Division of Cancer Epidemiology and Genetics

DCEG

Linkage

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HUMAN PAPILLOMAVIRUS AND CERVICAL CANCER

Mark Schiffman, M.D., M.P.H., of the Environmental Epidemiology Branch, sees a problem with the way we screen for cervical cancer: the Papanicolaou (Pap) smears and biopsies that women normally undergo are not as reliable as they should be. "The measures are so subtle that someone else or the same person on another day could tell you something different," he says. "We can't rely on them sufficiently—we should be searching for ancillary methods."

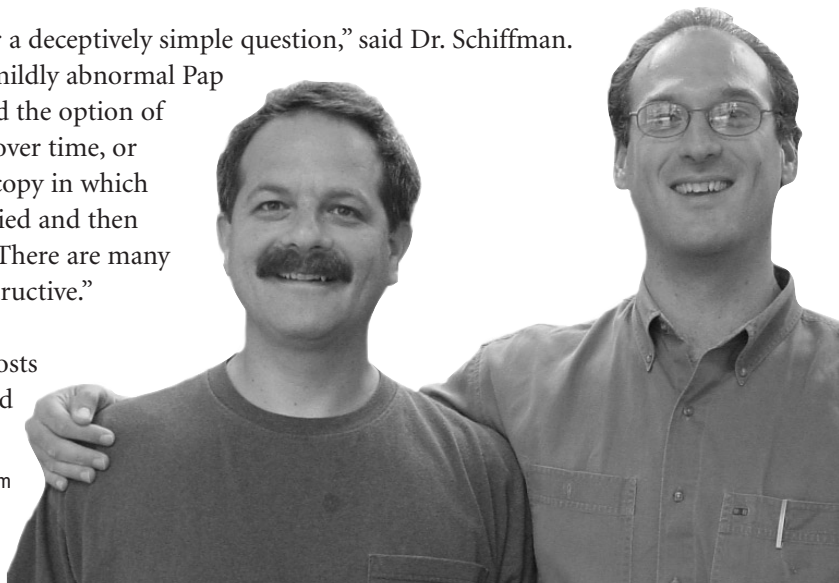
Dr. Schiffman and a group of NCI investigators have looked more closely at cervical cancer to determine better screening methods and possible vaccines against it. They recently published three articles on human papillomavirus (HPV) infections and their role in cervical cancer in the February 21 issue of the *Journal of the National Cancer Institute* (volume 93, issue 4). A related article by Dr. Schiffman and Dr. Mark Stoler, of the University of Virginia, also appeared in the *Journal of the American Medical Association* (volume 285, issue 11) on interobserver reproducibility of colposcopy. They found that reproducibility is mediocre to poor for three specimen types: thin-layer cytology, punch biopsy, and loop electrosurgical excision procedure.

Cervical cancer is one of the most common cancers worldwide among women, affecting more than 400,000 women and causing 200,000 deaths each year. More than 100 types of HPV exist; of these, several dozen affect the genital tract and more than a dozen are linked to cervical cancer. HPV-16 is implicated in about half of cervical cancer cases, and HPV-18, HPV-31, and HPV-45 account for another 25 to 30 percent combined.

Each year, more than 2.5 million women have Pap tests with mildly abnormal results. These tests exhibit atypical squamous cells of undetermined significance (ASCUS) or more definite mild changes called low-grade squamous intraepithelial lesions (LSILs). The ASCUS/LSIL Triage Study (ALTS), a randomized trial of management strategies for women with mildly abnormal Pap test results, was a collaboration between DCEG and Dr. Diane Solomon of the Division of Cancer Prevention (DCP).

"The trial attempts to answer a deceptively simple question," said Dr. Schiffman. "What should we do with a mildly abnormal Pap smear? In the past, you've had the option of getting repeated Pap smears over time, or getting an immediate colposcopy in which any suspicious tissue is biopsied and then you're treated appropriately. There are many ways to treat, but they're destructive."

And expensive. The annual costs in the United States associated



Drs. Mark Schiffman and Allan Hildesheim

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

Technical Editors
B.J. Stone (stoneb@mail.nih.gov)
Shelia Hoar Zahm (zahms@mail.nih.gov)

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

DCEG Linkage **Reporters**
Office of the Director, DCEG
Catherine McClave (mcclavec@mail.nih.gov)
Office of Division Operations and Analysis, OD, DCEG
Sandy Rothschild (rothschs@mail.nih.gov)
Office of the Director, EBP
Katrina Wahl (wahlk@mail.nih.gov)
Biostatistics Branch, EBP, DCEG
B.J. Stone (stoneb@mail.nih.gov)
Clinical Genetics Branch, HGP, DCEG
Ruthann Giusti (giustir@mail.nih.gov)
Environmental Epidemiology Branch, EBP, DCEG
Patricia Madigan (madiganp@mail.nih.gov)
Genetic Epidemiology Branch, HGP, DCEG
Mary Fraser (fraserm@mail.nih.gov)
Barbara Rogers (rogersb2@mail.nih.gov)
Laboratory of Population Genetics, HGP, DCEG
Leslie Derr (derrl@mail.nih.gov)
Jenny Kelley (kelleyj@mail.nih.gov)
Nutritional Epidemiology Branch, EBP, DCEG
Usha Singh (singhu@mail.nih.gov)
Occupational Epidemiology Branch, EBP, DCEG
Joanne Colt (coltj@mail.nih.gov)
Radiation Epidemiology Branch, EBP, DCEG
Ruth Kleinerman (kleinerr@mail.nih.gov)
Viral Epidemiology Branch, EBP, DCEG
Beth Maloney (maloneyb@mail.nih.gov)
DCEG Committee of Scientists
Tom O'Brien (obrient@mail.nih.gov)
DCEG Representative to the NIH Women Scientists Advisory Group
Martha Linet (linetm@mail.nih.gov)
DCEG Representative to the Tenure-track Committee
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DCEG Representatives to the NIH Fellows Committee
Dawn Elizabeth McNeil (mcneile@mail.nih.gov)
Tatiana Dracheva (dracheta@mail.nih.gov)
DCEG Representative to the NIH pre-IRTA Committee
Neely Kazerouni (kazeroun@mail.nih.gov)

Contractor Support
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(mbarker@palladianpartners.com)

with cervical cancer screening and managing abnormal test results top $5 billion.

The ASCUS portion of the trial involved 3,488 women who were randomly assigned to one of three management strategies to detect grade 3 cervical intraepithelial neoplasia:

- Colposcopy (the standard strategy), which involved a visual examination using a magnifying instrument. If abnormal tissue was found it was biopsied, and treatment was provided if necessary.

- HPV triage, in which the results of repeated Pap tests were combined with those of a test for oncogenic types of HPV. If the cells contained genetic material from any of 13 types of HPV (including 16, 18, 31, and 45), colposcopy was performed.

- Conservative management, which involved repeated Pap tests only. If the tests showed more severe cellular abnormalities, colposcopy was performed.

About 5 to 10 percent of women with ASCUS had a very-high-grade cancer precursor or cancer, and 96 percent of this small subset of women had a positive HPV test. Among all women with ASCUS, 55 percent tested positive for HPV. The 45 percent that were HPV negative would normally have received colposcopy, but their negative test results exempted them from the procedure.

Thus, "you can effectively reduce the worry of half the women because half are HPV negative," said Dr. Schiffman. "We know that if you don't have HPV, you almost certainly don't have cervical cancer."

In another project, a group of DCEG investigators including Drs. Schiffman, Allan Hildesheim, Mark Sherman, and Phil Castle (a DCP fellow working in DCEG) are currently assessing whether HPV testing is a more effective primary screening mode than the Pap smear in two large cohorts of women.

Allan Hildesheim, Ph.D., a recently tenured researcher in the Environmental Epidemiology Branch, and Dr. Schiffman led a study of HPV-16 among women from Guanacaste, Costa Rica, a province with very high rates of cervical cancer. The researchers screened more than 10,000 women and compared the viral DNA of HPV-16-positive women who had cancer or high-grade cancer precursors with that of HPV-16-positive women who had normal cells or mild changes. They found a strong association between certain variants and both cancer and high-grade precursors. The variants—dubbed non-European variants to distinguish them from the prototype virus—were associated with more than a 10-fold increased risk of cancer and a 3-fold risk of precursors. Women with cancer or precursors who had non-European variants did not significantly differ from other HPV-16-infected women in age, geography, or socioeconomic status. The variants differed from one another by less than two percent of nucleotide sequences.

The increased risk from non-European variants "is above and beyond the already 100-fold increase that comes from being infected with HPV-16," said Dr. Hildesheim. But the significance of the differences is not yet clear. Dr. Hildesheim believes they may result from functional differences among the variants or differences in the way certain people's immune systems handle the variants. Because infection with HPV-16 already poses such a high relative risk by itself, however, it is unlikely that this

research will have implications for screening.

Screening for HPV can be effective, but its costs are tremendous and often result in overtreatment. Ultimately, an HPV vaccine may significantly affect cervical cancer rates around the world. Dr. Hildesheim believes that in developing countries, "the impact of an HPV vaccine could be large. In the United States and Europe, the vaccine might reduce the economic burden of cervical cancer and might reduce morbidity associated with screening programs." DCEG investigators are launching a large vaccine trial in Costa Rica that will begin in the coming year.

In another *Journal of the National Cancer Institute* article, NCI presented results from a placebo-controlled, double-blind phase I trial of a vaccine for HPV-16. The vaccine contained the L1 structural protein of HPV-16 in its three-dimensional structure. Seventy-two volunteers (58 women and 14 men) who were at low risk for exposure to HPV were divided into various groups. Some volunteers received either placebo or a 10-microgram dose of the vaccine (with or without an adjuvant). Once the 10-microgram dose was established as safe, additional volunteers received either placebo or a 50-microgram vaccine dose (with or without an adjuvant). Each volunteer received three injections over four months, and investigators checked antibody levels at monthly intervals after each vaccination. The vaccine was well-tolerated and elicited a strong immune response. One month after the third injection, those given the vaccine had antibody levels up to 40 times higher than levels found in people naturally infected by HPV. The 50-microgram dose without adjuvant proved to be the most effective dose, and side effects were minimal.

You can effectively reduce the worry of half the women because half are HPV negative…. We know that if you don't have HPV, you almost certainly don't have cervical cancer.

This study was an NCI-wide effort, said Dr. Hildesheim. Dr. Douglas Lowy and Dr. John Schiller, both from the NCI Center for Cancer Research, led the phase I study in collaboration with Dr. Clayton Harro from the Johns Hopkins Center for Immunization Research. A phase II trial, similar to the phase I trial but larger in size, was completed at Johns Hopkins. Results of the phase II trial are pending, but Dr. Hildesheim said that "preliminary findings show similar results, with respect to both antibody titers and side effects." ■

—Nancy Volkers

PATRICIA HARTGE RECEIVES NIH MENTORING AWARD

In June, Patricia Hartge, Sc.D., received the NIH Award for Mentoring in recognition of her many contributions on behalf of postdoctoral fellows at NCI and throughout NIH. In her capacity as Deputy Director of the Epidemiology and Biostatistics Program, Dr. Hartge has actively sought opportunities to mentor fellows and other junior staff across all disciplines in DCEG, where she has provided expert advice and consultation and has served as primary mentor to fellows. She also serves as a mentor to her peers and is frequently called on for advice in study design, site visit preparation, and setting of scientific priorities.

Over the past year, Dr. Hartge played a key role by serving as Acting Dean of DCEG's newly established Office of Education. In this capacity, she coordinated the recruitment and training of postdoctoral fellows within the Division and assisted NCI and NIH with developing policies and programs for postdoctoral training. Within the Institute, Dr. Hartge assisted the Deputy Director of NCI in his efforts to create an NCI Fellowship Office and met with other NCI division deans to develop and recommend Institute-wide policies for postdoctoral training. Dr. Hartge also provided advice to the NIH Office of Education and designed an instrument that was used by the NIH Deputy Director of Intramural Research to survey fellows throughout NIH.

Dr. Patricia Hartge (second from right) with interns

ASSESSING EXPOSURE AND SUSCEPTIBILITY TO CARCINOGENS

Benzene, asbestos, vinyl chloride—these chemicals were first identified as known human carcinogens because people who had worked with these agents were found to be at increased risk for specific cancers. Indeed, "studies in the occupational environment have been the basis for much of what has been identified as carcinogenic," noted Joseph Coble, Sc.D., of the Occupational Epidemiology Branch. Understanding cause is key to preventing cancer. The reduction of occupational exposures to these compounds has reduced the risk for workers as well as the general population.


Dr. Joseph Coble

But quantifying these exposures to carcinogens is difficult. Most cancers have a long latency period, and new cases result from exposures that happened one or two decades ago. Linking chemical exposures to these cancers often involves going back in time and trying to quantify the various exposures. This is the science of retrospective exposure assessment.


Dr. Mustafa Dosemeci

Work history records help identify likely exposures, even though the exact frequency or concentration of the exposure for each worker may not be known. Mustafa Dosemeci, Ph.D., also of the Occupational Epidemiology Branch, pointed out that 20 to 30 years ago, epidemiologists used those records to estimate exposure levels for anyone working in the same occupation or industry. Such classification approaches, however, failed to account for differences in the extent of exposure, which for managers was quite different than the one based on the level of the individual factory worker. Similarly, Dr. Dosemeci described three people doing the same job in a benzene-exposed room: the first person is standing without protective equipment, the second person is wearing a respirator, and the third person is using a self-contained breathing apparatus. "It would be a big mistake to say that all three of those people had the same exposure to benzene."

Some epidemiologists assign estimates by job title. But "even using job titles isn't optimal," Dr. Dosemeci said. "All job titles in an industry aren't necessarily going to be exposed to the same level of exposure. What happens is you have misclassification, and that generally weakens any link between exposure and cancer."

To reduce such misclassification, researchers have been using detailed questionnaires in case-control and cohort studies to collect subject-specific exposure information. Data from these methodologies are combined into job exposure matrices whereby exposure levels are assigned to study subjects on the basis of work histories. This approach "links occupation with exposure to specific agents," said Dr. Coble. "What it allows you to do is group populations not by job titles, but by exposures."

For example, if you were interested in solvent exposure and risk of cancer, the job exposure matrix would identify painters, printers, furniture finishers, and others as having considerable exposure to solvents. Although these industries are rather different, these workers' exposures are similar. "It's a little bit of detective work," Dr. Coble said. "It boils down to looking at all available sources of information."

The science of assessing the effects of environmental exposure to carcinogens has recently advanced again to involve the field of gene–environment interactions. It is no longer enough to know to which carcinogens, how much, and for how long a person has been externally exposed. We now need to know that how each person's body deals with exposure is critical in the development of cancer. "The way our enzymes clear different toxins from the body ultimately determines the effect an exposure will have in the body," Dr. Dosemeci explained.

Various polymorphisms in the genes encoding these enzymes may lead to products that differentially activate or deactivate chemicals that enter the body. Thus, the presence or absence of certain polymorphisms can affect the level of chemical activation or deactivation, which in turn determines a person's susceptibility to a substance. "In some ways, these genetic factors can serve as our internal protective respirator," Dr. Dosemeci said. "Certain polymorphisms of a gene controlling levels of a deactivating enzyme can reduce the amount of exposure by as much as 50 percent."

A challenge for researchers is estimating the biologically effective dose that causes cancer in the body. The sheer number of possible markers presents a sample size problem for researchers involved in gene–environment studies. Dr. Dosemeci indicated that as many as 50 to 100 genes could interact with occupational exposures. But finding these markers can bring epidemiologists a long way from guessing on the basis of industry-wide estimates. He said, "the more we know about the relationship between gene and environment, the more accurately we can estimate risk of exposure." ■

—Lisa Chiu

A GLIMPSE FROM SPACE OF PESTICIDE EXPOSURE

Turn on the television these days and you'll find that satellite images are as ubiquitous as commercials. Nightly, viewers tune into their local news and see weather forecasters track storms in the brightly colored pixels of computer-enhanced satellite images. This imaging technology has aided everything from spy operations to mapping efforts, but it has not played much of a role in cancer epidemiology until now.

Dr. Mary Ward holding one of the satellite maps

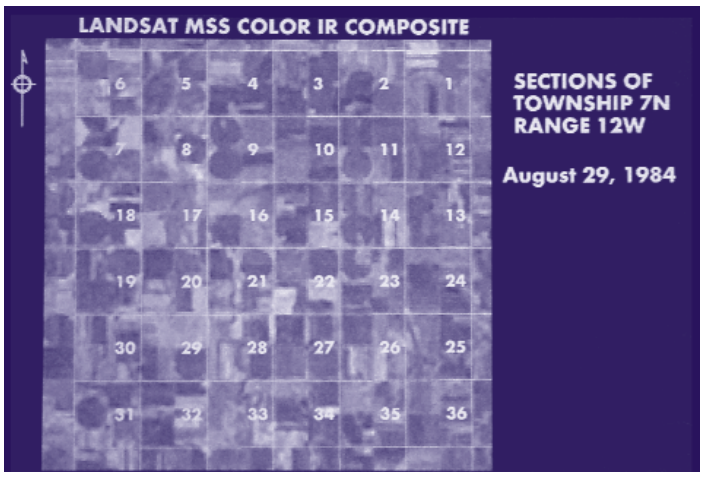
Mary Ward, Ph.D., of the Occupational Epidemiology Branch, and Colorado State University's Jay Nuckols, Ph.D., have demonstrated that orbiting technology can help identify homes that may have been exposed to specific agricultural pesticides. They are now working on refining their method to see if they can use such satellite information as a reasonable way to assess chemical exposures. "These are studies you can't do with a questionnaire, because people don't know what chemicals have been used on nearby fields," Ward said.

Dr. Jay Nuckols

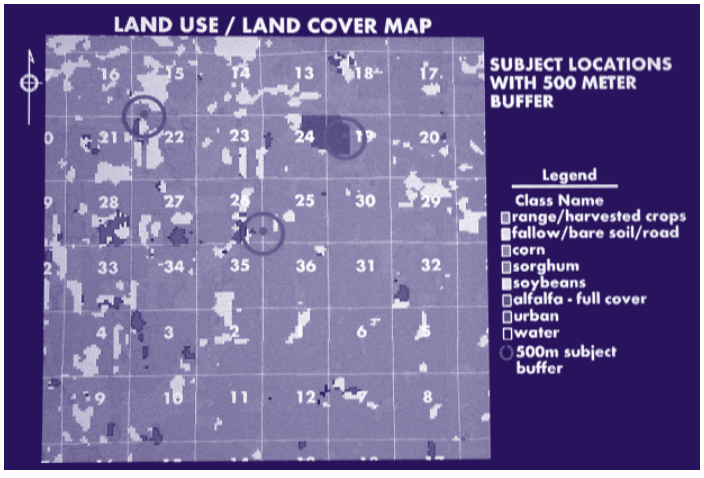
In their January 2000 *Environmental Health Perspectives* article (2000;108: 5-12), Dr. Ward, Dr. Nuckols, and their co-authors laid the groundwork for using satellite imaging for exposure assessment. They gathered imagery for two summer dates in 1984 that included three Nebraska counties that are part of the study region in an NCI population-based, case-control study of non-Hodgkin's lymphoma. From the photos, they set out to determine where different crops had been planted and the likely pesticides that had been used proximate to the residences of the study participants. "A satellite image is not that useful for identifying crops until you figure out a way to relate the reflectance measurements to what is on the ground," Nuckols said. "Since the images were from 1984, we needed to find a way to 'ground truth' since we were not able to go to the site and see what was there."

In previous epidemiologic studies of agricultural pesticides, people who lived in town and didn't farm were typically classified as unexposed…. In fact their homes may have been close enough to crop fields to result in exposure from pesticide drift.

Dr. Ward and Dr. Nuckols turned to Farm Service Agency records from the three counties, which contained information on the location and type of crops planted in 1984. The pesticides used on these crops were ascertained from a 1982 survey of pesticide use among farmers conducted by the University of Nebraska Institute of Agriculture and Natural Resources. By estimating chemical use for each crop type, these researchers identified crop fields with a high probability of agricultural pesticide use within a 500-meter radius around each residence. The 500-meter buffer zone was chosen as a median distance that could encompass the drift of chemicals from both



One square mile per block



Buffered sections

aerial and ground-based application methods, Dr. Ward said. She pointed out, however, that aerial applications are generally associated with considerably more pesticide drift.

"In previous epidemiologic studies of agricultural pesticides, people who lived in town and didn't farm were typically classified as unexposed," Dr. Ward explained. Whereas "in fact their homes may have been close enough to crop fields to result in exposure from pesticide drift." Indeed, she and Dr. Nuckols found that 22 percent of the homes in the three-county area were within 500 meters of pesticide use and could have had exposure to some agricultural pesticides.

Their study did not account for wind velocity and direction or for application method. Furthermore, there was no way to validate whether pesticides actually drifted into the homes of the participants in a study conducted over 15 years ago. To address this limitation, Dr. Ward and Dr. Nuckols are now working with a research group at the Iowa Department of Natural Resources to create crop maps from satellite imagery for Iowa. They will correlate the agricultural pesticides predicted by the metrics with the occurrence of pesticides measured in house dust samples collected from people's homes as part of a recently completed population-based, case-control study of non-Hodgkin's lymphoma. One aim of this next round of research will be to determine how best to modify the satellite method for predicting residential pesticide exposure.

Dr. Nuckols is pleased that satellite technology can be used to assess pesticide exposure beyond the farm. "We used to concern ourselves primarily with farmers and their families when we considered these exposures," he said. "With the use of this technology, we've moved to a much more integrated view of exposures for the entire population." ■

—Lisa Chiu

We used to concern ourselves primarily with farmers and their families when we considered these exposures…. With the use of this technology, we've moved to a much more integrated view of exposures for the entire population.


Dr. Anand Chokkalingam


Dr. David Kaufman


Dr. Aparna Mohan


Dr. Tara Vogt

NIH GRADUATES

Anand Chokkalingam, Ph.D., of the Environmental Epidemiology Branch (EEB), David Kaufman, Ph.D., of the Laboratory of Population Genetics (LPG), Aparna Mohan, M.D., Ph.D., of the Radiation Epidemiology Branch (REB), and Tara Vogt, Ph.D., M.P.H., of the Nutritional Epidemiology Branch (NEB) were awarded NIH graduate certificates at a ceremony led by Dr. Michael Gottesman and Dr. Ruth Kirschstein on May 9. The occasion honored NIH doctoral students who completed their dissertation research at NIH.

Dr. Chokkalingam successfully defended his thesis and completed the requirements for his Ph.D. in epidemiology at the University of Maryland School of Medicine, Department of Epidemiology and Preventive Medicine. He conducted his doctoral research, "Vitamin D Receptor Gene Polymorphisms, Insulin-like Growth Factors, and Prostate Cancer Risk: A Population-based Case-control Study in China," under the guidance of Dr. Paul Stolley of the University of Maryland and Drs. Ann Hsing and Katherine McGlynn of EEB. Dr. Chokkalingam will continue his postdoctoral research on prostate cancer and other hormonally related cancers at DCEG.

Dr. Kaufman successfully defended his Ph.D. in epidemiology at the Johns Hopkins University Bloomberg School of Public Health in July. His dissertation, "Segregation Analysis for Evidence of an Additional Breast Cancer Susceptibility Gene in Ashkenazi Jewish Families," was mentored by Dr. Terri Beaty from Johns Hopkins and Dr. Jeffery Struewing of LPG, where Dr. Kaufman will remain to learn about bioinformatics.

Dr. Mohan received her Ph.D. from the Johns Hopkins University Bloomberg School of Public Health. Her dissertation was entitled "Cause-specific Cancer Mortality and Incident Hematopoietic Malignancies among Radiologic Technologists in the United States." Dr. Mohan was mentored by Dr. Genevieve Matanoski of Johns Hopkins and Dr. Martha Linet of REB. She will continue her research in REB.

Dr. Tara Vogt earned her Ph.D. in epidemiology from Yale University after successfully defending her dissertation, "Diet and Prostate Cancer: Investigating the Relationship between Risk of Prostate Cancer and Serum Concentrations of Individual Carotenoids, Selenium, and Alpha-tocopherol in U.S. Black and White Men." Dr. Vogt will continue her research in cancer etiology as a postdoctoral fellow in NEB. Dr. Vogt was mentored by Dr. Susan Taylor Mayne from Yale and Dr. Regina Ziegler of the Office of the Director, Epidemiology and Biostatistics Program.

RASHMI SINHA, NUTRITIONAL EPIDEMIOLOGIST


Dr. Rashmi Sinha

The road to nutritional epidemiology for Rashmi Sinha, Ph.D., began with studying nucleic acid synthesis in bread molds as a biochemist. At the University of Stirling, Scotland, she focused on basic cellular pathways and the mysteries of messenger RNA. Although biochemistry first triggered her interest in science, Dr. Sinha began to feel too focused on minutiae, studying nucleic acids in a simple organism. She decided to take a wider view of science and work on mammalian systems. "It was at this point that my interest started to advance toward the field of nutrition," Dr. Sinha said. "Coming from India, I saw nutrition as a very important issue. So I tried to integrate nutrition with my biochemistry background."

A study in India will allow us to explore a diet–gene interaction in a population that is genetically similar to the Western population but has very different dietary and other exposures….

The Nutritional Epidemiology Branch's newest tenured researcher credits her biochemistry background with giving her a mechanistic point of view. "When I first came to NCI, many dietary tools to assess nutrition were being developed," Dr. Sinha said. "I felt that I had come at the right time. Rather than only thinking about associations, I try to figure out molecular mechanisms that may be involved in how a dietary component could trigger a certain disease."

Dr. Sinha started at NCI as a Fogarty Visiting Fellow in the Laboratory of Chemical Carcinogenesis and Tumor Promotion, studying the role of vitamin A in cellular differentiation. She came to DCEG as a staff fellow studying whether cooked meat increases the risk of cancer. Laboratory studies had demonstrated that meat cooked at high temperatures contains heterocyclic amines (HCA) and polycyclic aromatic hydrocarbons (PAH), which are mutagenic and carcinogenic.

But Dr. Sinha noted that the early epidemiologic studies did not differentiate between cooking methods, which produce widely different levels of HCA and PAH. For example, roast beef and steak are in the same meat category on questionnaires, but they are cooked differently. By separating meat categories into cooking methods and level of doneness, Dr. Sinha was able to look more specifically at the association between cooked meat and cancer in a case-control study. She found that meat cooked at higher temperatures and more well-done meat increase the risk for developing cancer, especially colon cancer. Dr. Sinha is now also reassessing how to categorize processed meat. "I'm trying to think about the different possible exposures from preservation methods," she said. "Is there a difference between smoking and salting or other methods of curing meat?"

To get conclusive information on the role of red meat and cooking methods in human cancers, Dr. Sinha believes she will need to look at populations with dietary habits different from those in the United States. She would like to look at populations in South America or New Zealand, where meat intake is high and both slow-cooking and high-temperature-cooking methods are used; in places like China and Japan, with their rapidly changing diets and increasing meat consumption; and in Europe, which has a wide range of meats and cooking methods.

Dr. Sinha is also interested in conducting a study in the country of her birth. Because the life expectancy rates in India are increasing and in some places are similar to those in United States, she wants to explore whether unique dietary exposures can be associated with the substantially lower cancer rates in India than in this country. One large difference between India and the United States is that a vast majority of Indians are vegetarian. Results from dietary studies of vegetarian Seventh Day Adventists in the United States are available, but India may provide interesting new pieces to the nutritional epidemiology puzzle. "Indian populations could be very interesting because although they are vegetarian, some people also consume a lot of fat," Dr. Sinha said. "Other low-meat-consuming populations, such as the Chinese, are being studied, but Indians are Caucasians and genetically closer to the Western population. So a study in India will allow us to explore a diet–gene interaction in a population that is genetically similar to the Western population but has very different dietary and other exposures, and also has low cancer rates."

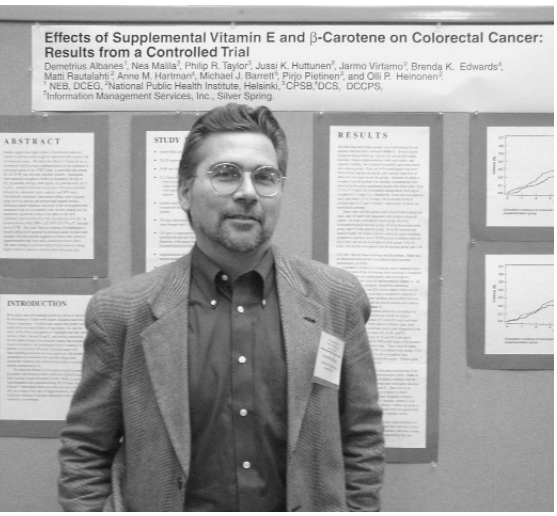
Because Indian cooking uses so many spices, Dr. Sinha would also like to explore whether the phytochemicals in the spices offer a protective effect. That, in addition to her work on cooked and processed meat and her interest in various population studies, gives her a lot to do. "I just feel like there are so many things to be done," Dr. Sinha said. "Sometimes, I wish there were 48 hours in a day." ■

—Lisa Chiu

DEMETRIUS ALBANES, CHIEF OF THE OFFICE OF EDUCATION

In December 2000, Demetrius Albanes, M.D., transferred from NCI's former Division of Clinical Sciences to DCEG to fill the newly created position of Chief of the Division's Office of Education (OE). Previously, Patricia Hartge, Sc.D.—with the assistance of Kristin Kiser, M.H.A.—had been covering DCEG's training-related activities in addition to her other responsibilities. OE promotes the recruitment and training of DCEG pre- and postdoctoral fellows, fosters career development for all DCEG research staff, coordinates the Division's seminar and didactic series, and develops training partnerships with schools of public health and departments of epidemiology.

Dr. Albanes plans to expand several areas of OE's work, but he says that many of the activities will continue as they are. "Overall, the system has been running quite well for a long time," he said, "but there are some aspects that we would like to continue to enhance." Advances in the molecular field, in particular, have increased opportunities for collaboration and have opened up a large and relatively new area for exploration and investigation. In addition to examining characteristics and exposures that may alter the risk for a cancer, epidemiologists now also evaluate genetic makeup and expression and increasingly incorporate biochemical and molecular processes. Recruitment and training programs must change to identify the best candidates and train them for the changing demands of molecular epidemiology.



Dr. Demetrius Albanes

The ultimate goal is to learn as much as we can about how cancer arises and why certain people are at greater risk, and to apply that knowledge to the development of more practical preventive strategies to lower the incidence of cancer. To do that, we need bright, dedicated young minds.

Dr. Albanes' top priority is to continue providing fellows the best research experience possible in cancer epidemiology. New aspects of training will include additional targeted multidisciplinary activities that provide some familiarity with laboratory methods, cancer treatment, and other aspects relevant to trainees' specific studies. "The Office is committed to guiding the career paths of the fellows," said Dr. Albanes. "They begin their fellowship by developing a research plan with their mentors, and they receive solid active guidance from these more senior researchers. The trainee–mentor collaboration is very important to high-quality research training."

Another priority is to develop joint training programs with graduate schools throughout the country, but especially locally. Along these lines, Dr. Albanes has already had discussions with departments at the Johns Hopkins and George Washington Universities to explore such collaborations.

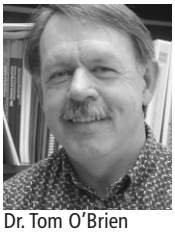
Dr. Albanes also places a high priority on career development. "We will be looking out for the best interests of all of our staff, not only the 45 fellows," he said. "Our principal investigators are already adept at keeping up with and leading the state of the science, and we want to continue to facilitate that in the best and most productive ways possible."

Though not an educator by training, Dr. Albanes is committed to nurturing young researchers. "I feel it's our responsibility as researchers, and in particular as researchers at NIH, to provide the highest quality training," he said. "I think the ultimate goal is to learn as much as we can about how cancer arises and why certain people are at greater risk, and to apply that knowledge to the development of more practical preventive strategies to lower the incidence of cancer. To do that, we need bright, dedicated young minds to come in and give their concerted effort and thought to the problems at hand and help develop new perspectives and approaches. If we're not committed to the next generation of cancer epidemiologists, we're going to fall short."

Dr. Albanes will divide his time between OE and the Nutritional Epidemiology Branch, where he will pursue his research interests, which include prostate cancer etiology and prevention, micronutrients such as vitamin E, and energy-related factors such as body size and physical activity. ■

—Nancy Volkers

PARTING WORDS FROM THE CHAIR, COMMITTEE OF SCIENTISTS


Dr. Tom O'Brien

I recently ended my 2.5-year term as Chair of the DCEG Committee of Scientists (COS), the mission of which is to enhance the environment for DCEG scientists by improving communication, reducing administrative obstacles, and promoting opportunities for career development. One might say that the mission of COS is to assess and build DCEG's "social capital." Cohen and Prusak define social capital as the stock of connections among people that makes cooperative action possible (Cohen D, Prusak L. *In Good Company: How Social Capital Makes Organizations Work*. Boston: Harvard Business School Press, 2001). These connections are important to the scientific mission of DCEG because the increasingly complex and collaborative nature of our research requires an increasing degree of cooperative action. It is also important to DCEG scientists because workplaces with high social capital are enjoyable places to work.

During my tenure, COS has undertaken three major initiatives to assess and build social capital within DCEG: a series of town meetings, an annual survey of branch management, and advocacy of management training for branch chiefs and other DCEG scientists.

The town meetings have provided opportunities for direct communication between DCEG scientists and Division Director Joseph Fraumeni, M.D. During the past year COS conducted forums for specific groups of DCEG scientists, rather than Division-wide meetings. These smaller, more focused town meetings were quite productive. Andrew Flood, Ph.D., M.A., of the Nutritional Epidemiology Branch and James Lacey, Ph.D., M.P.H., of the Environmental Epidemiology Branch moderated the Fellows Town Meeting, which addressed training and mentoring issues, including a discussion of recommendations from the National Academy of Science report *Enhancing the Postdoctoral Experience*. Ruth Kleinerman, M.P.H., of the Radiation Epidemiology Branch and Robert Clifford, Ph.D., of the Laboratory of Population Genetics led the Staff Scientists Town Meeting, which focused on the role of the staff scientist in the DCEG research program. This meeting resulted in the initiation of an annual award for the best original research by a staff scientist and discussions between Dr. Fraumeni and Michael Gottesman, M.D., NIH Deputy Director for Intramural Research, regarding the eligibility of staff scientists for the NIH Loan Repayment Program. During the Principal Investigators Town Meeting, discussion focused on the DCEG budget, the tenure process, and the balance between collaboration and independence for DCEG principal investigators.

About 85 percent of the respondents consider the intellectual environment of their branch or lab to be good or excellent.

The second major COS effort has been the implementation of the annual survey of branch management. Because the branch or lab is the organizational unit that affects DCEG scientists most directly, COS developed an anonymous, web-based survey in which branch members were asked to evaluate how well their branch was functioning. COS presented the results to Dr. Fraumeni and to Deputy Division Director Shelia Zahm, Sc.D. Dr. Fraumeni shared these results with the Epidemiology and Biostatistics Program Director, Robert Hoover, M.D., Sc.D., and to each branch chief as part of the DCEG annual personnel review. Besides their value for evaluating the specific branches, the aggregated results of this survey provide an assessment of the level of social capital within the Division. These results are heartening in that about 85 percent of the respondents consider the intellectual environment of their branch or lab to be good or excellent. The results for the 2000 survey of branch management are available on the DCEG intranet (http://intranet-dceg.ims.nci.nih.gov/scientists.html).

Although the survey results have indicated a high degree of satisfaction, they have also identified areas for improvement. One such issue is the need for management training. Although branch chiefs and other DCEG scientists have considerable management responsibilities, many do not have formal training in managing time, people, and other resources. COS has worked with Dr. Zahm and the NIH Office of Human Resource Management to develop a management training curriculum for DCEG. To date, branch chiefs have received training in strategic planning, time management and delegation, and staff development and conflict resolution. On July 26, the Division will offer a time-management training session for all interested DCEG staff.

In closing, I thank my COS colleagues for their creative ideas, wisdom, and hard work. And I thank Dr. Fraumeni and Dr. Zahm for their strong support in our efforts to build social capital within DCEG. ■

—Tom O'Brien

SAM MBULAITEYE, MEDICAL ONCOLOGIST


Dr. Sam Mbulaiteye

In the spring of this year, Sam Mbulaiteye, M.D., a medical oncologist from the Uganda Cancer Institute in Kampala, joined the Viral Epidemiology Branch as a research fellow. *DCEG Linkage* recently met with Dr. Mbulaiteye to discuss his research interests in HIV/AIDS, its impact on cancer pathogenesis and natural history, and his plans while at DCEG.

What interested you in public health and epidemiology rather than more traditional clinical patient care?

I became interested in public health during my medical training at Makerere Medical School in Kampala. I noticed that Uganda, like the rest of sub-Saharan Africa, was experiencing an overwhelming burden of disease. Doctors had been trained since the turn of the century and an excellent health infrastructure was in place, but they seemed to be fighting a losing battle.

I noticed that Uganda, like the rest of sub-Saharan Africa, was experiencing an overwhelming burden of disease. Doctors had been trained since the turn of the century and an excellent health infrastructure was in place, but they seemed to be fighting a losing battle.

More people sought care, but new diseases and resistance to known treatments were emerging. And although medical advances were proceeding elsewhere at an ever-increasing pace, doctors did not know how to apply this knowledge in Uganda. I thought my career interests would be best served by seeking a branch of medicine that would provide me with an understanding of diseases in populations. That branch is public health, and epidemiology is its scientific arm.

What drew your interests to the impact of HIV/AIDS on cancer pathogenesis?

I trained in Uganda at a time when HIV was just being described. Like the United States, Uganda was experiencing an unprecedented increase in the incidence of Kaposi's sarcoma (KS), particularly among adults in their 20's and 30's. I learned that HIV increases the risk for cancers, such as Burkitt's lymphoma and KS, that are also associated with other viral infections. Because the prevalence of HIV and some of these viral infections in Uganda is high, my curiosity was piqued as to what impact HIV infection would have on the risk of cancer or its clinical presentation.

U.S. studies have shown that AIDS only slightly elevates the overall risk for cancer, but greatly increases the risk for viral-associated cancers such as KS, non-Hodgkin's lymphoma, Hodgkin's disease, and cervical cancer. The risk of KS is similar in Uganda and the United States, but studies in Uganda have not revealed the AIDS-associated increase in risk for lymphoma or cervical cancer seen in the United States, and in Uganda there is a marked increase in incidence of cancer of the conjunctiva.

So far, changes in liver cancer that may be attributable to AIDS have not been observed.

Cancer is a slowly growing disease, and the HIV epidemic is still raging in Uganda. Findings to date are therefore not definitive. I believe there is still much to study on the multifactorial etiology of cancer afforded by the HIV epidemic in Uganda.

Has working on HIV/AIDS opened new directions for research?

The finding of a new herpesvirus associated with KS has opened up a new area of research. For example, what is the distribution of this virus in Uganda, how is it spread, and what causes some people infected with the virus to develop KS while others do not? I am pursuing the hypothesis that in sub-Saharan Africa this herpesvirus is transmitted through blood transfusions. I hope to test this hypothesis, together with colleagues here at NCI and in Uganda, by studying Ugandan children with sickle cell anemia, who usually receive many transfusions.

What is the situation for patients with HIV/AIDS in Uganda?

Uganda has been fortunate in having reacted swiftly to the epidemic. The epidemic may be declining in response to educational messages. But the more that is known about HIV infection and its complications, the better the chance to reduce rates of HIV-related diseases. My being here at NCI is a step in the right direction—it should foster an international collaboration that will take knowledge that has given hope to AIDS patients in the west and translate it into hope for those in Africa.

How do you feel your research will affect the long-term prognosis of HIV patients?

First of all, improved links between NCI and Uganda could well result in an increase in the volume of research directly relevant to Ugandan patients with HIV/AIDS. We shall learn the spectrum of cancers occurring in HIV-infected persons in Uganda, the risk factors for these various cancers, and how these risks can be modified. For patients, this research will lead to more information regarding cancer etiology, surveillance, diagnosis, early detection, and treatment. Doctors will know what risks a patient faces and how to advise the patient, and they will have the information needed to perform the proper tests, make the correct diagnosis, and work with the patient for longer lasting results. In the long run, this research will lead to improved patient care and a better doctor-patient relationship.

Are there any other cancer problems that interest you?

As a matter of fact, I'm also interested in breast cancer. Although breast cancer is rare in Uganda, it is the second most common tumor among Ugandan women. It is a very aggressive disease, occurring at young ages among women who have had many children and have breastfed, often for up to 60 months. This is a very different profile from breast cancer in other parts of the world, which intrigues me. I hope I will get to study this disease and these unusual patterns in the future.

What are your goals for the future?

I hope to be able to pass on to my colleagues in Uganda, and in Africa in general, the knowledge and skills I have learned. In the 1960's, NIH established the Uganda Cancer Institute (UCI) as a research institute. This institute was key in characterizing Burkitt's lymphoma and showing that this lymphoma could be cured. Unfortunately, UCI was dismantled during the years of Ugandan turmoil and now exists only as a treatment and counseling center. My hope is to see UCI return to its former position of prominence in medical research. ■

Uganda has been fortunate in having reacted swiftly to the epidemic.... But the more that is known about HIV infection and its complications, the better the chance to reduce rates of HIV-related diseases.

—Sandy Rothschild

CANCER ATLAS WEB SITE UPDATED

An enhanced version of the *Cancer Mortality Maps and Graphs* web site, which provides interactive maps, graphs, text, tables, and figures showing geographic patterns and time trends of cancer death rates for more than 40 types of cancer from 1950 through 1994, is now available at http://cancer.gov/atlasplus/. New data on this site include cancer rates for blacks at the county level from 1970 through 1994, five-year mortality rates from 1950–1954 through 1990–1994, and cancer rates for four age groups (0–19, 20–49, 50–74, and 75 years and over). The site uses state-of-the-art features, such as the following:

- GIF (graphic interchange format) and HTML (hypertext markup language) with links;
- PDF (portable document format), which allows printing, searching, copying, pasting, and zooming of the document;
- SVG (scalable vector graphics), which is like PDF, but also includes "pop-up" text boxes within the document; and
- [D]-Link, which makes the charts and graphic data accessible to the visually impaired.

The site also has some new features:

- Interactive charts created over the internet with "drilldown" capability, which enables the user to go from state mortality rates to county or state economic area (SEA) rates;
- Five-year rates over time for the United States overall, each state, and each SEA that can be viewed on the same graph;
- State-by-state cancer rates for all the cancers available on the site;
- Multiple geographic pattern and time trend maps (*J Natl Cancer Inst* 2000;92:534-543), which can be "animated" into a slide show; and
- Links to related U.S. and international web sites.

MINGDONG ZHANG, RESEARCH FELLOW


Dr. Mingdong Zhang

Before joining the Viral Epidemiology Branch (VEB) last year as a research fellow, Mingdong Zhang, M.D., Ph.D., was a research fellow in the National Institute of Allergy and Infectious Diseases (NIAID). His research has focused on hepatitis viruses, hepatocellular carcinoma, and host genetics. *DCEG Linkage* had a chance to chat with Dr. Zhang about his work and insights from his training both in China and in the United States.

What encouraged you to conduct epidemiologic research on liver cancer at Shanghai Medical University? How did you end up at NCI?

Losing two relatives to cancer motivated me to go to medical school. While conducting public health studies during my internship, I became interested in epidemiology, which I think has more impact on the health of the general population than does clinical medicine. After medical school, I entered an epidemiology graduate program at the University of Iowa. For my thesis project, I conducted a population-based, case-control study of liver cancer in endemic areas of southwest China. I especially focused on hepatitis B infection, aflatoxin intake, family history, and other risk factors related to liver cancer.

During my studies at the University of Iowa, I developed an interest in molecular biology. Because I could not find a dissertation advisor working on the molecular biology of hepatitis viruses, I transferred to a Ph.D. program in molecular virology at Baylor College of Medicine in Houston. At Baylor, I eventually joined a laboratory where I worked on the molecular pathogenesis of rotavirus, which causes diarrhea in infants and young children. My dissertation focused on the molecular mechanisms of the viral nonstructural protein NSP4 in causing disease.

In the spring of 1999, I joined the hepatitis viruses lab at NIAID, with an interest in studying the hepatitis C virus. But there my projects were limited to the hepatitis E virus (HEV), an RNA virus that causes acute hepatitis and has no implications to the development of liver cancer. While I was scanning the NCI web site, my attention was drawn to the research being conducted in DCEG. I contacted Dr. Jim Goedert, Chief of VEB, and Dr. Tom O'Brien, also of VEB, and I was brought to DCEG to conduct molecular epidemiologic studies of hepatitis B and C viruses, with a focus on host genetic susceptibility.

By studying the interactions between viruses and host genes, we might find new clues to how the host responds to a viral infection and how the host interacts with viruses during their replication and during oncogenesis.

What was the importance of your work with HEV?

I was able to construct a full-length cDNA clone of the viral RNA. From this clone, I made RNA transcripts *in vitro* and introduced HEV RNA into the livers of rhesus monkeys and chimpanzees. If the reconstructed RNA represented an authentic virus genome sequence, it would initiate HEV replication in the liver of these animals and infectious virus particles would be recovered.

An infectious cDNA clone is very important for studies of an RNA virus. Once we have a clone, we can modify and study the function of individual genes. At the same time, we can find a way to adapt the virus to grow in the cell culture. Ultimately, we can develop an attenuated live vaccine to prevent virus infection.

How does your role in VEB enhance the mission of DCEG?

Many viruses cause human cancer. By studying the interactions between viruses and host genes, we might find new clues to how the host responds to a viral infection and how the host interacts with viruses during their replication and during oncogenesis. These studies may help us identify new targets or pathways to develop preventive or therapeutic approaches to cancer.

What will likely affect the outcome of your research?

The development of new technologies and the support of the Division in terms of scientific guidance, research resources, and network of collaborators will all strongly affect the outcome of my research.

What impact might this research have on future NIH studies?

Most important is the identification of potential host genes and the polymorphisms associated with host susceptibility to infection by hepatitis B and C viruses. If we can achieve that goal, it will open the door to opportunities for future hepatitis virus and liver cancer research. ■

—Sandy Rothschild

RECENT SCIENTIFIC HIGHLIGHTS

BREAST CANCER

Benign Breast Disease and Mammographic Density in Relation to Breast Cancer

This case-control study, nested within the prospective follow-up of the Breast Cancer Detection Demonstration Project, evaluated information on benign breast histology and mammographic density from 347 women who later developed breast cancer and from 410 age- and race-matched control subjects. After adjustment for mammographic density, the odds ratio (OR) for atypical hyperplasia was 2.1, and after adjustment for benign histology, the OR for at least 75 percent density was 3.8. Women with nonproliferative benign disease and at least 75 percent density had an OR of 5.8, while those with atypical hyperplasia and less than 50 percent density had an OR of 4.1. Women with proliferative benign disease and at least 75 percent density did not have as high a risk for breast cancer arising from the combination of effects ($p = 0.002$) as women with only one of these factors. **(Byrne C, Schairer C, Brinton LA, Wolfe J, Parekh N, Salane M, Carter C, Hoover R. Effects of mammographic density and benign breast disease on breast cancer risk.** *Cancer Causes Control* **2001;12:103-110)**

Lactation and Breast Cancer Risk

The relationship between lactation and breast cancer risk was examined in a case-control study of 608 women with incident breast cancer and 609 control subjects, aged 30 to 80 years, in Connecticut. Parous women who reported ever lactating had a slightly reduced risk of breast cancer (odds ratio [OR] = 0.8, 95 percent CI = 0.6–1.1) compared with parous women who had never lactated. Women who had breast fed more than three children had an OR of 0.5 (95 percent CI = 0.3–1.0), and women who had breast fed their first child for more than 13 months had an OR of 0.5 (95 percent CI = 0.2–0.9). **(Zheng T, Holford TR, Mayne ST, Owens PH, Zhang Y, Zhang B, Boyle P, Zahm SH. Lactation and breast cancer risk: a case-control study in Connecticut.** *Br J Cancer* **2001;84:1472-1476)** ■

BREAST IMPLANTS

Risk of Cancers among Women with Augmentation Mammoplasty

A retrospective cohort study was conducted to assess long-term health effects among 13,488 women who received cosmetic breast implants and 3,936 patients with other types of plastic surgery. Following a study that showed no relation between breast implants and breast cancer (Brinton et al., 2000), this paper focused on the 359 other incident cancer cases among the implant patients versus 296 expected based on population rates (standardized incidence ratio = 1.2). Elevated ratios were observed for cancers of the stomach (2.6), cervix (3.2), vulva (2.5), and brain (2.2) and for leukemia (2.2). When implant recipients were compared with the other plastic surgery patients, no overall increase in cancer risk was observed, suggesting that many previously observed elevations were attributable to lifestyle factors. However, elevated relative risks did persist for cancers of the cervix (1.8), respiratory tract (2.4), and brain (2.8). **(Brinton LA, Lubin JH, Burich MC, Colton T, Brown SL, Hoover RN. Cancer risk at sites other than the breast following augmentation mammoplasty.** *Ann Epidemiol* **2001;11:248-256)**

Mortality Patterns among Women with Augmentation Mammoplasty

In the same cohort, both the implant and other plastic surgery groups had lower death rates than the general population, which suggested that patients who seek elective surgery are generally healthy. Yet implant patients had higher overall mortality (relative risk = 1.3) than other plastic surgery patients, reflecting increases in risk for respiratory tract cancer (3.0), brain cancer (2.2), and suicide (4.2). **(Brinton LA, Lubin JH, Burich MC, Colton T, Hoover RN. Mortality among augmentation mammoplasty patients.** *Epidemiology* **2001;12:321-326)** ■

CERVICAL CANCER

Human Papillomavirus Cofactors Related to Cervical Cancer

Factors associated with high-grade squamous intraepithelial lesions (HSIL) and cervical cancer were examined in a case-control study within a population-based cohort of human papillomavirus (HPV)-positive women in Costa Rica. Women with HPV-positive HSIL or cancer (HSIL/CA; n = 146) were compared with HPV-positive women without HSIL/CA (n = 843). The risk of HSIL/CA increased with number of live births (p for trend = 0.04) and was elevated among women who smoked more than six cigarettes a day (relative risk = 2.7, 95 percent CI = 1.1–6.7). Current use of barrier contraceptives reduced the risk (relative risk = 0.4, 95 percent CI = 0.2–0.96). Oral contraceptive use was associated with HSIL/CA among women with fewer than three pregnancies, but no associations were observed between risk and sexual behavior or a self-reported history of sexually transmitted diseases. Results were similar among women positive for high-risk HPV types. **(Hildesheim A, Herrero R, Castle PE, Wacholder S, Bratti MC, Sherman ME, Lorincz AT, Burk RD, Morales J, Rodriguez AC, Helgesen K, Alfaro M, Hutchinson M, Balmaceda I, Greenberg M, Schiffman M. HPV co-factors related to the development of cervical cancer: results from a population-based study in Costa Rica.** *Br J Cancer* **2001;84:1219-1226)**

Homocysteine Levels and Risk of Cervical Cancer

In a large case-control study, 183 case subjects and 540 control subjects were assessed for cervical cancer risk factors and serum homocysteine levels. The risk for invasive cervical cancer was elevated in women in the upper three homocysteine quartiles (more than 6.31 μmol/L; odds ratio = 2.4–3.2, *p* for trend = 0.01). Odds ratios were similar when case subjects were compared with human papillomavirus 16-seropositive control subjects. Thus, serum homocysteine levels may predict the risk of invasive cervical cancer. **(Weinstein SJ, Ziegler RG, Selhub J, Fears TR, Strickler HD, Brinton LA, Hamman RF, Levine RS, Mallin K, Stolley PD. Elevated serum homocysteine levels and increased risk of invasive cervical cancer in US women. *Cancer Causes Control* 2001;12:317-324)** ■

DIETHYLSTILBESTROL

Cancer Risk among Women Given Diethylstilbestrol during Pregnancy

Compared with women not given diethylstilbestrol (DES) during pregnancy, women given DES showed a modest but statistically significant increase in breast cancer risk (relative risk = 1.3). The increased risk was not exacerbated by family history of breast cancer, use of oral contraceptives, or hormone replacement therapy. The study found no evidence that DES was associated with risk of ovarian, endometrial, or other cancer. **(Titus-Ernstoff L, Hatch EE, Hoover RN, Palmer J, Greenberg ER, Ricker W, Kaufman R, Noller K, Herbst AL, Colton T, Hartge P. Long-term cancer risk in women given diethylstilbestrol (DES) during pregnancy. *Br J Cancer* 2001;84:126-133)**

Cancer Risk among Males with *In Utero* Exposure to Diethylstilbestrol

A total of 3,613 men with prenatal DES exposure were studied from 1978 through 1994. Overall, cancer rates among DES-exposed men were similar to those among unexposed men (relative risk [RR] = 1.1) and to national rates for all men (RR = 0.99). The RR for testicular cancer among exposed men was 3.1 times that among unexposed men and 2.0 times the population-based rate. **(Strohsnitter WC, Noller KL, Hoover RN, Robboy SJ, Palmer JR, Titus-Ernstoff L, Kaufman RH, Adam E, Herbst AL, Hatch EE. Cancer risk in men exposed *in utero* to diethylstilbestrol. *J Natl Cancer Inst* 2001;93:545-551)** ■

INFECTIOUS AGENTS

Helicobacter pylori Seropositivity and Gastric Cancer in Linxian, China

In this prospective nested case-control study, 99 patients with gastric cardia cancer, 82 patients with noncardia gastric cancer, and 192 cancer-free control subjects were selected from participants in a nutrition intervention trial previously conducted in Linxian, China. The estimated odds ratio for *H. pylori* seropositivity was 1.9 for gastric cardia cancer, 2.3 for noncardia gastric cancer, and 2.0 for gastric cardia and noncardia cancers combined. Thus, *H. pylori* carriage may increase the risk of cancer throughout the stomach. **(Limburg PJ, Qiao YL, Mark SD, Wang GQ, Perez-Perez GI, Blaser MJ, Wu YP, Zou XN, Dong ZW, Taylor PR, Dawsey SM. *Helicobacter pylori* seropositivity and subsite-specific gastric cancer risks in Linxian, China. *J Natl Cancer Inst* 2001;93:226-233)**

Helicobacter pylori and Pancreatic Cancer

The association of *H. pylori* with exocrine pancreatic cancer was examined in a nested case-control study within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study cohort of male Finnish smokers aged 50 to 69 years. Seroprevalence of *H. pylori* was 82 percent for subjects diagnosed with pancreatic cancer (n = 121) and 73 percent for control subjects (n = 226). Subjects with *H. pylori* or CagA+ strains demonstrated an elevated risk of pancreatic cancer (odds ratio = 1.9, 95 percent CI = 1.1–3.3) compared with seronegative subjects (odds ratio = 2.0, 95 percent CI = 1.1–3.7). Thus, *H. pylori* carriage may play a role in the development of exocrine pancreatic cancer. **(Stolzenberg-Solomon RZ, Blaser MJ, Limburg PJ, Perez-Perez G, Taylor PR, Virtamo J, Albanes D. *Helicobacter pylori* seropositivity as a risk factor for pancreatic cancer. *J Natl Cancer Inst* 2001;93:937-941)**

Cancers after AIDS-related Immunosuppression in Adults

Analyses of population-based AIDS and cancer registry data from 11 geographically diverse areas in the United States, representing 302,834 adults aged 15 to 69 years with HIV/AIDS, revealed an excess of AIDS-defining cancers. Non-AIDS-defining cancers also occurred in significant excess (n = 4,422, overall risk ratio [RR] = 2.7). Hodgkin's disease (n = 612, RR = 11.5)—particularly of the mixed cellularity subtype (n = 217, RR = 18.3) and the lymphocytic depletion subtype (n = 36, RR = 35.3), lung cancer (n = 808, RR = 4.5), penile cancer (n = 14, RR = 3.9), soft tissue malignancies (n = 78, RR = 3.3), lip cancer (n = 20, RR = 3.1), and testicular seminoma (n = 115, RR = 2.0) met criteria for potential association with immunosuppression. However, except for Hodgkin's disease and possibly lip cancer and testicular seminoma, most non-AIDS-defining cancers did not appear to be influenced by the advancing immunosuppression associated with HIV disease progression. Some may have occurred excessively because of heavy smoking (lung cancer), frequent exposure to human papillomavirus (penile cancer), or inaccurately recorded cases of Kaposi's sarcoma (soft-tissue malignancies) in this population. **(Frisch M, Biggar RJ, Engels EA, Goedert JJ. Association of cancer with AIDS-related immunosuppression in adults. *JAMA* 2001;285:1736-1745)**

Risk of T-cell Lymphomas in Persons with AIDS

The risk of T-cell lymphoma in the two years after AIDS onset was examined by linking data from 302,834 adults with AIDS to cancer registry data. Of 6,788 cases of non-Hodgkin's lymphoma with specified histologies, 96 (1.4 percent) were T-cell lymphomas. The relative risk of T-cell lymphoma, estimated by the standardized incidence ratio, was 15.0. Risk was increased for all subtypes, including mycosis fungoides, peripheral or cutaneous lymphomas, and adult T-cell leukemia or lymphoma. HIV-related immunodeficiency may be an important risk factor, but being an immigrant from the Caribbean region and other factors might independently increase the risk for T-cell lymphoma. **(Biggar RJ, Engels EA, Frisch M, Goedert JJ. Risk of T-cell lymphomas in persons with AIDS. *J Acquir Immune Defic Syndr* 2001;26:371-376)**

SV40 Detection and Mesothelioma

The sensitivity, specificity, and reproducibility of various detection assays for the simian virus SV40, particularly in mesotheliomas, were assessed in a multicenter study. Assays were tested using fresh-frozen mesothelioma and normal human lung specimens. All of the PCR-based assays demonstrated high specificity and reproducibility in most laboratories, but none of the mesothelioma or normal lung samples obtained from archival samples at a single center was reproducibly positive for SV40 DNA. **(Strickler HD, The International SV40 Working Group. A multicenter evaluation of assays for detection of SV40 DNA and results in masked mesothelioma specimens. *Cancer Epidemiol Biomarkers Prev* 2001;10:523-532)** ■

LEUKEMIA

Childhood Leukemia and Exposure to Household Solvents

This study explored the risk of acute lymphoblastic leukemia in childhood in association with participation in hobbies or other home projects involving organic solvents. Leukemia was associated with frequent (more than four times/month) exposure to model building (odds ratio [OR] = 1.9) and with artwork using solvents (OR = 4.1). Children whose mothers lived in homes painted extensively (more than four rooms) in the year before the children's birth also exhibited elevated risk (OR = 1.7). **(Freedman DM, Stewart P, Kleinerman RA, Wacholder S, Hatch EE, Tarone RE, Robison LL, Linet MS. Household solvent exposures and childhood acute lymphoblastic leukemia. *Am J Public Health* 2001;91:564-567)** ■

LUNG CANCER

Trends in U.S. Lung Cancer Mortality

Lung cancer trends, including trends among birth cohorts born after 1950, were examined. Results revealed an unexpected, significant moderation in the rate of decrease in lung cancer mortality for whites born after 1950 and a corresponding smaller and nonsignificant moderation for blacks. These data are consistent with trends in smoking initiation rates for both cigarettes and marijuana, which increased among children aged 12 to 17 years from 1965 through 1977. A significant decrease in the slope of the calendar-period trend for lung cancer mortality was observed in 1990 for both whites and blacks. **(Jemal A, Chu KC, Tarone RE. Recent trends in lung cancer mortality in the United States. *J Natl Cancer Inst* 2001;93:277-283)**

Previous Pulmonary Disease and Lung Cancer

A population-based, case-control study in Gansu Province, China, identified 656 men and 230 women with lung cancer diagnosed between 1994 and 1998. After data were adjusted for active smoking and socioeconomic status, significantly increased risks were related to pulmonary tuberculosis (odds ratio [OR] = 2.1) and chronic bronchitis or emphysema (OR = 1.4). Nonsignificantly increased ORs for asthma (1.4) and pneumonia (1.5) were also observed. **(Brenner AV, Wang ZY, Kleinerman RA, Wang LD, Zhang SZ, Metayer C, Chen K, Lei SW, Cui HX, Lubin JH. Previous pulmonary diseases and risk of lung cancer in Gansu Province, China. *Int J Epidemiol* 2001;30:118-124)**

DIETARY IODINE AND RADIOACTIVE IODINE

The major fallout from the nuclear power station accident at Chernobyl in 1986 occurred in regions of Ukraine and Belarus, where the population may currently have a moderate iodine deficiency. A workshop was held in November 2000, in conjunction with the Ukraine-Belarus-USA study of thyroid disease in persons exposed as children, to review what is known about iodine nutrition in these regions, how it might affect the risk of thyroid tumor formation resulting from exposure to radioiodine, and how to monitor iodine nutrition. No precise information about iodine intake was available for 1986, but a moderate deficiency was suggested by the prevalence of mild goiter in the region's children, and this suggestion was supported by urinary iodine measurements that started in 1990. The effects of iodine deficiency on increased thyroid size and increased iodine uptake by the thyroid in 1986 are not known. Also missing are experimental and clinical data on the effects of increased thyroid cellular activity, following the accident, on the risk of tumorigenesis. Despite these limitations, iodine nutrition should be monitored in persons exposed to radioiodine as children. **(Robbins J, Dunn JT, Bouville A, Kravchenko VI, Lubin J, Petrenko S, Sullivan KM, Vanmiddlesworth L, Wolff J. Iodine nutrition and the risk from radioactive iodine: a workshop report on the Chernobyl long-term follow-up study. Thyroid 2001;11:487-491)**

p53 Gene Expression and Indoor Exposure to Smoky Coal in China

Ninety-seven newly diagnosed lung cancer patients and 97 control subjects individually matched by age, sex, and type of home fuel were enrolled in a population-based study in Xuan Wei County, China. In these poorly ventilated homes, a greater level of lifetime use of smoky coal was associated with an overall increase in lung cancer risk. Compared with subjects who used less than 130 tons of smoky coal during their lifetime, the odds ratio for lung cancer was 1.48 for subjects exposed to 130 to 240 tons of smoky coal and 3.21 for subjects who used more than 240 tons (p for trend = 0.01). This effect was found almost exclusively among women, nearly all of whom were nonsmokers, and was primarily seen only among patients with sputum samples positive for *p53* overexpression (odds ratio = 18.72 versus 4.80 for *p53*-negative women). **(Lan Q, Feng ZM, Tian D, He XZ, Rothman N, Tian LW, Lu XB, Terry MB, Mumford JL. *p53* Gene expression in relation to indoor exposure to unvented coal smoke in Xuan Wei, China. *J Occup Environ Med* 2001;43:226-230)** ■

MELANOMA

Recent Trends in U.S. Whites

In cohort analysis of data from the Surveillance, Epidemiology, and End Results program, melanoma incidence increased among females born since the 1960's. From 1974–1975 through 1988–1989, upward incidence trends were seen for localized tumors and downward trends for distant-stage tumors in the under-40 age group. From 1990–1991 through 1996–1997, age-specific rates among females compared with males generally remained stable or declined more for distant-stage tumors and increased less for local-stage tumors. The increase in thin tumors (less than 1 mm) was significant in all age groups ($p < 0.05$ for all) except men under 40 years. In contrast, the increase in rates for thick tumors (4 mm or more) was significant only for males aged 60 years and older ($p = 0.0003$). The recent trends appear to reflect increases in sunlight exposure. **(Jemal A, Devesa SS, Hartge P, Tucker MA. Recent trends in cutaneous melanoma incidence among whites in the United States. *J Natl Cancer Inst* 2001;93:678-683)** ■

NUTRITION

Empirical Evidence of Correlated Biases in Dietary Assessment Instruments

A new model of dietary assessment was introduced that includes, for both the food frequency questionnaire (FFQ) and the dietary report reference instrument, group-specific biases related to true intake and correlated person-specific biases. Data were obtained from a dietary assessment validation study among 160 women at the Dunn Clinical Nutrition Center, Cambridge, United Kingdom, in 1988–1990. Using biomarker measurements and dietary report measurements, the new model suggests that measurement error in the FFQ could lead to a 51 percent greater attenuation of true nutrient effect. It also demonstrates the need for a study 2.3 times larger than what would be estimated by the dietary report reference instrument. **(Kipnis V, Midthune D, Freedman LS, Bingham S, Schatzkin A, Subar A, Carroll RJ. Empirical evidence of correlated biases in dietary assessment instruments and its implications. *Am J Epidemiol* 2001;153:394-403)** ■

OCCUPATION

Diesel Engine Emissions and Cancer

Job and industry titles from the Swedish Cancer Environment Register III—which contains data on cancer incidence, from 1971 to 1989, by occupation and industry of employment from the 1960 and 1970 census reports—were classified according to the estimated probability and intensity of exposure to diesel emissions. Compared with no exposure, men who were exposed at high or medium intensity in 1960 experienced an increased risk of lung cancer (relative risk [RR] = 1.3, 95 percent CI = 1.3–1.4 for high intensity; RR = 1.1, 95 percent CI = 1.1–1.2 for medium intensity), but results did not suggest an effect among women (RR = 1.1, 95 percent CI = 0.6–1.8 for high or medium intensity). Among men, the risk was higher for squamous cell carcinoma of the lung than for other histological types, and small increases in risk were also observed for cancers of the stomach (standard incidence ratio [SIR] = 1.06), pancreas (SIR = 1.05), larynx (SIR = 1.09), and kidney (SIR = 1.06). Women experienced nonsignificant increases in risk for stomach, pancreatic, and laryngeal cancers and significant increases for oral or pharyngeal cancer (SIR = 1.64) and cervical cancer (SIR = 1.48). No increased risk of bladder cancer was observed for either gender. **(Boffetta P, Dosemeci M, Gridley G, Bath H, Moradi T, Silverman D. Occupational exposure to diesel engine emissions and risk of cancer in Swedish men and women. *Cancer Causes Control* 2001;12:365-374)**

Occupation and Brain Cancer

A population-based, case-control study of 375 persons with incident brain glioma and 2,434 population-based control subjects in Iowa showed an increased risk among men employed for more than 10 years in roofing, siding, sheet-metalworking, newspaper work, rubber and plastic products, wholesale trade of durable goods and grain, cleaning and building service occupations, certain manufacturing industries, as well as miscellaneous mechanics and repairers. Risk was also increased for subjects who worked in plumbing, heating and air conditioning, electrical services, gasoline service stations, and the military. Among women, excess risk was associated with work in agricultural services

and farming, apparel and textile products, electrical and electronic equipment manufacturing, various retail sales, record keeping, and restaurant service. These associations may provide clues to environmental determinants of brain tumors about which little is known. **(Zheng TZ, Cantor KP, Zhang YW, Keim S, Lynch CF. Occupational risk factors for brain cancer: a population-based case-control study in Iowa. *J Occup Environ Med* 2001;43:317-324)**

Philadelphia Firefighters

In a retrospective cohort mortality study of 7,789 Philadelphia firefighters employed between 1925 and 1986, the firefighters had similar mortality from all causes of death combined and from all cancers (standard mortality ratio = 0.96 and 1.10, respectively) as white men in the United States. Increased mortality was observed for cancers of the colon and kidney, non-Hodgkin's lymphoma, and multiple myeloma, which may be associated with the chemical exposures experienced by firefighters. **(Baris D, Garrity TJ, Telles JL, Heineman EF, Olshan A, Zahm SH. Cohort mortality study of Philadelphia firefighters. *Am J Ind Med* 2001;39:463-476)** ■

OVARIAN CANCER

Ovarian Cancer Risk by Parity and Oral Contraceptive Use among Carriers and Noncarriers of *BRCA1* or *BRCA2* Mutations

In a population-based case-control study of Jewish women in Israel, 840 women with ovarian cancer and 751 control subjects were tested for the founder mutations in *BRCA1* and *BRCA2* that are common among Jews. The effects of parity and oral contraceptive use on ovarian cancer risk were estimated for carriers and noncarriers. Of the women with ovarian cancer, 29.0 percent carried a *BRCA1* or *BRCA2* mutation; 1.7 percent of control subjects did. Overall, multiparity and the use of oral contraceptives lowered the risk of ovarian cancer. Multiparity was protective among both carriers and noncarriers, and oral contraceptive use was protective only among noncarriers. Among carriers, the risk was reduced by 12 percent per birth (95 percent CI = 2.3–21.0) and by 0.2 percent per year of oral contraceptive use (95 percent CI = 4.9–5.0). On the basis of these results, it is premature to advise use of oral contraceptives as chemoprevention among carriers of *BRCA1* and *BRCA2* mutations. **(Modan B, Hartge P, Hirsh-Yechezkel G, Chetrit A, Lubin F, Beller U, Ben-Baruch G, Fishman A, Menczer J, Struewing JP, Tucker MA, Ebbers SM, Friedman E, Piura B, Wacholder S. Parity, oral contraceptives, and the risk of ovarian cancer among carriers and noncarriers of a *BRCA1* or *BRCA2* mutation. *N Engl J Med* 2001;345:235-240)** ■

PROSTATE CANCER

Insulin-like Growth Factors and Prostate Cancer: A Chinese Prospective, Case-control Study in China

To assess whether insulin-like growth factors and binding proteins (IGF-I, IGF-II, IGFBP-1, and IGFBP-3) are associated with prostate cancer in a low-risk population, plasma concentrations of these factors were measured among 128 men with incident prostate cancer and 306 population control subjects in Shanghai, China. The risk for prostate cancer was significant for the highest quartile of IGF-1 compared with the lowest (odds ratio [OR] = 2.6, p for trend = 0.01) and for the IGF-I:IGFBP-3 molar ratio, an indirect measure of free IGF-I (OR = 2.5, p for trend < 0.001). Risk was nonsignificant for IGFBP-3 (OR = 0.5, p for trend = 0.08) and for IGFBP-1 (OR = 0.6, p for trend = 0.25). These four associations were more pronounced after data were adjusted for serum 5α-androstane-3α,17β-diol glucuronide and sex hormone-binding globulin levels. No significant association with IGF-II concentration was observed. **(Chokkalingam AP, Pollak M, Fillmore CM, Gao YT, Stanczyk FZ, Deng J, Sesterhenn IA, Mostofi FK, Fears TR, Madigan MP, Ziegler RG, Fraumeni JF Jr, Hsing AW. Insulin-like growth factors and prostate cancer: a population-based case-control study in China. *Cancer Epidemiol Biomarkers Prev* 2001;10:421-427)**

Serum Insulin and Leptin Concentrations and Their Associations with Prostate Cancer

Blood samples from the same prostate cancer study population were analyzed for insulin and leptin levels. After data were adjusted for body mass index, waist-to-hip ratio (WHR), insulin-like

JONI RUTTER, MEMBER OF FELLOWS COMMITTEE


Dr. Joni Rutter

Joni Rutter, Ph.D., a postdoctoral fellow in the Laboratory of Population Genetics, is finishing her term as one of the NCI representatives on the NIH Fellows Committee (Felcom). Dr. Tatiana Dracheva, of the Laboratory of Population Genetics, will be taking her place this summer. Felcom is composed of fellows from each Institute and serves to enhance the intramural training experience. Subcommittees focus on such career issues and opportunities as the annual NIH Job Fair, the Fellows Award for Research Excellence (FARE) competition, and mentoring. Dr. Rutter chaired the Mentoring Subcommittee, which gathered information on the mentoring received by postdoctoral fellows during their tenure at NIH. Dr. Rutter described her experience as a Felcom representative and mentoring at NIH in the May 18 U.S.A. issue of *Science* magazine's *Next Wave*, available at http://nextwave.sciencemag.org/cgi/content/full/2001/05/17/1.

growth factor I, and sex hormone levels, higher serum insulin concentration was significantly and positively associated with prostate cancer ($p < 0.001$); men in the highest tertile had a 2.6-fold risk of prostate cancer compared with men in the lowest tertile. Regardless of the tertile level of WHR, higher insulin concentration was positively associated with the disease. Men in the highest tertiles of WHR (greater than 0.900) and insulin (more than 8.83 μM/mL) had 8.6 times the risk of men in the lowest tertiles of both, and those in the lowest tertile of WHR (less than 0.873) and the highest tertile of insulin had 4.3 times the risk. By contrast, the association between leptin concentration and prostate cancer risk was not significant. **(Hsing AW, Chua S Jr, Gao Y-T, Gentzschein E, Chang L, Deng J, Stanczyk FZ. Prostate cancer risk and serum levels of insulin and leptin: a population-based study.** *J Natl Cancer Inst* **2001;93:783-789)**

Vitamin D Receptors, Insulin-like Growth Factors, and Prostate Cancer

The association of vitamin D receptor gene polymorphisms and insulin-like growth factor-binding protein (IGFBP) with prostate cancer risk was examined in 191 newly diagnosed prostate cancer patients and 304 control subjects in Shanghai, China. No significant association was observed for the *Bsm*I or *Fok*I gene polymorphism, but decreased risk was observed among men with the ff *Fok*I genotype with higher plasma IGFBP-3 level (odds ratio = 0.14, 95 percent CI = 0.04–0.56, p for trend < 0.01) or IGFBP-1 level (odds ratio = 0.25, 95 percent CI = 0.07–0.85, p for trend = 0.02). IGFBP-3 level was not associated with risk among men with the FF or Ff genotype, and no effects were observed for IGF-I or IGF-II. Therefore, the IGF and vitamin D regulatory systems may interact to affect prostate cancer risk. **(Chokkalingam AP, McGlynn KA, Gao YT, Pollak M, Deng J, Sesterhenn IA, Mostofi FK, Fraumeni JF, Hsing AW. Vitamin D receptor gene polymorphisms, insulin-like growth factors, and prostate cancer risk: a population-based case-control study in China.** *Cancer Res* **2001;61:4333-4336)** ■

RADIATION

Cancer Mortality and Nasopharyngeal Radium Irradiation

A retrospective cohort study of all-cause and cancer-related mortality was conducted for 5,358 subjects exposed to nasopharyngeal radium irradiation (NRI) and 5,265 nonexposed subjects who as children had been treated at nine ear, nose, and throat clinics in The Netherlands from 1945 through 1981. Average radiation doses of 275 cGy for the nasopharynx, 10.9 cGy for the pituitary, 1.8 cGy for the brain, and 1.5 cGy for the thyroid were observed. Of the NRI-exposed subjects, 302 had died (standard mortality ratio [SMR] = 1.1, 95 percent CI = 1.0–1.3), and 315 of the nonexposed subjects had died (SMR = 1.1, 95 percent CI = 0.99–1.2). Ninety-six cancer-related deaths (SMR = 1.2, 95 percent CI = 0.95–1.4) among exposed subjects and 87 among nonexposed subjects (SMR = 1.0, 95 percent CI = 0.8–1.3) were documented. Although no excess deaths from cancers of the head and neck were found among exposed subjects, findings did indicate excess deaths from lymphoproliferative and hematopoietic cancers (SMR = 1.9, 95 percent CI = 1.1–1.3). These deaths resulted mainly from non-Hodgkin's lymphoma (SMR = 2.6, 95 percent CI = 1.0–5.3). These results do not indicate increased mortality in a population exposed to NRI during childhood. **(Ronckers CM, Land CE, Verdujin PG, Hayes RB, Stovall M, van Leeuwen FE. Cancer mortality after nasopharyngeal radium irradiation in the Netherlands: a cohort study.** *J Natl Cancer Inst* **2001;93:1021-1027)** ■

STATISTICS

A Marginal Likelihood Approach for Estimating Penetrance from a Kin-cohort Design

A marginal likelihood approach to estimate penetrance of a rare autosomal mutation was developed to be computationally simple to implement, more flexible than the original kin-cohort analytic approach proposed by Wacholder et al. (1998), and more robust than the likelihood approach to the presence of residual familial correlation considered by Call et al. (1999). The trade-off between robustness and efficiency was examined using simulation experiments. The method is illustrated by analysis of the data from the Washington Ashkenazi Study. **(Chatterjee N, Wacholder S. A marginal likelihood approach for estimating penetrance from kin-cohort designs.** *Biometrics* **2001;57:245-252)** ■

Pseudo-likelihood Estimates of Cumulative Risk of an Autosomal Dominant Disease from a Kin-cohort Study

The kin-cohort method by Wacholder et al. (1998) used to estimate the cumulative risk of breast cancer among *BRCA1* and *BRCA2* mutation carriers, while asymptotically correct, does not necessarily produce monotone estimates in small samples. In a quest to obtain monotone, weakly parametric estimates, separate piecewise exponential models for carriers and noncarriers were explored. Because the number of intervals on which constant hazards are assumed increased, however, the maximum likelihood score equations became unstable and difficult to solve. Therefore, alternative pseudo-likelihood procedures that were readily solvable were developed for piecewise exponential models with many intervals. **(Moore DF, Chatterjee N, Pee D, Gail MH. Pseudo-likelihood estimates of the cumulative risk of an autosomal dominant disease from a kin-cohort study.** *Genet Epidemiol* **2001;20:210-227)** ■

DCEG PEOPLE IN THE NEWS


Dr. Louise Brinton

In April, **Louise Brinton, Ph.D.,** of the Environmental Epidemiology Branch, presented a talk entitled "Etiologic Leads for Breast Cancer" at the First Joint U.S.–Egypt Meeting on Cancer, held in Sharm El Sheikh, Egypt. Also in April, she spoke on "Long-term Follow-up Study of Women with Augmentation Mammoplasty," as the First Invited Scholar in Residence Lecturer, to the Department of Epidemiology and Preventive Medicine at the University of Maryland School of Medicine in Baltimore. In May, Dr. Brinton spoke at the Canadian Breast Cancer Research Initiative Conference, held in Quebec, about emergent hypotheses on the etiology of breast cancer.


Dr. Kenneth Cantor

Kenneth Cantor, Ph.D., of the Occupational Epidemiology Branch, was appointed in May to the National Academy of Sciences subcommittee to update the 1999 report *Arsenic in Drinking Water*, on the basis of new studies and analyses published since that report was released.


Dr. Neil Caporaso

Neil Caporaso, M.D., of the Genetic Epidemiology Branch, organized and chaired the Behavioral Genetics and Cancer symposium at the 92nd Annual Meeting of the American Association for Cancer Research (AACR) held in New Orleans in March 2001. Speakers (including Dr. Andrew Bergen, a Branch special volunteer) presented overviews on the genetics of behavior, alcohol consumption, obesity, and tobacco use and addiction. Emphasis was placed on the parallel challenges that behavioral and cancer geneticists face in characterizing the genes involved in complex conditions.


Dr. Ruthann Giusti

Ruthann Giusti, M.D., of the Clinical Genetics Branch, and her collaborator, Dr. Thomas Ried of the NCI Center for Cancer Research, received a FY2001 Bench-to-Bedside Award from the NIH intramural research program. Their proposed project is entitled "Genomic Changes in Pre-malignant, Pre-invasive, and Invasive Breast Cancer in Women Genetically at High Risk for Breast Cancer."

Alisa Goldstein, M.D., Maria Teresa Landi, M.D., Ph.D., and **Margaret Tucker, M.D.,** all of the Genetic Epidemiology Branch, presented data from the Branch's genetic epidemiology and case-control studies of melanoma and dysplastic nevi at the Fifth World Conference on Melanoma in Venice, Italy, held February 28–March 3. This conference, held under the auspices of the Italian Ministry of Health, was part of the Melanoma Programme, World Health Organization. Dr. Goldstein presented "Genotype-phenotype Relationships in Melanoma-prone Families with *Cdkn2a* and *Cdk4* Mutations," Dr. Landi presented "Melanocortin-1 Receptor Gene Variants in Italian Melanoma-prone Families," and Dr. Tucker presented "Melanonocytic Lesions Do Not Vary by Mutation Type in Melanoma-prone Families." Abstracts of the meeting were published in *Melanoma Research* 2001;11(suppl 1):S1-S241. Also in Venice, Drs. Goldstein, Landi, and Tucker met with members of the International Melanoma Genetics Consortium to discuss findings and to plan future collaborative studies.


Dr. Mark Greene

As a member of the Clinical Cancer Genetics Subcommittee of the American Society of Clinical Oncology's (ASCO's) Education Committee, **Mark Greene, M.D.,** of the Clinical Genetics Branch, gave a lecture on genodermatoses at the ASCO Comprehensive Review of Clinical Cancer Genetics course in San Francisco in May. This intensive, two-day symposium served as a review mechanism for the newly developed credentialing procedure created by ASCO and the American Board of Internal Medicine through the independent Institute for Clinical Evaluation. This procedure will benefit health care providers (M.D.s, R.N.s, genetic counselors, social workers, etc.) who engage in familial cancer risk management and assessment.


Dr. Robert Hoover

Robert Hoover, M.D., Sc.D., Director of the Epidemiology and Biostatistics Program, received the Physician Researcher of the Year award from the PHS Physicians' Professional Advisory Committee. Dr. Hoover was presented with the award in May at the annual meeting of the PHS Commissioned Officers Association held in Washington, DC. The award recognizes individual initiative, accomplishment, and accountability for actions that increase the overall effectiveness of PHS through research.


Dr. David Kaufman

In March, **Dr. David Kaufman,** a predoctoral fellow in the Laboratory of Population Genetics, was honored at the AACR annual meeting in New Orleans with a 2001 AACR-AFLAC Scholar in Cancer Research Award. The award recognizes promising cancer research and the submission of a meritorious abstract selected for presentation. Dr. Kaufman's abstract was titled "Segregation Analysis of 236 Families of Breast Cancer Cases without *BRCA1/2* Mutations Provides Statistical Evidence of a Major Recessive Breast Cancer Susceptibility Gene with High Penetrance."

Nathaniel Rothman, M.D., M.P.H., M.H.S., of the Occupational Epidemiology Branch, and Dr. Stefano Bonassi of the Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy, organized and co-chaired the symposium Chromosomal Aberrations, Somatic Mutations, and Cancer Risk at the Environmental Mutagenesis Society in San Diego in March. Dr. Rothman also organized and co-chaired, with Dr. Stephen Chanock of the NCI Center for Cancer Research, the symposium How Do We Capitalize on the New Tools of Genomics in Cohort and Case-control Studies of Cancer? at the annual AACR meeting in New Orleans in March.


Dr. Arthur Schatzkin

Arthur Schatzkin, M.D., Dr.P.H., of the Nutritional Epidemiology Branch, recently received the Master Teacher Award in Preventive Medicine from the Alumni Association of the College of Medicine, State University of New York at Brooklyn (Downstate). In March, he gave a presentation, "Can Dietary Change Inhibit Colorectal Adenoma Pathogenesis?" at the Cancer Research Foundation of America Symposium for National Colorectal Cancer Awareness Month in Bethesda, MD. Also in March, Dr. Schatzkin gave the Gibson Lecture at the University of Virginia School of Medicine titled "Can Dietary Change Prevent Colorectal Cancer—Or Not?" And in April, at the First Joint U.S.–Egypt Meeting on Cancer Research in Sharm El Sheikh, Egypt, he spoke on "Can Dietary Change Prevent Colorectal Cancer?"


Dr. Rachael Stolzenberg-Solomon

Rachael Stolzenberg-Solomon, Ph.D., M.P.H., a cancer prevention fellow in the Nutritional Epidemiology Branch, won the prize for the best poster at the American Society of Preventive Oncology meeting in New York in March. Her poster was entitled "*H. pylori* and Pancreatic Cancer Risk in a Cohort of Male Smokers."

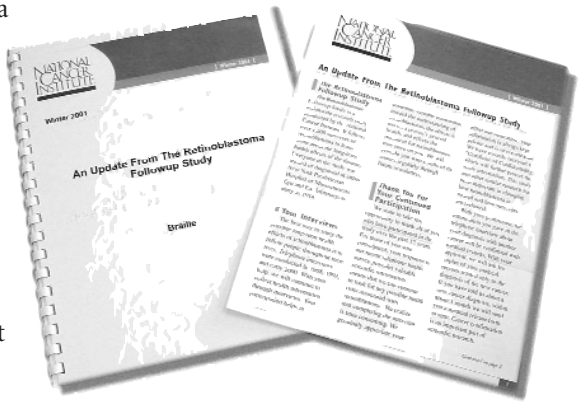

Dr. B.J. Stone

In May, **B.J. Stone, Ph.D.,** received the Blue Cross/Blue Shield Distinguished Federal Employee Award for her volunteer efforts in the community and within NIH. Dr. Stone has participated in the Recording for the Blind and Dyslexic program for over twenty-five years by recording mathematics textbooks on tape. Her dedicated service has helped an entire generation of blind scholars. At NIH, Dr. Stone is a regular donor to the Blood Bank, and she has donated over 100 units of blood. She also serves as the Division's volunteer fire drill coordinator. ■

RETINOBLASTOMA NEWSLETTER

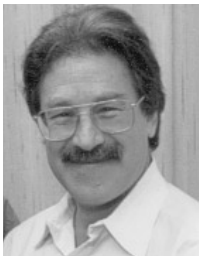
Ruth Kleinerman, M.P.H., of the Radiation Epidemiology Branch and Margaret Tucker, M.D., Chief of the Genetic Epidemiology Branch have published a newsletter, *An Update from the Retinoblastoma Followup Study*, for participants in a longitudinal study of retinoblastoma, a rare eye cancer occurring in early childhood. Because the vision of many patients is limited by their disease, the newsletter is produced in braille as well as large type.

Retinoblastoma patients are at increased risk of melanoma, and the current issue of the newsletter provides advice on avoiding sun exposure, explains warning signs for melanoma, and describes Dr. Tucker's clinical examination study of retinoblastoma patients with melanoma. This issue also warns about an increased risk of lung cancer for these patients, a result recently reported by Ms. Kleinerman and other DCEG investigators, and provides resources av able for smoking cessation.



Retinoblastoma braille and large-type newsletters

TOWN MEETING AWARDS


Dr. Richard Klausner

Dr. Richard Klausner (Director, NCI) presented the following awards to DCEG staff members at his annual DCEG Town Meeting on March 9.

DCEG Award for the Outstanding Research Paper in 2000 by a Fellow

Qing Lan, M.D., for Lan Q, He X, Costa DJ, Tian L, Rothman N, Hu G, Mumford JL. Indoor coal combustion emissions, *GSTM1* and *GSTT1* genotypes, and lung cancer risk: a case-control study in Xuan Wei, China. *Cancer Epidemiol Biomarkers Prev* 2000;9:605-608.


Dr. Qing Lan

Maria T. Sgambati, M.D., for Sgambati MT, Stolle C, Choyke PL, Walther MM, Zbar B, Linehan WM, Glenn GM. Mosaicism in von Hippel-Lindau disease: lessons from kindreds with germline mutations identified in offspring with mosaic parents. *Am J Hum Genet* 2000;66:84-91.

DCEG Award for the Outstanding Research Paper in 2000 by a Staff Scientist

Ruth A. Kleinerman, M.P.H., for Kleinerman RA, Tarone RE, Abramson DH, Seddon JM, Li FP, Tucker MA. Hereditary retinoblastoma and risk of lung cancer. *J Natl Cancer Inst* 2000;92:2037-2039.


Ms. Ruth Kleinerman

DCEG Outstanding Mentor Awards

Sholom Wacholder, Ph.D.

Nathaniel Rothman, M.D., M.P.H., M.H.S.


Dr. Sholom Wacholder


Dr. Nathaniel Rothman

DCEG Award for Exemplary Service

Martha S. Linet, M.D., M.P.H.


Dr. Martha Linet

RADIOACTIVE FALLOUT FROM NUCLEAR WEAPONS TESTS

Researchers have made preliminary estimates of radiation doses experienced by representative persons in the contiguous United States by examining their individual exposures to a set of radionuclides produced by nuclear weapons tests between 1951 and 1963. Andre Bouville, Ph.D., Ethel Gilbert, Ph.D., Kiyo Mabuchi, Ph.D., M.P.H., Elaine Ron, Ph.D., and Steve Simon, Ph.D., all from the Radiation Epidemiology Branch, Ms. Betsy Duane of the Office of the Director, and scientists from the Centers for Disease Control and Prevention have co-authored a report, "A Feasibility Study of the Health Consequences to the American Population of Nuclear Weapons Tests Conducted by the United States and Other Nations," for the U.S. Congress. The report makes recommendations for the study of the health risks from exposure to fallout, and for the development of a health communication strategy for the public and health care providers. The National Academy of Sciences is currently reviewing the report on behalf of the Department of Health and Human Services.

FELLOWSHIP ACHIEVEMENT AWARDS

Congratulations to the recipients of the 2001 DCEG Fellowship Achievement Awards: Lawrence Engel, Ph.D., of the Occupational Epidemiology Branch, Aparna Mohan, M.D., Ph.D., of the Radiation Epidemiology Branch, and Joni Rutter, Ph.D., of the Laboratory of Population Genetics. This performance award recognizes outstanding Cancer Research Training Award (CRTA) fellows by increasing their annual stipend as if they had an additional year of experience. Fellows are nominated by their branch chiefs and are evaluated by a selection committee on the basis of scientific productivity as demonstrated by high-quality scientific publications and ongoing research projects.

COMINGS … GOINGS


Dr. Marie Cantwell

In May, **Marie Cantwell, Ph.D.,** joined the Nutritional Epidemiology Branch as a visiting fellow. Dr. Cantwell received a B.Sc. in human nutrition and dietetics and a Ph.D. in human nutrition from the University of Dublin, Trinity College, Ireland. Her research focused on the development and validation of a food frequency questionnaire to assess dietary intake of fatty acid, as well as an assessment of the acute postprandial effects of hydrogenated fat compared with alternative fats used by the food industry. Currently, her main interests include dietary assessment methodology and biological markers of dietary intake. She is located in EPS/7045 and can be reached at 301-594-7905.


Ms. Annette Cunningham

Ms. Annette Cunningham, who had worked as an office automation assistant in the Biostatistics Branch since 1988, left in June to take a position at the Uniformed Services University of the Health Sciences. As a valued member of the support staff, Ms. Cunningham provided many services to the Branch and Division. This year she received an award for her work on the Combined Federal Campaign.


Dr. Mohamed Eltom

Mohamed Eltom, M.D., has joined the Viral Epidemiology Branch as a postdoctoral fellow. Dr. Eltom was trained in medicine at Juba University in Khartoum, Sudan. Before coming to DCEG, he was a project coordinator with the Johns Hopkins University project on perinatal HIV research at Queen Elizabeth Central Hospital in Malawi. There he helped manage clinical studies on the efficacy of antiretroviral drugs in preventing mother-to-infant HIV transmission, as well as studies of mastitis and HIV transmission. At DCEG, Dr. Eltom will be collaborating with Dr. Robert Biggar, Dr. Denise Whitby, and others to establish a repository of tumor tissues suitable for exploring new viruses. He is also interested in studying human herpesvirus 8 transmission in Africa. Dr. Eltom is located in EPS/8015 and can be reached at 301-435-4721.


Dr. Ahmedin Jemal

Ahmedin Jemal, D.V.M., Ph.D., who started work in the Biostatistics Branch as a fellow in 1998, left in late May to take a new position as Program Director for Cancer Surveillance at the American Cancer Society in Atlanta. Dr. Jemal worked with Dr. Susan Devesa and other members of DCEG, and during his stay at DCEG he published several descriptive articles on lung cancer, melanoma, retinoblastoma, and other cancers.


Dr. Zhaohai Li

Zhaohai Li, Ph.D., will be a visiting scientist in the Biostatistics Branch until early 2002 while on sabbatical from George Washington University's Biostatistics Center. Dr. Li will work to improve sib-pair identity-by-descent methods to detect genetic links to disease. He will also extend the transmission disequilibrium test based on parent-child triads to quantitative traits that have been dichotomized.


Dr. Roxana Moslehi

Roxana Moslehi, Ph.D., M.Sc., has joined the Genetic Epidemiology Branch as a visiting fellow in the Cancer Genetics and Epidemiology Training Program. She recently received a Ph.D. from the Department of Medical Genetics, University of British Columbia, Vancouver. Before that, she obtained an M.Sc. in medical genetics from the University, with an emphasis on cancer genetics. For her doctoral thesis project, she estimated the frequency and penetrance of the three founder *BRCA1* and *BRCA2* mutations among Jewish women with ovarian cancer according to histologic type. Dr. Moslehi also evaluated a variety of factors modifying the risk for tumors associated with these mutations. She is located in EPS/7002 and can be reached at 301-594-7648.


Ms. Stephanie Mulherin

Stephanie Mulherin, M.S.P.H., joined the Viral Epidemiology Branch as a predoctoral fellow. She received her M.S.P.H. in epidemiology, with a concentration in infectious

diseases, from the University of North Carolina at Chapel Hill, where she is enrolled in the Ph.D. program. For her master's thesis, Ms. Mulherin used enzyme immunoassay data to analyze the spectrum effect in the diagnosis of *Chlamydia trachomatis*. She has a strong interest in diseases that may be related to polymorphisms in the genes encoding cytokines, such as tumor necrosis factor alpha and the interleukins. Under the supervision of Dr. Charles Rabkin, she will work with several other Branch investigators through July. Ms. Mulherin is located in EPS/8011 and can be reached at 301-435-4730.


Ms. Barbara Rogers

In April, **Ms. Barbara Rogers** joined the Genetic Epidemiology Branch as an epidemiology program specialist. Previously, she was a management analyst in the Quality Management Department at the Veterans Affairs Medical Center in Washington, DC. Prior to that she worked as a consultant and senior project manager in health care for both the public and private sectors. Ms. Rogers is located in EPS/7002 and can be reached at 301-594-7665.


Ms. Tawanda Roy

Ms. Tawanda (Tee) Roy joined the Nutritional Epidemiology Branch in February as a program assistant. Previously, Ms. Roy worked at the Food and Drug Administration as a technical information assistant. She has completed the lead user program and is now certified as a Microsoft Office user specialist. She is located in EPS/7033 and can be reached at 301-594-7924.


Dr. Mark Sherman

Mark Sherman, M.D., recently joined the Environmental Epidemiology Branch as an NCI expert. Dr. Sherman has an M.D. from the University of Chicago and further residency and fellowship training in pathology from New England Deaconess Hospital, Harvard Medical School, and Montefiore Medical Center. As an associate professor in the Departments of Gynecology and Obstetrics and Oncology at the Johns Hopkins University School of Medicine, he has collaborated with DCEG for a number of years. Dr. Sherman's unique insights into pathology, clinical issues, and epidemiology will enhance the biologic perspective and approach to studies throughout the Division. Although he will focus his research on breast and gynecologic cancers, he will be available to consult and train others in the Division on a number of issues relevant to the integration of pathology and epidemiology. He is located in EPS/7080 and can be reached at 301-594-7661.


Dr. Rachael Stolzenberg-Solomon

Rachael Stolzenberg-Solomon, Ph.D., M.P.H., joined the Nutritional Epidemiology Branch as a cancer prevention fellow. She has a B.S. in dietetics from the University of California at Davis, dietetic internship training at Vanderbilt University Medical Center, and an M.P.H. and Ph.D. in epidemiology from the Johns Hopkins University School of Hygiene and Public Health. She has worked for a number of years as a clinical dietitian. She did her Ph.D. work, which focused on indicators of methyl-group availability and pancreatic cancer, as a Cancer Research Training Award (CRTA) predoctoral fellow in the Cancer Prevention Studies Branch in the Division of Clinical Sciences. Dr. Stolzenberg-Solomon has been in the Cancer Prevention Fellowship Program since July 1999. Her interests are gastrointestinal cancers (primarily pancreatic and esophageal cancers) and colorectal polyps. She has been working with Drs. Demetrius Albanes, Steven Mark, and Rashmi Sinha. She is located in EPS/7039 and can be reached at 301-594-2939.


Dr. Wei-Cheng You

Wei-Cheng You, M.D., left the Biostatistics Branch in June to assume his new positions as Director of the Beijing Institute for Cancer Research and Dean of the School of Oncology, Peking University. Dr. You arrived at DCEG in 1990 as a visiting scientist and became a principal investigator in 1997. His research focused on gastric cancer, and he played a central role in the Shandong Intervention Trial, which is testing the effectiveness of various supplements in reversing premalignant changes in the stomach. ■

FAREWELL TO *DCEG LINKAGE* MANAGING EDITOR

Michelle Renehan, the *DCEG Linkage* Managing Editor since 1998, is leaving DCEG for a position as an Administrative Officer in NCI's Center for Cancer Research. We are grateful for the quiet excellence that Ms. Renehan brought to the myriad tasks involved in overseeing the production of this newsletter.

Ms. Renehan holding a page proof of this issue.

CHAMPIONS RECOGNIZED

Recently, the "champions" who have worked to help Richard Klausner, M.D., create the Extraordinary Opportunities component of the 2002 Bypass Budget were recognized for their contributions. The plan, with its associated budget proposal, has been a centerpiece of Dr. Klausner's successful efforts to highlight the importance of enhanced support for cancer research in an era when new tools (e.g., molecular biology, informatics, genetics) and new approaches have provided dramatic insights into the fundamental nature of cancer. Neil Caporaso, M.D., was a co-champion for "Research on Tobacco and Tobacco-related Cancers," while Robert Hoover, M.D., Sc.D., and Kenneth Buetow, Ph.D., were co-champions for "Genes and the Environment." Each received a plaque and a photo of themselves along with Dr. Klausner and the other champions set on the background of a *Wheaties* box portraying the champion theme.