100 x 10^6 cells/L decline), or high HIV RNA level (HR = 3.96; CI = 2.19–7.16 per $\log_{10}$). KS herpesvirus (KSHV) viremia was observed at generally low levels in 9 of 70 evaluated subjects and was associated with increased KS risk (OR = 11.7; CI = 1.8–76). Among K8.1-seropositive subjects, KS incidence was tenfold higher in those with KSHV viremia (30.3 per 100 person years versus 3.4 per 100 person years in those without viremia). Among individuals with HIV-KSHV coinfection, KSHV viremia identifies a subgroup with extremely high risk for developing KS. **(Engels EA, Biggar RJ, Marshall VA, Walters MA, Gamache CJ, Whitby D, Goedert JJ. Detection and quantification of Kaposi's sarcoma-associated herpesvirus to predict AIDS-associated Kaposi's sarcoma.** ***AIDS*** **2003;17:1847–1851)**

Immune Responses to HPV Vaccine

Current candidate vaccines for prevention of human papillomavirus (HPV) infection and cervical neoplasia include noninfectious VLPs, composed of the L1 major capsid protein. In a phase II trial to study the immunogenicity of a recombinant HPV-16 L1 VLP vaccine, cell-mediated immune responses were evaluated in peripheral blood mononuclear cells (PBMCs) from 43 individuals receiving the vaccine intramuscularly at 0, 1, and 6 months and from 10 individuals receiving placebo. Vaccination resulted in increases in T-cell-proliferative response to HPV-16 L1 VLPs ($p < 0.001$). Significant increases in cytokine (interferon-gamma, interleukin [IL]-5 and IL-10) responses to L1 VLPs were observed after vaccination ($p < 0.001$). The strongest cytokine responses at month 7 were observed in individuals with high antibody titers at month 2, suggesting that neutralizing antibodies generated by initial vaccination may augment T-cell responses to subsequent booster vaccinations. No significant

increases in lymphoproliferative or cytokine responses to L1 VLPs were observed in individuals receiving placebo. The HPV-16 L1 vaccine induces not only robust B-cell responses but also L1-specific T-cell responses. **(Pinto LA, Edwards J, Castle PE, Harro CD, Lowy DR, Schiller JT, Wallace D, Kopp W, Adelsberger JW, Baseler MW, Berzofsky JA, Hildesheim A. Cellular immune responses to human papillomavirus (HPV)-16 L1 in healthy volunteers immunized with recombinant HPV-16 L1 virus-like particles. *J Infect Dis* 2003;188:327–338)**

KIDNEY CANCER

Long-Term Smoking Cessation Reduces Risk of Kidney Cancer

To better characterize the magnitude and timing of decrease in risk of renal cell carcinoma (RCC) associated with smoking cessation, cases (n = 387) that were identified through the Iowa Cancer Registry were compared to randomly selected population controls (n = 2,333). Smoothing spline regression analysis provided evidence of a consistent inverse linear trend between years of cessation and risk of RCC (Figure 1). In categorical analysis, compared with current smokers, those quitting ≥ 30 years ago experienced a 50 percent reduced risk (OR = 0.5, CI = 0.3–0.8). Risk among long-term quitters was similar to risk among never smokers (OR = 0.6, CI = 0.4–0.8). In contrast, cessation of < 10 years, 10 to 19 years, and 20 to 29 years all resulted in a less pronounced reduction in RCC risk of approximately 20 to 30 percent. **(Parker AS, Cerhan JR, Janney CA, Lynch CF, Cantor KP. Smoking cessation and renal cell carcinoma. *Ann Epidemiol* 2003;13:245–251)**

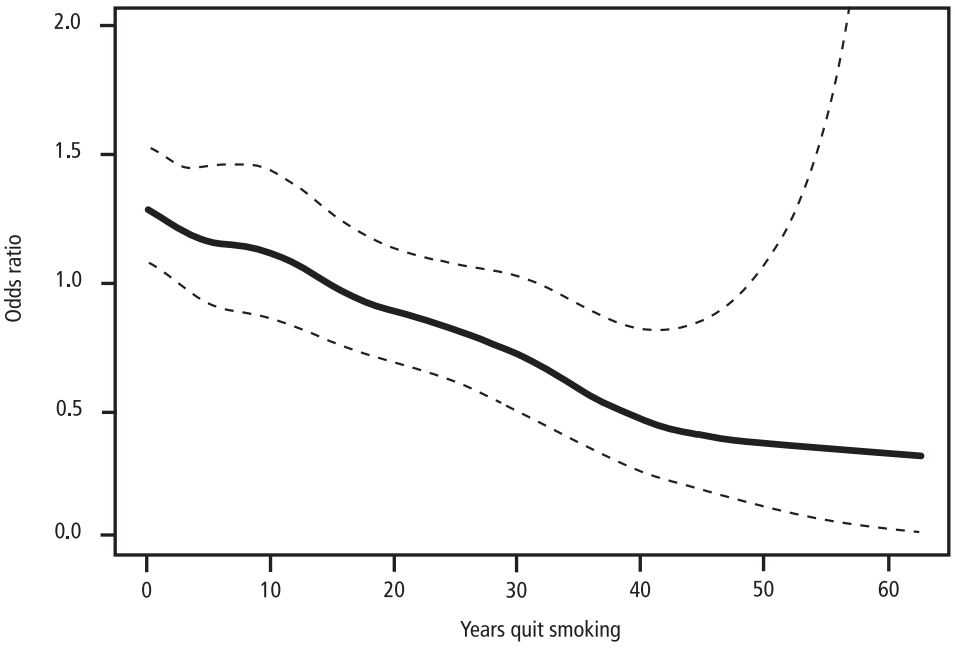


Figure 1. Association [OR (solid line) and 95 percent CI (dotted lines)] of cessation years with risk of RCC in a univariate generalized additive model controlling for age, BMI, hypertension, and pack years of smoking. Current smokers have a value of zero for cessation years and never smokers are excluded from the analyses (Parker, et al. *Ann Epidemiol* 2003;13:245–251).

MELANOMA

Trends in Ocular Melanoma Incidence

Data collected through the Surveillance, Epidemiology, and End Results (SEER) program were studied for melanoma incidence among U.S. whites. The incidence of ocular melanoma decreased over time in both sexes, with no indication of an increase during the 1990's, as might have been expected on the basis of a recent German study linking this tumor to cell phone use. The annual percent change was -0.7 percent for males (CI = -2.3–0.9) and -1.2 percent for females (CI = -2.5–0.0). Time trends appeared to differ by subsite of ocular melanoma, with rates being flat for the choroid, decreased for the ciliary body, and increased for the conjunctiva (among males only) beginning in the 1980's. In contrast, all subsites of cutaneous melanoma, including the face and adjacent areas, showed marked increases in incidence over the observation period. Further study is required to explain the different time trends for subsites of ocular melanoma, and for ocular versus facial and other cutaneous melanomas. **(Inskip PD, Devesa SS, Fraumeni JF Jr. Trends in the incidence of ocular melanoma in the United States, 1974–1998. *Cancer Causes Control* 2003;14:251–257)**

METHODS

Electron-Beam Irradiation Reduces the Yield and Quality of Buccal-Cell DNA

Buccal cells were collected from 29 participants, by use of mouthwash rinses, and were split into equal aliquots, with one aliquot irradiated by electron-beam (E-beam) irradiation equivalent to the sterilizing dosage used by the U.S. Postal Service and with the other left untreated. Irradiated aliquots had lower median DNA yields than untreated aliquots (3.7 versus 7.6 mg/aliquot, $p < 0.0005$) and were more likely to have smaller maximum DNA fragment size ($p < 0.0005$). Irradiated aliquots showed poorer PCR amplification of a 989-bp beta-globin target than untreated aliquots (Figure 2), but 536-bp and 268-bp beta-globin targets were amplified from all aliquots. There was no detectable irradiation effect on single-nucleotide polymorphism assays, but there was a trend for decreased detection of longer single tandem repeats ($p = 0.01$) in irradiated versus untreated aliquots. E-beam irradiation reduces the yield and quality of buccal-cell specimens. Although irradiated specimens may retain sufficient

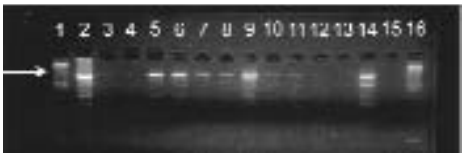


Figure 2. Irradiated aliquots show poorer PCR amplification of a 989-bp (arrow) beta-globin target (Castle, et al. *Am J Hum Genet* 2003;73:646–651).

DNA integrity for some amplified analyses of many common genomic targets, assays that target longer DNA fragments (> 989 bp) or require whole-genome amplification may be compromised. **(Castle PE, Garcia-Closas M, Franklin T, Chanock S, Puri V, Welch R, Rothman N, Vaught J. Effects of Electron-Beam Irradiation on Buccal-Cell DNA. *Am J Hum Genet* 2003;73:646–651)**

NUTRITION

Follow-up in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study

In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study, alpha-tocopherol supplementation decreased prostate cancer incidence, whereas beta-carotene increased the risk of lung cancer and total mortality among Finnish male smokers. Post-intervention follow-up for cancer incidence and cause-specific mortality was conducted on 25,563 men. The link between beta-carotene supplementation and lung cancer risk disappeared (relative risk [RR] =1.06; CI = 0.94–1.20, recipients of beta-carotene versus nonrecipients) (Figure 3). For prostate cancer, the RR was 0.88 (CI = 0.76–1.03) for participants that had received alpha-tocopherol compared with non-recipients. No late preventive effects on other cancers were observed for either supplement. Among the 7,261 individuals who died during the post-trial follow-up period, the RR was 1.01 (CI = 0.96–1.05) for alpha-tocopherol recipients versus non-recipients and 1.07 (CI = 1.02–1.12) for beta-carotene recipients versus non-recipients. The beneficial and adverse effects of supplemental alpha-tocopherol and beta-carotene disappeared during

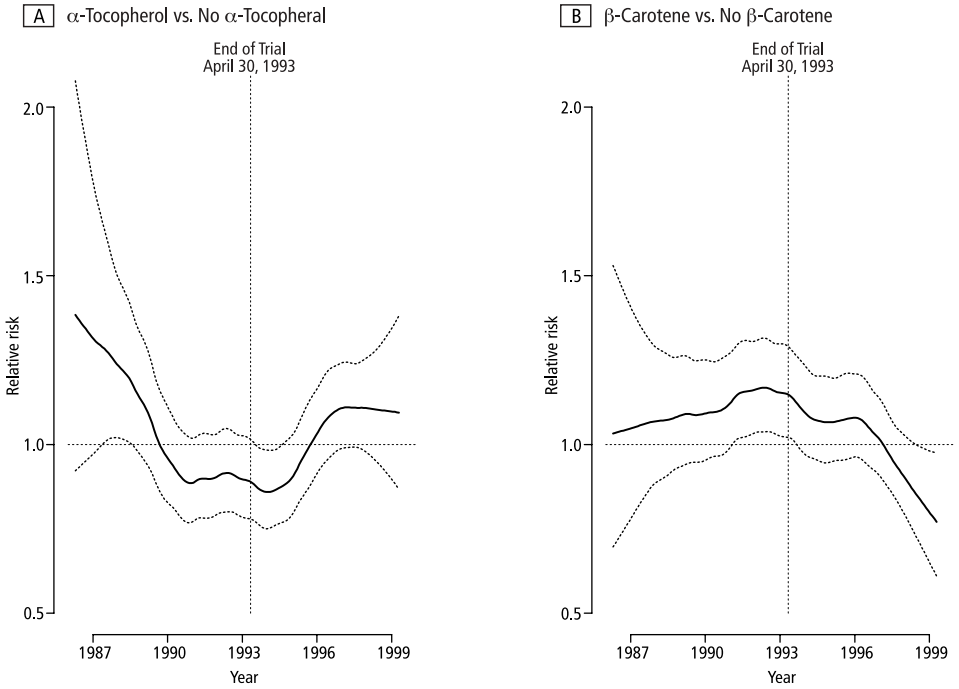


Figure 3. Lung cancer incidence for participants in the ATBC study. Smoothed relative risk curves and 95 percent pointwise confidence intervals in calendar time (The ATBC Study Group. *JAMA* 2003;290:476–485).

postintervention follow-up. The preventive effects of alpha-tocopherol on prostate cancer require confirmation in other trials. **(Virtamo J, Pietinen P, Huttunen JK, Korhonen P, Malila N, Virtanen MJ, Albanes D, Taylor PR, Albert P, ATBC Study Group. Incidence of cancer and mortality following alpha-tocopherol and beta-carotene supplementation: A postintervention follow-up. *JAMA* 2003;290:476–485)**

Biomarkers Confirm Underreporting on Dietary Instruments

The Observing Protein and Energy Nutrition (OPEN) Study was conducted to assess dietary measurement error using two self-reported dietary instruments—the food frequency questionnaire (FFQ) and the 24-hour dietary recall (24HR)—and biomarkers of energy and protein intakes: doubly labeled water and urinary nitrogen. Participants were 484 men and women aged 40 to 69 years from Montgomery County, Maryland. Nine percent of men and 7 percent of women were defined as underreporters of both energy and protein intake on 24HRs; for FFQs, the comparable values were 35 percent for men and 23 percent for women. On average, men underreported energy intake compared with total energy expenditure by 12 to14 percent on 24HRs and 31 to 36 percent on FFQs and underreported protein intake compared with a protein biomarker by 11 to 12 percent on 24HRs and 30 to 34 percent on FFQs. Women underreported energy intake on 24HRs by 16 to 20 percent and on FFQs by 34 to 38 percent and underreported protein intake by 11 to 15 percent on 24HRs and 27 to 32 percent on FFQs. These findings have important implications for nutritional epidemiology and dietary surveillance. **(Subar AF, Kipnis V, Troiano RP, Midthune D, Schoeller DA, Bingham S, Sharbaugh CO, Trabulsi J, Runswick S, Ballard-Barbash R, Sunshine J, Schatzkin A. Using intake biomarkers to evaluate the extent of dietary misreporting in a large sample of adults: The OPEN study. *Am J Epidemiol* 2003;158:1–13)**

ORAL CANCER

Occupational Exposures and Risk of Oral Cancer

Data from a population-based, case-control study conducted in Puerto Rico were analyzed using a job-exposure

matrix to investigate the relationship between occupational exposures and cancers of the oral cavity or pharynx. The risk for cancer of the oral cavity, but not the pharynx, was significantly elevated among farm workers in the sugarcane industry (OR = 4.4; CI = 1.4–13.6). An exposure-response trend was seen for cumulative exposure to solvents, with an OR = 3.2 (CI = 0.8–12.6) in the highest exposure category. The overall contribution to the risk of cancer of the oral cavity or pharynx associated with occupational exposures in Puerto Rico appears to be small; however, elevated risks were seen among sugarcane farmers and subjects with high cumulative exposure to solvents. **(Coble JB, Brown LM, Hayes RB, Huang WY, Winn DM, Gridley G, Bravo-Otero E, Fraumeni JF Jr. Sugarcane farming, occupational solvent exposures, and the risk of oral cancer in Puerto Rico. *J Occup Environ Med* 2003;45:869–874)**

RADIATION

Russian Nuclear Workers Have Increased Risks of Solid Tumors and Leukemia

The cancer risks associated with protracted exposure to external whole-body gamma radiation at high cumulative doses were studied in a cohort of 21,500 Russian nuclear workers who began working at the Mayak complex between 1948 and 1972. Both solid cancer and leukemia death rates increased significantly with increasing gamma-ray dose ($p < 0.001$). Plutonium exposure was associated with increased risks for lung, liver, and skeletal cancers and for other solid cancers as a group, but not with leukemia. Under a linear dose-response model, the excess relative risk (ERR) for lung, liver, and skeletal cancers as a group (668 deaths) adjusted for plutonium exposure was 0.30/Gy ($p < 0.001$) compared to 0.08/Gy ($p < 0.001$) for all other solid cancers (1,062 deaths) (Figure 4). For leukemia, the ERR/Gy was estimated to be 7 ($p < 0.001$) for doses received within 3 to 5 years of death and 0.45 ($p = 0.02$) for doses received 5 to 45 years prior to death. **(Shilnikova NS, Preston DL, Ron E, Gilbert ES, Vassilenko EK, Romanov SA, Kuznetsova IS, Sokolnikov ME, Okatenko PV, Kreslov VV, Koshurnikova NA. Cancer mortality risk among workers at the Mayak nuclear complex. *Radiat Res* 2003;159:787–798)**

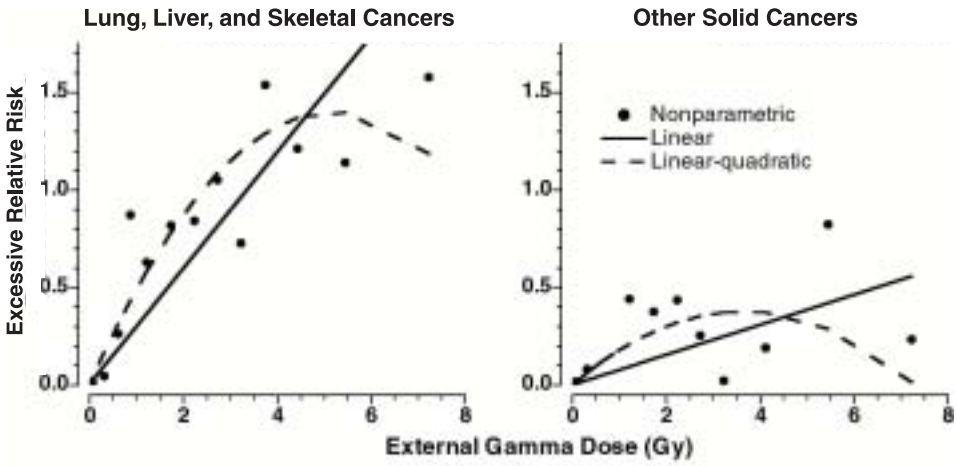


Figure 4. Parametric and nonparametric descriptions of the external dose response for the solid cancer excess relative risk in the Mayak worker cohort (Shilnikova, et al. *Radiat Res* 2003;159:787–798).

MARTHA LINET ELECTED PRESIDENT OF THE AMERICAN COLLEGE OF EPIDEMIOLOGY

Martha S. Linet, M.D., M.P.H., who is Chief of the Radiation Epidemiology Branch, was recently elected President of the American College of Epidemiology (ACE) at the annual September meeting in Chicago. Dr. Linet will begin her term in September 2004 and serve for three years (president-elect, president, past-president). Dedicated to continued education and advocacy for epidemiologists in their efforts to promote public health, ACE serves the interests of its members through sponsorship of scientific meetings, publications, educational activities, recognition of outstanding contributions to the field, and advocacy for issues pertinent to the practice of epidemiology. ACE currently has close to 1,000 members and sponsors the journal *Annals of Epidemiology.*

Martha Linet

DCEG PEOPLE IN THE NEWS

Juan Alguacil, M.D., Ph.D., M.P.H., of the Occupational and Environmental Epidemiology Branch (OEEB), gave talks during June on "Urinary pH and bladder cancer risk" at the Institut Municipal d'Investigació Mèdica in Barcelona, at the National Institute of Health in Madrid, and at the University Miguel Hernandez in Alicante. He also was invited to speak on "*NAT1* and *NAT2* polymorphisms, red meat and prostate cancer risk" at the Catalan Institute of Oncology in Barcelona. While in Barcelona, Dr. Alguacil co-directed a course: "Use of biomarkers in epidemiological studies on environmental and occupational health."

Blanche Alter, M.D., M.P.H., Mark H. Greene, M.D., and **June Peters, M.S., C.G.C.,** all of the Clinical Genetics Branch (CGB), will serve as adjunct faculty in the National Human Genome Research Institute's Medical Genetics Fellowship Training program. The three-year program entails 18 months of laboratory experience, 18 months of clinical experience, and classroom lectures. As part of their clinical research, fellows will participate in the CGB Familial Cancer Clinics.

Aaron Blair, Ph.D. (OEEB), delivered the plenary lecture on "Cancer and chronic diseases in the Agricultural Health Study cohort" at the conference on Future of Rural Peoples held during October in Saskatoon, Canada. Dr. Blair also gave a keynote lecture on "Occupational and environmental cancer" at the Annual Conference of the Korean Society of Preventive Medicine held at the National Cancer Institute in Seoul during October.

Andre Bouville, Ph.D., of the Radiation Epidemiology Branch (REB), gave an invited presentation at a National Research Council meeting in Washington, DC, which was held to assess the distribution and administration of potassium iodide in the event of a nuclear accident.

Philip Castle, Ph.D., of the Hormonal and Reproductive Epidemiology Branch (HREB), gave talks on "Human papillomavirus and the development of cervical pre-cancer and cancer" at the University of Texas Southwestern in Dallas and at the University of New Mexico in Albuquerque. He also spoke on "Cervical cancer risk factors —HPV vaccines" at the Latin American Federation of Oncology Societies meeting held in Córdoba, Argentina. In addition, Dr. Castle recently joined the editorial board of the *Journal of Lower Genital Tract Disease.*

In July, **Jinbo Chen, Ph.D.** (BB), gave an invited talk on "Haplotype analysis for cohort and nested case-control studies" at the National Heart, Lung, and Blood Institute.

Seven DCEG investigators taught in the Division of Cancer Prevention 2003 Cancer Prevention Fellowship Summer Curriculum: **Susan Devesa, Ph.D.,** and **Barry Graubard, Ph.D.,** (BB); **Mark H. Greene, M.D.** (CGB); **Robert Hoover, M.D., Sc.D.,** Epidemiology and Biostatistics Program; **Arthur Schatzkin, M.D., Dr.P.H.,** Nutritional Epidemiology Branch (NEB); **Aaron Blair, Ph.D.,** and **Nathaniel Rothman, M.D., M.P.H., M.H.S.** (OEEB).

Mustafa Dosemeci, Ph.D. (OEEB), gave an invited seminar on "Assessing occupational exposures in respiratory epidemiological studies" at a meeting of the National Institute for Occupational Safety and Health held in Morgantown, West Virginia.

Alisa Goldstein, Ph.D. (GEB), gave an invited talk on "Familial melanoma, pancreatic cancer and germline *CDKN2A* mutations" at the First International Melanoma Research Congress during June in Philadelphia. At the same meeting, **Margaret Tucker, M.D.,** (GEB), spoke on "Host factors and risk of melanoma." Drs. Goldstein and Tucker also spoke on "Modification of *CDKN2A*-associated melanoma risk" and "Genetic epidemiology of melanoma," respectively, at the annual meeting of the American Association for Cancer Research (AACR) to be held in Washington, DC.

Andrea Baccarelli and Nathaniel Rothman

Andrea Baccarelli, M.D., M.P.H., of the Genetic Epidemiology Branch (GEB), and **Nathaniel Rothman, M.D., M.P.H., M.H.S.** (OEEB), were invited speakers at the 2003 Congress of the European Societies of Toxicology, held in Florence, Italy, in September. Dr. Baccarelli lectured on "Aryl-hydrocarbon receptor-dependent pathway and toxic effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin: A population-based study in Seveso, Italy" and Dr. Rothman spoke on "Application of new technologies to molecular epidemiology studies of occupational cancer."


Deirdre Hill

Deirdre Hill, Ph.D. (REB), received the Radiation Research Society 2003 Scholars-in-Training Travel Award. The award recognizes young investigators who are making significant contributions in radiation research and provides financial assistance to attend the 12th International Congress of Radiation Research. Dr. Hill presented her work on "Diagnostic and therapeutic radiation in relation to risk of glioma, meningioma, and acoustic neuroma" at the 2003 congress, which was held during August in conjunction with the 50th Annual Meeting of the Radiation Research Society in Brisbane, Australia.

Lifang Hou, M.D., Ph.D. (OEEB), received a Takeda Scholar-in-Training Award to attend the AACR meeting on "SNPs, haplotypes, and cancer: Applications in molecular epidemiology" in Key Biscayne, Florida. Dr. Hou presented her research on *CYP1A1* and *NQ01* polymorphisms and their relationship to smoking and risk of colorectal adenoma.


Lifang Hou

In August, **Ann Hsing, Ph.D.** (HREB), served as the DCEG representative for the External Advisory Board overseeing proposed epidemiologic studies within the Prostate Cancer Prevention Trial. The studies are aimed at clarifying the reasons for the elevated incidence of high-grade prostatic tumors in subjects treated with finasteride, a 5-alpha reductase inhibitor.


Peter Inskip

Peter Inskip, Sc.D. (REB), gave an invited talk on "Etiology of brain tumors: Recent findings and possible leads" at the annual meeting of the Genetics and Environmental Mutagenesis Society held during April in Research Triangle Park, North Carolina.

Greg Kirk, M.D., Ph.D., M.P.H., of the Viral Epidemiology Branch (VEB) received his doctoral degree in Epidemiology from Johns Hopkins University in May. Dr. Kirk's dissertation was titled "The epidemiology of viral, environmental, and genetic factors in hepatocellular carcinoma: A case-control study from The Gambia, West Africa." In April, he presented findings at the 11th International Symposium of Viral Hepatitis in Sydney and at the National Institute of Allergy and Infectious Diseases (NIAID) Grand Rounds. Dr. Kirk also completed a fellowship in infectious diseases at NIAID in June and will remain in VEB to continue studies of hepatocellular carcinoma.


Greg Kirk


James Lacey

James Lacey, Ph.D. (HREB), spoke on "Menopausal hormone therapy and the risk of ovarian cancer" at the Department of Obstetrics & Gynecology at the University of Utah during April, and at the Twelfth Annual Carroll W. Feist Symposium at the Louisiana State University Health Sciences Center in Shreveport, Louisiana, during May.

Martha Linet, M.D., M.P.H. (REB), spoke on "Cancer in children: Possible links to environmental contaminants" at the Annual Meeting of the Pediatric Academic Societies held during May in Seattle.


Gladys Glenn

Gladys M. Glenn, M.D., Ph.D. (GEB), gave two invited talks on "Clinical evaluation, molecular genetics, and epidemiology of von Hippel-Lindau Syndrome (VHL)" and "Pheochromocytomas in VHL" at a meeting during June in Nashville, Tennessee, which celebrated the 10th anniversary of the VHL Family Alliance, an international support organization. Dr. Glenn received a plaque recognizing her contributions to the advancement of knowledge about the syndrome.


Elizabeth Maloney

Elizabeth Maloney, Dr.P.H. (VEB), gave an invited presentation at the Gorgas Memorial Laboratory Scientific Conference held in August in Panama. Dr. Maloney's talk, "HTLV-II in the Guaymi Amerindians of Panama," summarized results of collaborative studies conducted by the VEB, the Centers for Disease Control and Prevention, and Gorgas Memorial Laboratory.

Mary Lou McMaster, M.D. (GEB), was promoted by the U.S. PHS to the rank of Commander in the Commissioned Corps.


June Peters

June Peters, M.S., C.G.C. (CGB), received the Region II leadership award from the National Society of Genetic Counselors at its annual meeting during September in Charlotte, North Carolina.


Ulrike Peters

Ulrike Peters, Ph.D. (NEB), gave invited talks on "Dietary risk factors and colorectal adenomas — results from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Trial" at the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina, during May and at the University of Minnesota in Minneapolis during July.

Preetha Rajaraman, M.S. (REB), was selected for a travel award to attend the student workshop at the 2003 Society for Epidemiologic Research meeting. She presented her dissertation work on "Occupational exposure to lead and the risk of adult brain tumors."

Nathaniel Rothman, M.D., M.P.H., M.H.S. (OEEB), co-chaired a session on "Study designs in molecular epidemiology" and spoke on "Sample size considerations for population-based studies of genetic susceptibility and cancer" at the annual AACR meeting held during July in Washington, DC. Dr. Rothman also co-chaired a poster discussion session on "SNPs and function."

Arthur Schatzkin, M.D., Dr.P.H. (NEB), delivered a keynote presentation on "Diet and cancer" at the Annual Meeting of the International Association of Cancer Registries held in Honolulu during June. Dr. Schatzkin also spoke on "Dietary fiber and colorectal cancer" at the International Conference on Health Effects of the Mediterranean Diet, held in Crete during June, and on "Promise and perils of surrogate endpoints" at a workshop held at the Fred Hutchinson Cancer Research Center in Seattle during May. In September, he addressed the AARP's National Event in Chicago on "A new partnership in biomedical and lifestyle research: The NIH-AARP Diet and Health Study."


Ruth Pfeiffer and Nilanjan Chatterjee

Nilanjan Chatterjee, Ph.D. (BB), spoke on "Semiparametric maximum-likelihood estimation in case-control studies of gene-environment interactions" at the Joint Statistical Meeting held in August in San Francisco. At the same conference **Ruth Pfeiffer, Ph.D.** (BB), delivered an invited talk "On a supplemented case-control design."

Mark Schiffman, M.D., M.P.H. (HREB), received a PHS Meritorious Service Medal in June at the NIH Director's Award Ceremony.

Lois Travis, M.D., Sc.D. (REB), gave five presentations at the International Conference on Hodgkin's Disease Survivorship To Formulate Global Recommendations for Patient Follow-up. The meeting was sponsored by Harvard Medical School and held in Bellagio, Italy, during July.

Sholom Wacholder, Ph.D. (BB), spoke on "Methodologic issues in studying the joint effects of genetic and environmental factors on cancer risk" at a session of "Meet the Expert" at the annual AACR meeting. Dr. Wacholder also spoke on "Case-control studies: Preventing worst-case scenarios."

Nancy Weissman, M.S.S.W. (CGB), co-authored a report on the "National Association of Social Workers standards


Nancy Weissman

for integrating genetics in social work practice." The document covers nine standards designed to enhance social workers' awareness of the skills and knowledge needed to work effectively with clients, families, health care providers, and the community and to increase social workers understanding of the impact on the field of genetics.

COMINGS…GOINGS

Ruth Ann Arnold, who served as the lead purchasing agent for DCEG from 1997 through 2003, retired in May. During her tenure with the Administrative Resource Center (ARC), Ms. Arnold received numerous awards for her vast knowledge of the rules and regulations of the procurement system and her dedication and service to the scientific staff.

Matthew Bonner, Ph.D., has joined the Occupational and Environmental Epidemiology Branch (OEEB) as a postdoctoral fellow. Dr. Bonner recently completed his doctoral degree in epidemiology at the University of Buffalo, where his dissertation focused on environmental exposures and breast cancer.


Matthew Bonner

Elizabeth Challenor-Reese has joined the Hormonal and Reproductive Epidemiology Branch (HREB) as a program assistant. Before coming to the NCI, she spent seven years working in the private non-profit sector.

Lawrence Engel, Ph.D., a postdoctoral fellow in OEEB, joined the epidemiology program of the Memorial Sloan-Kettering Cancer Center in May. During his fellowship, Dr. Engel examined occupational risk factors for stomach cancer, genetic polymorphisms and bladder cancer, and serum organochlorine levels and cancer risk.

Jennifer Fergenbaum, M.S., a visiting predoctoral fellow from Canada, left HREB in July to pursue a doctoral degree at the University of Toronto. Ms. Fergenbaum worked on breast cancer risk factors in relation to tumor hormone receptor status, and she investigated quality assurance issues related to breast tissue microarrays.


Jill Gianessi

Jill Gianessi, B.S.N., joined the Office of the Director in June 2003 as a communications intern. Ms. Gianessi received a Bachelor of Science degree in nursing from Illinois Wesleyan University in 1998, and she will complete a Master of Science degree in Environmental Health and Safety at Illinois State University in December 2003. Prior to coming to the NCI, she held staff nurse positions and worked at a local health department.


Ruthann Giusti

Ruthann Giusti, M.D., M.S., who was a staff clinician in the Clinical Genetics Branch (CGB), has joined the Food and Drug Administration's Center for Biologics Evaluation and Research. Dr. Giusti, who joined the NCI as a medical oncology fellow and was a special assistant for cancer genetics to the DCEG Director before becoming a clinical investigator in the CGB in 2000. Her research work focused on the clinical implications of cancer susceptibility genes. During her time at DCEG, she received a Bench-to-Bedside Award for her project on "Genomic changes in pre-malignant, pre-invasive, and invasive breast cancer in women genetically at high risk for breast cancer" and was recognized with a PHS Commissioned Corps Outstanding Service Medal. Dr. Giusti will continue to be an adjunct investigator in the CGB.

Mina Ha, M.D., Ph.D., M.P.H., recently joined the Radiation Epidemiology Branch (REB) as a visiting fellow. Dr. Ha was an Associate Professor in the Department of Preventive Medicine of the Dankook University College of


Mina Ha

Medicine in Korea and received her degrees from the Seoul National University College of Medicine. For the past three years, Dr. Ha has been the epidemiologist in charge of the Korean Electromagnetic Field Project, a community-based study evaluating risks for brain tumors, leukemia, and lymphoma associated with residential exposure to broadcast transmitters.

Michelle Khan, from the Howard Hughes Medical Institute-National Institutes of Health Research Scholars Program, recently joined the HREB. Ms. Khan is currently in the M.D./M.P.H. program at the Robert Wood Johnson Medical School and School of Public Health in New Jersey. She is currently working with Dr. Mark Schiffman, focusing on the effect of human papillomavirus tests with differing sensitivities on the projected performance of the assays in epidemiologic research and clinical practice.


Michelle Khan

Vicki Kirsh, M.Sc., a predoctoral fellow in OEEB, returned to Yale University in September to complete work on her doctoral dissertation, which will focus on dietary factors and prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, including lycopene and tomato products, antioxidant micronutrient intake, and fruit and vegetable intake.

Manolis Kogevinas, M.D., Ph.D., returned to the Institut Municipal d'Investigació Mèdica in Barcelona, Spain, in July after spending a year in OEEB as a visiting scientist. Dr. Kogevinas

was a Principal Investigator in Spain for the DCEG Interdisciplinary Case-Control Study of Bladder Cancer and during the past year analyzed data from this investigation.

Ursula Leitzmann, M.S., joined REB as a program analyst in July. Before coming to NCI, she coordinated a program on conflict resolution in an academic setting. Ms. Leitzmann holds a master's degree in communication from the Ludwig-Maximilians-University, Munich, Germany; has a graduate certificate in administration and management from Harvard University; and is completing a master's degree in intercultural relations with the University of the Pacific, Stockton, California.


Ursula Leitzmann

Michael Martin, M.D., Ph.D., has joined CGB as a postdoctoral fellow. Dr. Martin trained in medical oncology at the University College in Dublin and holds a doctoral degree in genetics from Trinity College, Dublin. He is at NCI under the auspices of an exchange program that is part of the Ireland–Northern Ireland–NCI Cancer Consortium. Dr. Martin has completed a year of clinical training at the Center for Cancer Research and now will be involved in CGB studies of hereditary breast/ovarian cancer as well as a project investigating the mammographic density in *BRCA* mutation carriers.


Michael Martin

Ruth Medler, an office automation assistant in the HREB since January 2002, left the branch in August. She is planning a mission trip with her church to India for several weeks, and then will start a new position working in a physician's office.

Dominique Michaud, Sc.D., of the Nutritional Epidemiology Branch (NEB), joined the Department of Epidemiology at the Harvard School of Public Health in June as an Assistant Professor in Cancer Epidemiology. Dr. Michaud joined NEB in December 2000 as a tenure-track investigator and worked on studies of dietary intake in relation to bladder cancer risk and recurrence. She will continue to collaborate with DCEG as an adjunct investigator.


Dominique Michaud

Pauline Mysliwiec, M.D., M.P.H., a postdoctoral fellow in the NEB, joined the University of California at Davis in September as an Assistant Professor in the Division of Gastroenterology and Internal Medicine. During her fellowship, Dr. Mysliwiec, a gastroenterologist, worked on numerous projects related to colon cancer and adenoma recurrence.


David Ng

David Ng, M.D., joined the Genetic Epidemiology Branch (GEB) as a clinical fellow. Dr. Ng received his medical degree from the Uniformed Services University of the Health Sciences and completed a residency in Internal Medicine at David Grant Medical Center, Travis Air Force Base, California. Most recently, he completed a fellowship with the National Human Genome Research Institute, where he was involved in a variety of research projects that combined both clinical and molecular components aimed at syndrome delineation and gene discovery.

Rachelle Ragland-Greene left the DCEG ARC in July and entered the two-year Administrative Careers and Development Program, which offers unique internship and career development opportunities. Ms. Ragland-Greene obtained her B.S.B.A. in Marketing from Grambling State University in 1991 and joined the DCEG ARC in 2001. Ms. Ragland-Greene reviewed and processed training, travel, and personnel actions. She served as a travel and subject matter expert for the Enterprise Human Resource and Payroll system, and received an award for training staff on the newly deployed web-based system.


Rachelle Ragland-Greene

Consol Serra Pujadas, M.D., Ph.D., was a visiting scientist in the OEEB this past summer. A physician with expertise in occupational health, she serves as Associate Professor in Preventive Medicine and Public Health at the University of Pompeu Fabra, Barcelona, Spain. During her visit, Dr. Serra Pujadas evaluated the risk for bladder cancer among textile workers.


Tammy Shields

Tammy Shields, Ph.D., an HREB pre- and postdoctoral fellow since 2000, recently left the branch to spend more time with her family. Dr. Shields completed her doctoral work in HREB on the relationship of endogenous hormones to cervical cancer. She also conducted research on other potential cervical cancer risk factors and on the relationship between occupation and ovarian cancer.


Laveta Stewart

Laveta Stewart, M.P.H., joined GEB in June as a research fellow after receiving her degree at Saint Louis University School of Public Health. Ms. Stewart conducted her

M.P.H. internship with GEB in 2002, working with Drs. Gladys Glenn and Jorge Toro on a newly described syndrome: hereditary leiomyomatosis and renal cell cancer. Ms. Stewart's current research is on uterine leiomyomas in women with this syndrome.


Abigail Ukwuani

Abigail Ukwuani, M.P.A., recently joined the Chornobyl Research Unit of REB. Mrs. Ukwuani obtained her master's degree in public administration from the University of Nigeria, Nsukka. Before coming to DCEG, she worked at the State Education Commission in Enugu, Nigeria, and at the Department of Epidemiology at the University of North Carolina at Chapel Hill.

Marianne Vidal, M.S., left the REB after two years as a special volunteer, and returned to the Institut de Radioprotection et de Sûreté Nucléaires (IRSN) in Fontenay-aux-Roses, in the suburbs of Paris, France. While in REB, she worked on improving the thyroid dose estimates for cohort studies of thyroid disease resulting from the Chornobyl accident. Ms. Vidal also wrote a review of the thyroid doses that occurred as a result of large environmental releases of iodine-131; this review will be part of a book being prepared by the IRSN.

JENNIFER DONALDSON LEAVES NCI AFTER 26-YEAR CAREER

Jennifer Donaldson, who served as an office manager in the Radiation Epidemiology Branch (REB), retired this past summer after a 26-year NCI career. In 1977, at the age of 19, Ms. Donaldson joined NCI's Laboratory of Chemical Pharmacology as a purchasing agent under the leadership of Drs. Richard Adamson and Susan Sieber. Recalling her interview for that job, Ms. Donaldson said, "I was told that one of my main duties would be 'to do travel.' I went home that night and told my parents that I would have to buy new luggage for all the travel I would be doing. Boy was I naïve! Only in the government can you 'do travel,' but never actually go anywhere."

In 1981, Ms. Donaldson joined the Biometry Branch—the predecessor to the current DCEG Biostatistics Branch—as an Epidemiology Research Assistant. Under the guidance of **Thomas Fears, Ph.D.,** she learned SAS programming and worked on NCI's first skin cancer survey. Acquiring these new skills and experiences helped move Ms. Donaldson into a Statistical Program Specialist position, which she held for thirteen years. During that time she worked with researchers **Mitchell Gail, M.D., Ph.D.; Jay Lubin, Ph.D.; Steven Mark, Ph.D.; Sholom Wacholder, Ph.D.;**

Philip Rosenberg, Ph.D.; Dr. Jacques Benichou; and Dr. Fears on hormone assay reliability studies and other projects. "I was most fortunate to work with this group," Ms. Donaldson acknowledges. "They taught me so much and gave me opportunities to grow and learn for which I am still very grateful."

Ms. Donaldson's final NCI stop was with REB, which she joined in 1998. In her new position she served as the office manager and became very involved in the branch budget process. "I thought it would be hard to call REB home after leaving the Biostatistics Branch," remarked Ms. Donaldson. "But within no time I was part of the team and gained many friendships that I know will continue." Under the leadership of **Elaine Ron, Ph.D.,** and **Martha Linet, M.D., M.P.H.,** Ms. Donaldson participated in many Branch projects, including the Surveillance, Epidemiology, and End Results Multiple Primary Cancer Monograph. Ms. Donaldson also continued with Division-wide duties and, shortly before retiring, worked with **Jim Vaught, Ph.D.** (Office of the Director), to track DCEG's biospecimens through DNA extraction and genotyping.

When asked about her favorite memories of working in DCEG, the list quickly grew, but among the highlights, Ms. Donaldson was grateful for the tremendous opportunities that **Joseph Fraumeni, M.D.,** and **Shelia Zahm, Sc.D.,** made available to anyone with the desire to learn and considered the on-the-job training and mentoring she received from DCEG to be the very best. She also cites the excitement of working with people from all over the world. "I love hearing about other cultures and customs and I will miss the diversity that is commonplace to DCEG," noted Ms. Donaldson, "I have always felt it an honor and privilege to work with people doing such important and worthwhile work…. I am proud to have been part of DCEG and look forward to reading about all the future discoveries made by DCEG investigators, my friends, who have meant so much to me over the years." ■

FAMILIAL MELANOMA STUDY NEWSLETTER ON SUN-PROTECTIVE CLOTHING

The Genetic Epidemiology Branch (GEB) has published the spring 2003 issue of *Familial Melanoma Study News,* a newsletter for families enrolled in the study "Clinical, Laboratory, and Epidemiologic Characterization of Individuals and Families at High Risk of Melanoma." **Margaret Tucker, M.D.,** Branch Chief, **Alisa Goldstein, Ph.D.,** Senior Investigator, **Mary Fraser, M.A., R.N.,** Clinical Nurse Specialist, and **Barbara Rogers,** Epidemiology Program Specialist, developed the newsletter, which was mailed to approximately 1,800 family members participating in the study.

The feature article discusses sun-protective clothing, including types of fabrics that provide the most protection from ultraviolet (UV) radiation; classifies sun-protective clothing according to the UV Protection Factor (UPF), of which there are three categories approved for use in the United States; identifies clothing that has met standards for manufacturing, testing, and labeling of sun-protective clothing; and discusses special products containing UV absorbers that can be added to laundry to increase the UPF of some fabrics.

Research findings from three recent GEB publications regarding melanoma risk are summarized (see November 2002 *Linkage* for more on melanoma research) and include:

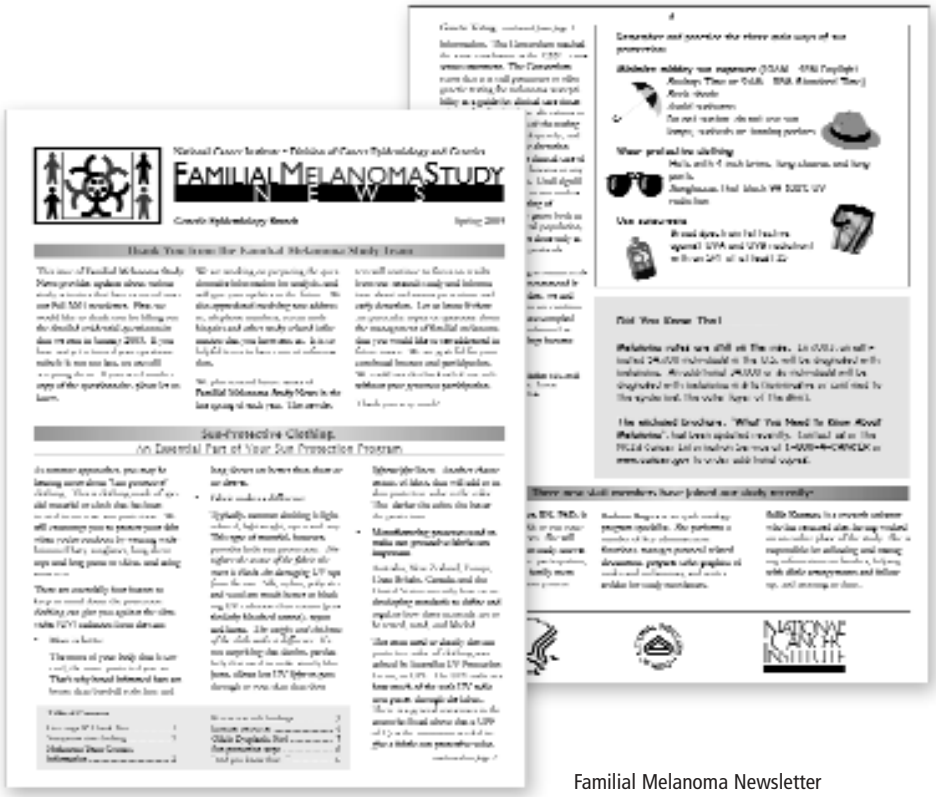
- A novel approach developed by DCEG study investigators to determine average annual UVB intensity showed, for the first time, that individual risk of melanoma is associated with the intensity of sunlight that a person receives over a lifetime. The study also found that the risk of melanoma increased with the amount of time outdoors, even for men and women who can develop a deep tan.

- The International Melanoma Genetics Consortium study evaluating the penetrance of *CDKN2A* mutations in 80 families from the United States, Australia, and Europe showed that the estimates of lifetime penetrance of *CDKN2A* mutations vary widely by locality, similar to the general population rates, suggesting that factors (such as sun exposure) affecting the general population also affect risk in mutation carriers.

- The International Melanoma Genetics Consortium also revised their clinical guidelines regarding genetic testing for melanoma susceptibility. Such testing remains of limited clinical utility, and it is still premature to offer such testing as a guide for clinical care.

Additional features of the newsletter include web sites offering extensive information about sun safety and melanoma, questions and answers about dysplastic nevi, and sun protection information. Copies of the newsletter can be obtained from GEB and will soon be available on the DCEG web site. ■

—Mary Fraser, R.N., and Barbara Rogers



Familial Melanoma Newsletter