DCEG Linkage

Division of Cancer Epidemiology and Genetics

National Cancer Institute

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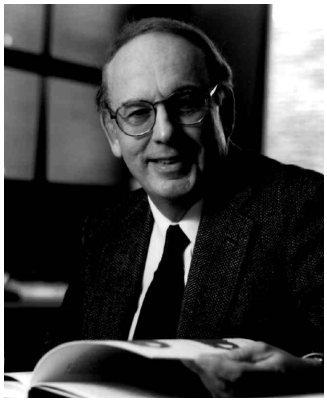
DIRECTOR'S PAGE

Mentoring on the Move

The primary motivation for becoming a good mentor is the natural human inclination to share knowledge and experience, according to the National Academy of Science's publication *Advisor, Teacher, Role Model, Friend: On Being a Mentor to Students in Science and Engineering* (copies available in my office). In addition, mentors enjoy the satisfaction of having a fellow succeed and become a friend and colleague. There is also the benefit of working with younger scientists to help mentors stay on top of a fast-breaking field and extend their own contributions. Finally, good mentoring is important in attracting and recruiting fellows of the highest caliber to participate actively in our research projects.



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

During the past year, NCI and NIH have been developing strategies to improve the quality of mentoring of predoctoral and postdoctoral scientists. In DCEG, we have already taken steps to improve communications between fellows and supervisors and to clarify the Division's position on career advancement within our intramural research program (see "On Postdoctoral Career Progression," p. 2). Because fellows are integral members of our larger research program, their intellectual contributions to projects are vital and deserve prompt feedback and suitable recognition. Mentors must therefore provide fellows with a candid evaluation of their progress and with guidance on career development through regular meetings and annual written assessments.

To ensure that fellows have a successful training experience during their time with us, it is essential that they receive sufficient opportunities and resources to carry out their research projects. New research directions and career shifts can arise when astute mentors identify skills and potential that a fellow may not be completely aware of. In addition, fellows should not be limited to advice from a single mentor, but should be encouraged to broaden their perspective by seeking guidance from other scientists in the Division. By providing a nurturing work environment, mentors can have an enormous impact on the productivity and career advancement of fellows, and can open doors for collaborative interactions and professional opportunities inside and outside NCI.

Ms. Joanne Colt is preparing a *DCEG Fellows Handbook*, which will help orient fellows when they join the Division. The handbook will provide information on a

variety of topics related to the practical aspects of conducting research. Fellows and their mentors also will benefit from a forthcoming NIH publication, *Guidelines for Training and Mentoring in the Intramural Research Program at NIH*. Prepared by Dr. Michael Gottesman, NIH Deputy Director for Intramural Research, with the assistance of the Scientific Directors, the booklet articulates expectations for the research training experience at NIH.

Recognizing that effective mentoring is not always an innate skill, DCEG's next goal is to help our scientific staff members improve their abilities in this area. As one means, we are planning a series of seminars by outside investigators who have a record of achievement as mentors. Mentoring will also be evaluated during annual performance reviews of each scientist, as well as at site visit reviews of tenured and tenure-track investigators. These evaluations will help us assess how well we as a Division are doing as mentors, and where we need to improve. Skilled mentors will not only be recognized through the evaluation process, but also by the fellows themselves. In 1997, the Division instituted an annual Outstanding Mentor Award, the recipient of which is selected by the fellows.

A primary goal of mentoring is to develop the next generation of scientists. An equally important goal is to maintain the vitality of our research program. It is thus to everyone's benefit to ensure that fellows have a successful experience as part of DCEG's research team. Homer described the original Mentor as a "wise and trusted counselor" who was placed in charge of the household by Odysseus during his travels. All of us must strive to be wise and trusted counselors to the training fellows working with us as they launch their scientific careers. ■

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Editor
Michelle Renehan renehanm@mail.nih.gov

DCEG Linkage Contacts
Administrative Resource Center
Mary Jude Jacobs
Biostatistics Branch
B.J. Stone
Committee of Scientists
Sholom Wacholder
DCEG Representatives to the NIH Fellows' Committee
Frank Groves and Sandra Petralia
DCEG Representative to the NIH pre-IRTA Committee
Rebecca Schiller
DCEG Representative to the NIH Women Scientists Advisory Group
Alisa Goldstein
Environmental Epidemiology Branch
Catherine Schairer
Genetic Epidemiology Branch
Mary Fraser
Nutritional Epidemiology Branch
Stephanie Weinstein
Occupational Epidemiology Branch
Ifetayo White
Office of Division Operations and Analysis
Michelle Renehan
Radiation Epidemiology Branch
Ruth Kleinerman
Research Contracts Branch
Sharon Miller
Viral Epidemiology Branch
Jim Goedert

MESSAGE FROM ODOA

On Postdoctoral Career Progression

Career progression of postdoctoral fellows was one of the major topics discussed at July's retreat of the DCEG Senior Advisory Group (SAG). Of particular concern were ways to ensure that progress and expectations are clearly communicated to fellows by their supervisors, and that fellows understand opportunities for career advancement within the Division. After the retreat, members of DCEG's leadership met to develop a formal policy with respect to these concerns. The policy was presented and approved at the October meeting of SAG, and is now incorporated into the Division's "Operating Philosophy and Principles," which can be accessed at DCEG's intranet site (*http://intranet-dceg.ims.nci.nih.gov/index.html*).

The Division's policy regarding postdoctoral fellows is based on the philosophy and requirements under which DCEG, NCI, and NIH operate with respect to these appointments. The NIH policy concerning postdoctoral fellows and tenure-track is as follows:

"The primary purpose of an NIH fellowship or clinical associateship is to provide time-limited research training and development opportunities to postdoctoral scientists. It is anticipated that, upon completion of their fellowship, the vast majority of all fellows will leave NIH to pursue careers at extramural institutions. The tenure-track has been created to provide an opportunity for outstanding postdoctoral scientists trained inside and outside the NIH Intramural Research Program to prove themselves as independent scientists and to compete for permanent positions as tenured independent investigators."

Some of the key elements of the Division's new policy are noted below.

- Supervisors (i.e., mentors) should meet at least every 6 months with each fellow to discuss performance and future plans. One of the meetings should be held in anticipation of the Division's annual personnel review, which usually occurs in early spring. After this meeting but before the personnel review, supervisors should provide each fellow with a candid written evaluation of the fellow's performance and goals for the coming year.

- If different from the supervisor, the Branch or Laboratory Chief should meet at least annually with each fellow to discuss the fellow's research program and other career-related issues.

- Postdoctoral fellows may compete for tenure-track positions at any time during their appointment, and they are considered on the basis of their record of accomplishment and potential for growth as an independent investigator.

- All tenure-track recruitments are fully open to all eligible investigators, regardless of their affiliation or duration of postdoctoral experience.

- Tenure-track investigators are evaluated by the Branch or Laboratory Chief or another reviewer designated by the Division Director. The reviewer meets annually with each tenure-track investigator to candidly discuss performance, expectations, and potential to achieve tenure, followed by a written evaluation addressing the following elements: (1) A focused and critical assessment of the scientific achievements of the investigator during the year under review, (2) a description and assessment of the investigator's research plans for the new year, plus an evaluation of the ability to meet the goals set forth in the individual's independent research program, and (3) a recommendation as to continuation of tenure-track.

- A recommendation for tenure may occur at any time during the period of tenure-track. ■

1998 Award for the Outstanding Research Paper by a Fellow

The award for the Outstanding Research Paper of the Year by a DCEG Fellow was established by the Division in 1997. This award honors a postdoctoral or predoctoral fellow for the best research paper published during the past calendar year. The winning paper is selected for its impact, innovation, and clarity of thought and language. The winner of the 1997 award was Dr. Lea Harty. (Harty LC, Caporaso NE, Hayes RB, Winn DM, Bravo-Otero E, Blot WJ, Kleinman DV, Brown LM, Armenian HK, Fraumeni JF, Shields PG. Alcohol dehydrogenase 3 genotype and risk of oral cavity and pharyngeal cancers. *J Natl Cancer Inst* 1997;89:1698-1705)

Eligibility criteria for the award are:

- The fellow must be the lead author;

- The paper must be based on research conducted while the author was a fellow within DCEG;

- The paper must be based on research supported by DCEG; and

- The paper must have appeared in print during the past year.

The publications are identified and submitted to the Office of Division Operations and Analysis in January by the DCEG Branch and Laboratory Chiefs. These papers are provided to the DCEG Senior Advisory Group members, who select the winning publication by secret ballot at their February meeting. The winner receives a plaque and a $1,000 cash award. ■

1998 DCEG Outstanding Mentor Award

In 1997, the Division established an annual award to honor the scientist deemed the most outstanding mentor by the DCEG fellows. Nomination of an

award candidate may be made by any fellow working in the Division at some time during the year. Any DCEG scientist (tenured investigator, tenure-track investigator, or staff scientist) who interacts with a fellow in any type of mentoring capacity is eligible for the award. Ascientist does not have to be the "official mentor" to be a candidate for the award.

The process for selecting the winner of the Outstanding Mentor Award is overseen by Ms. Joanne Colt, the DCEG Fellowship Coordinator, and involves the following:

- Nominations are submitted to Ms. Colt in December.
- Each fellow may nominate up to two DCEG scientists for the award. Award nominations should describe the fellow's relationship to the nominee and the rationale supporting the submission.
- During the first 2 weeks of January, fellows are invited to Ms. Colt's office to read the material supporting each nominee and to vote for the outstanding mentor.
- Votes are tabulated by Ms. Colt, and the award winner is announced by the end of January.

The winner of the Outstanding Mentor Award receives a plaque and a $3,000 Special Act Cash Award. Additional information about the award can be accessed at the Division's intranet site at *http://intranet-dceg.ims.nci.nih.gov/index.html.* ■

Student Loan Repayment Program

Several DCEG staff members have successfully competed for the NIH student loan repayment program (LRP). The LRP is designed to help defray the debt that is often part of graduate education. Open to persons with postdoctoral degrees, the LRP is composed of (1) the AIDS LRP, geared toward AIDS research, (2) the Clinical Research LRP, designed to attract physicians from disadvantaged backgrounds, and (3) the General Research LRP, aimed at highly qualified physicians and scientists. LRPs pay lending institutions up to $20,000 per year toward outstanding educational debts. Participants must agree to conduct research at NIH for a minimum of 2–3 years. To qualify for an LRP, an applicant must have an educational debt in excess of 20 percent of his or her annual NIH salary. More information can be obtained by calling 1-800-528-7689 or by visiting the web site *http://www.training.nih.gov/postdoctoral/loanrepay.html.* ■

DCEG Summer Internship Program

The DCEG Summer Internship Program is committed to supporting students interested in exploring careers in cancer epidemiology and genetics. It is open to high school, college, and graduate students. Successful applicants join the Division for at least 8 weeks between June and August. Under supervision, interns conduct research in selected areas of epidemiologic or laboratory investigation. Students are encouraged to attend lectures in the Summer Seminar Series, participate in DCEG meetings and seminars, attend formal NIH lectures and symposia, and participate in the Summer Research Program Poster Day. Students interested in applying to this program should send a cover letter indicating interests relevant to the Division's research mission, along with a curriculum vitae, to Ms. Michelle Renehan, Summer Internship Coordinator, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Executive Plaza North, Room 543, Bethesda, MD 20892-7399. ■

Jim Sontag and Michelle Renehan

THE NEW WHO AND PARTNERSHIPS FOR THE FUTURE

DCEG and the Office of the NIH Director sponsored a special lecture on October 29 by Dr. Gro Harlem Brundtland, Director-General of the World Health Organization (WHO). She spoke on "The New WHO and Partnerships for the Future," in which she stressed the importance of partnerships between WHO, NIH, and other public and private biomedical institutions in the United States and around the world. Dr. Brundtland was Prime Minister of Norway for 10 years. She stepped down from the post in 1996 and was elected Director-General of WHO last May. This was the first time that a Director-General of WHO has visited NIH.

A reception with poster presentations followed Dr. Brundtland's lecture. Ms. Linda Morris Brown

Joseph F. Fraumeni, Jr., M.D., and Gro Harlem Brundtland, M.D.

(Biostatistics Branch) presented "A randomized multi-intervention trial to inhibit precancerous gastric lesions in Shandong, China." She outlined a collaborative, randomized, multi-intervention trial with the Beijing Institute for Cancer Research to evaluate *Helicobacter pylori* antibiotic treatment, garlic extract, and certain micronutrient supplements in preventing the development of gastric cancer. In addition, Dr. Wong-Ho Chow (Occupational Epidemiology Branch) presented "The Shanghai women's cohort study." She described a prospective, population-based cohort study of 75,000 Chinese women and their husbands, which was recently initiated to examine dietary, hormonal, and other risk factors of cancer.

Dr. Mark Schiffman (Environmental Epidemiology Branch) presented "The success of NCI–IARC collaborative work to understand and prevent cervical cancer." He outlined the collaborations between NCI and the International Agency for Research on Cancer (IARC), which have confirmed that most cases of cervical cancer worldwide are caused by persistent infection with oncogenic types of human papillomavirus (HPV). NCI and IARC continue to collaborate on natural history and prevention studies to develop a vaccine against HPV. In addition, Dr. Angela Manns (Viral Epidemiology Branch) presented "Frequency of antibodies to human herpes virus type 8 (HHV-8) in multiple myeloma and B-cell non-Hodgkin's lymphoma in Jamaica and Trinidad." She summarized results from a study of seroprevalence of HHV-8 among incident cases and controls enrolled in parallel case-control studies. The data suggest that HHV-8 is not associated with multiple myeloma, but may play a role in the etiology of non-Hodgkin's lymphoma.

Dr. Richard Hayes (Occupational Epidemiology Branch) and Dr. Martha Linet (Radiation Epidemiology Branch) presented "Benzene and cancer risk in China." In a cohort study of benzene-exposed workers, the risks of nonlymphocytic leukemia, myelodysplastic syndromes, and non-Hodgkin's lymphoma increased with increasing exposure to benzene, but the temporal patterns of benzene-associated conditions appeared to be disease-specific. In addition, Ms. Gloria Gridley (Biostatistics Branch) presented the question "Is there a healthy worker effect for cancer incidence among women in Sweden?" She compared cancer incidence rates for women who reported employment in both the 1960 and 1970 Swedish censuses with those who reported no employment in either census. Employed women had a slightly higher overall cancer incidence in the follow-up period (1971–89), with a 20 percent increased risk of cancers of the lung and bladder and a 10 percent increased risk of reproductive cancers. There was no evidence of a healthy worker effect that introduces a bias in most occupational cohort studies. ■

ASTUTE CLINICIAN LECTURE

On October 15, J. Bruce Beckwith, Professor of Pediatric Pathology at Loma Linda University, gave the first Astute Clinician Lecture, which honors a scientist whose research began with an unusual clinical observation and, through subsequent laboratory studies, opened a new area of investigation.

In 1963, Dr. Beckwith, a resident in Pathology at Los Angeles Children's Hospital, saw a child who had died of congenitally large abdominal organs, a huge umbilical hernia due to the overcrowded abdominal cavity, and a large tongue. He then found two similar cases among the records at the hospital. Dr. Hans Wiedemann independently described the syndrome the following year in Kiel, Germany. Sometimes seen in this disorder, now known as Beckwith-Wiedemann syndrome (BWS), is an overgrowth of a segment of the body (hemihypertrophy).

Laboratory studies focused on three lines of research. First, the gene was mapped to chromosome *11p15*, the locus for insulin-like growth factor 2, a product that may be associated with bodily overgrowth. The second line of research revealed that BWS involves genomic imprinting, a newly identified genetic mechanism. Normally the maternal gene for BWS is silent because of imprinting, and the child is unaffected. When the silence of the gene is broken before conception, BWS occurs. The syndrome also

Ms. Nancy Browning (wife of Dr. Beckwith), Dr. Robert W. Miller, Dr. J. Bruce Beckwith, Dr. John Gallin (Director of the Warren Grant Magnuson Clinical Center), and Mrs. Robert W. Miller after the Astute Clinician Lecture.

occurs when the maternal gene remains silent, but the paternal gene is duplicated through a biological error.

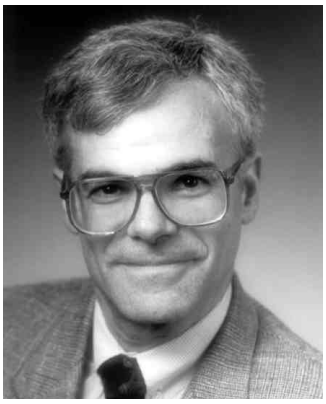
Dr. Beckwith pursued a third line of research involving Wilms tumor, which is the most frequent of the childhood cancers that occur excessively in BWS. Coincidentally, the National Wilms Tumor Study (NWTS) registry had been initiated in 1969 to track the tumor's response to therapies and late effects of the disease. The registry covers about 85 percent of cases in the United States, and now contains data on almost 9,000 cases. The pathology for each case was reviewed by Dr. Beckwith, who found that more than 500 were misdiagnosed as Wilms tumor and were actually other neoplasms—some previously unknown and more malignant than Wilms tumor, and others benign.

Dr. Beckwith found that Wilms tumor arises from abnormally persistent clusters of renal embryonal cells (nephrogenic rests). These rests seem to represent the second step in Knudson's two-step mechanism of carcinogenesis involving tumor suppressor genes. The type of Wilms tumor that occurs with congenital absence of the iris (aniridia) is associated with the *WT-1* gene and generally originates *within* the lobes of kidney tissue. The type of Wilms tumor associated with BWS (*WT*-2 gene) commonly arises at the *periphery* of the renal lobes. For more than 20 years, it has been known that Japanese children have half the rate of Wilms tumor found in Caucasian children. The reason, based on Dr. Beckwith's studies, is that Asian children have a near absence of tumors with perilobar precursor lesions. The two forms of Wilms tumor, which look alike at the bedside, arise from teratogenic precursor lesions that differ at the molecular, histologic, and epidemiologic levels.

With Dr. Beckwith's retirement in 1999, the NWTS Pathology Center will be moved to the Johns Hopkins Division of Pediatric Pathology in the Department of Pathology.

The annual Astute Clinician Lecture is supported by a gift from Dr. and Mrs. Robert W. Miller. Dr. Miller holds the title of NIH Scientist Emeritus, and is located in the Genetic Epidemiology Branch of DCEG. Please contact Dr. Miller (301-496-5785) if you would like to nominate a candidate for next year's lecture. Candidates may come from any area of clinical investigation. ■

DCEG TOWN MEETING WITH DR. GOTTESMAN



Michael Gottesman, M.D.

Dr. Michael Gottesman, NIH Deputy Director for Intramural Research, was the guest of the DCEG Committee of Scientists at a town meeting on September 24. He spoke about tenure and promotion policy, recruitment, and the fellowship program at NIH. Some of the topics he covered were:

- The different personnel systems at NIH and the opportunities provided by some of them for salaries above those allowed by the Civil Service system;
- The new NIH tenure policy and the commitment to salary and research support that tenure entails;
- NIH's commitment to postdoctoral fellows to provide the best possible training;
- Mentoring as an essential element of the training program; and
- NIH's commitment to uphold agreements with tenure-track investigators in providing resources to maximize their chance of success.

Summarized below are Dr. Gottesman's responses to some of the subjects raised during the question period following his presentation.

- Of 100 tenure-track searches, about half were filled from within the branch or laboratory, and approximately two-thirds of the other half came from outside NIH. Since NIH trains about 15 percent of NIH-supported postdocs, Dr. Gottesman considers about one-third as the ideal fraction of new tenure-track positions from the outside. About 150 scientists were grandfathered into tenure-track in 1994.

- Scientists are not guaranteed a staff scientist or tenure-track position at NIH on completing a postdoctoral appointment. Dr. Gottesman noted that there are about 2,500 postdocs and 30 tenure-track openings each year, and there is no quota for the number of tenure-track scientists that can be tenured from within an institute.

- In Dr. Gottesman's view, with few exceptions, salaries at NIH are competitive with the extramural community. Title 42 provides a mechanism to provide higher salaries for postdocs in exceptional circumstances, but such positions require an FTE.

- Dr. Gottesman stressed the importance of collaboration. In collaborative efforts, investigators need to carve out a niche, so their individual contributions are recognized by their peers at meetings and in publications. Dr. Gottesman believes that developing social skills is important to effectively network with colleagues.

- The extension of tenure-track to 8 years for scientists involved in population-based studies is prospective. Since it does not automatically apply to current tenure-track scientists, modification of their tenure-track agreement beyond 6 years would be necessary if additional time is needed. ■

Sholom Wacholder

GENETIC INFLUENCES ON SMOKING BEHAVIOR

Despite widespread knowledge of the health consequences of cigarette smoking, almost 26 percent of Americans older than age 17 smoke. Efforts to quit smoking have a poor success rate (about 10 to 15 percent), so a better understanding of the underpinnings of smoking dependency may be key to strategies to prevent smoking and reduce smoking-related diseases.

Smoking results in the release of neurotransmitters, including beta-endorphin, dopamine, serotonin, and norepinephrine. The release of beta-endorphin is associated with reduced anxiety and tension, whereas release of dopamine and norepinephrine result in smoking-related stimulation. The release of this mix of neurotransmitters helps to explain one of the apparent paradoxes of smoking: Smokers report feeling more relaxed and composed after smoking, yet exhibit increased heart rate, blood pressure, and constriction of blood vessels (resembling the "fight or flight" response). Unfortunately, all these factors work against efforts to quit smoking, particularly among persons with depression. In earlier work led by Dr. Caryn Lerman (Lombardi Cancer Center, Georgetown University), we showed that a substantial proportion of smokers experience depression and use nicotine to "reduce negative affect." (Lerman C, Audrain J, Orleans CT, Boyd R, Gold K, Main D, Caporaso N. Investigation of mechanisms linking depressed mood to nicotine dependence. *Addict Behav* 1996;21:9-19) Nicotine withdrawal is particularly tough on depressed persons, and they are unlikely to successfully quit smoking without attention to these conditions.

Findings from twin studies suggesting an hereditary component to smoking encouraged us in the early 1990's to pursue studies to explore associations between candidate genes and smoking habits. We established a collaboration with Dr. Lerman and Dr. Peter Shields (Laboratory of Human Carcinogenesis, Division of Basic Sciences) in which we assembled a group of smokers enrolled in a smoking cessation clinic and matched them to nonsmokers on age, race, and gender. Our first work involved *CYP2D6*, a gene inherited in different forms in the general population and originally thought to be involved in the metabolism of nicotine. Our studies demonstrated that nicotine elimination does not differ between persons with the functional version of the gene and

those without it. This finding and other evidence reduce the putative importance of this gene in influencing smoking habits.

We then focused on polymorphisms involving dopamine, a neurotransmitter that may be responsible for the reinforcing properties of nicotine. Numerous genes influence the disposition of nicotine, including ones that code proteins for dopamine transport (*SLC6A3*) and various dopamine receptors (e.g., *DRD2, DRD4*). In a group of 230 smokers and 230 nonsmokers matched on race, we observed that subjects with the *SLC6A3-*9* variant of the dopamine transporter (present in about one-half the population) were less likely to be smokers (P=0.03). We also observed that among the smokers, persons with this genotype had significantly longer quit periods (480 days vs. 233 days, P=0.05), but no significant difference in age at initiation of smoking or in smoking intensity. The *DRD2* gene has been previously studied in relation to smoking and to psychiatric disorders, such as alcoholism and compulsive gambling. We found no association of this gene with smoking, but interestingly, there was an interactive effect, as persons having both variants *DRD2-A2* and *SLC6A3-*9* had only half the risk of being smokers. These findings will appear in the January issue of *Health Psychology*, (Lerman C, Caporaso N, Main D, Audrain J, Bowman ED, Lockshin B, Boyd NR, Shields PG. Genetic risk factors for smoking) along with a companion piece with a similar finding involving the *SLC6A3* gene and an editorial on this topic.

Although these results require confirmation, it is certain that future attention will focus on identifying genes that account for smoking habituation. It was shown recently that persons receiving bupropion (Wellbutrin), a selective dopamine reuptake inhibitor, had significantly greater success at smoking cessation. (Hurt RD, et al. Acomparison of sustained-release bupropion and placebo for smoking cessation. *N Engl J Med* 1997;337:1195-1202) This antidepressant drug works by inhibiting the transport of dopamine from the synapse, thus increasing the level of synaptic dopamine available for neurotransmission. The drug may be effective through its relief of the underlying depression or through action on the dopamine transporter gene. Regardless, it is noteworthy that a gene that influences smoking behavior might also influence smoking-related disease. In the Genetic Epidemiology Branch, Dr. Andrew Bergen, Dr. Maria Teresa Landi, and I are currently developing study designs to explore these questions. ■

Neil Caporaso

SCIENTIFIC HIGHLIGHTS

Biostatistics Branch

Kin-cohort Method of Analysis

The kin-cohort method was devised as a means for quickly estimating penetrance of an autosomal dominant gene within a population-based setting, rather than from high-risk families. It was first used to estimate the risk of cancer among Jewish carriers of breast cancer susceptibility genes in the Washington, DC, area. (Struewing JP, Hartge P, Wacholder S, Baker SM, Berlin M, McAdams MS, Timmerman BS, Brody LC, Tucker MA. The risk of cancer associated with specific mutations of *BRCA1* and *BRCA2* among Ashkenazi Jews. *N Engl J Med* 1997;336:1401-1408) In this study, a 63 percent risk was estimated for first occurrence of breast or ovarian cancer by age 70 among carriers of three specific *BRCA1* and *BRCA2* mutations common in this eastern European Jewish population. The risk estimates were much higher than in noncarriers, but lower than estimates based on high-risk families. The details of the kin-cohort approach, with its strengths and limitations, have been described in a recent paper. (Wacholder S, Hartge P, Struewing, JP, Pee D, McAdams M, Brody L, Tucker M. The kin-cohort study for estimating penetrance. *Am J Epidemiol* 1998;148:623-630)

The Washington, DC, Ashkenazi study was also used recently to evaluate the effect of a distinctive *APC* gene mutation (*I1307K*), which is relatively common in this population group, on the risk of cancer. Modestly increased risk of breast and colorectal cancers was seen among carriers. (Woodage T, King SM, Wacholder S, Hartge P, Struewing JP, McAdams M, Laken SJ, Tucker MA, Brody, LC. The *APC I1307K* allele and cancer risk in a community-based study of Ashkenazi Jews. *Nat Genet* 1998;20:62-65) In Iceland, the kin-cohort method was used to estimate gene penetrance among carriers of a founder *BRCA2* mutation. This study relied on data from population-based cancer registries, rather than reports from volunteers, thus reducing opportunities for biased estimates of risk. Results of this study are described below under the Genetic Epidemiology Branch.

Changing Patterns in the Incidence of Esophageal and Gastric Carcinoma

Data from the Surveillance, Epidemiology, and End Results (SEER) program were used to calculate age-

adjusted incidence rates for esophageal carcinoma by histologic type and for gastric adenocarcinoma by anatomic subsite through 1994. Among white males, the incidence of esophageal adenocarcinoma increased more than 350 percent since the mid-1970's, and now surpasses the incidence of squamous cell carcinoma. Rates have also risen among black males, but at much lower levels. To a lesser extent, the incidence of gastric cardia adenocarcinoma increased steadily among white males, to nearly equal the rate for noncardia tumors of the stomach, and among black males. The upward trend for both tumors was much greater among older than younger males. Although incidence also rose among females, the rates were much lower than those among males. Cigarette smoking may contribute to the continuing upward trend of these tumors through an early-stage carcinogenic effect, and obesity may contribute through increasing intra-abdominal pressure and predisposing to gatroesophageal reflux disease. (Devesa SS, Blot WJ, Fraumeni JF Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer* 1998:83:2049-2053)

Helicobacter Pylori Infection and Mode of Transmission

In a study of *H. pylori* infection and mode of transmission in Linqu County, a high-risk area of gastric cancer in China, the prevalence rate of infection varied as a function of age, rising from about 50 percent at ages 3 to 4 to 85 percent at ages 9 to 10, before falling to 67 percent at ages 11 to 12. Sixty-eight percent of adults were *H. pylori* positive, with a somewhat higher rate of positivity in younger than in older age groups. In families with at least one infected parent, 85 percent of children were *H. pylori* positive, whereas in families with both parents uninfected, only 22 percent of children were *H. pylori* positive. The patterns are consistent with person-to-person transmission of *H. pylori* infection between parents and very young children. (Ma JL, You WC, Gail MH, Zhang L, Blot WJ, Brown LM, Xu GW, Fraumeni JF Jr. *Helicobacter pylori* infection and mode of transmission in a population at high risk of stomach cancer. *Int J Epidemiol* 1998;27:570-573)

Thromboembolism and Risk of Cancer

Using Swedish national inpatient and cancer registries, a record-linkage study of 62,000 patients was carried out to clarify the relation between venous thromboembolism (VTE) and risk of cancer. Within the first year after VTE diagnosis, the standardized incidence ratio was 12.9 for polycythemia vera and greater than 5.0 for cancers of the liver, pancreas, ovary, and brain and for non-Hodgkin's lymphoma. After the first year, a 30 percent increase in cancer risk persisted over time, suggesting that premalignant change may predispose to VTE. (Baron JA, Gridley G, Weiderpass E, Nyrén O, Linet M. Venous thromboembolism and cancer. *Lancet* 1998;351:1077-1080)

Trends in HIV Incidence among Young Adults

Back-calculation analyses were used to study trends in HIV incidence and prevalence in persons born between 1960 and 1974. Among persons aged 20 to 25 years, HIV incidence from homosexual contact or injected-drug use decreased between 1988 and 1993, but this favorable trend was partially offset by increasing heterosexual transmission, especially in minority populations. (Rosenberg PS, Biggar RJ. Trends in HIV incidence among young adults in the United States. *JAMA* 1998;279:2894-2899)

Increased Hypermutation in Immunoglobulin Variable Genes

Novel methods were developed for analyzing mutational spectra of DNA repair genes in the process of hypermutation of immunoglobulin variable genes. Mutational spectra were examined in the *Ig* variable genes of knockout mice lacking the nucleotide excision repair gene *Xpa* and the mismatch repair genes *Pms2* and *Msh2*. The results suggest that an *MSH2*-dependent pathway preferentially corrects mismatches at *G* and *C* nucleotides, and that tandem substitutions are processed by a *Pms2*-dependent pathway. (Winter DB, Phung QH, Umar A, Baker SM, Tarone RE, Tanaka K, Liskay RM, Kunkel TA, Bohr VA, Gearhart PJ. Altered spectra of hypermutation in antibodies from mice deficient for the DNA mismatch repair protein *PMS2*. *Proc Natl Acad Sci USA* 1998;95:6953-6958; Phung QH, Winter DB, Cranston A, Tarone RE, Bohr VA, Fishel R, Gearhart PJ. Increased hypermutation at *G* and *C* nucleotides in immunoglobulin variable genes from mice deficient in the *MSH2* mismatch repair protein. *J Exp Med* 1998;187:1745-1751) ■

Environmental Epidemiology Branch

Use of Electric Blankets and Risk of Breast Cancer in Younger Women

A population-based case-control study investigated use of electric blankets (one of the largest sources of

electromagnetic field exposure in the home) and risk of breast cancer among newly diagnosed women under age 55 years. Little or no increased risk was associated with ever having used electric blankets, mattress pads, or heated water beds, and there was no substantial variation in risk with duration of use, menopausal status, hormone receptor status, or stage of disease. These data do not support an association between magnetic field exposure from electric blankets and breast cancer risk among women under age 55 years. (Gammon MD, Schoenberg JB, Britton JA, Kelsey JL, Stanford JL, Malone KE, Coates RJ, Brogan DJ, Potischman N, Swanson CA, Brinton LA. Electric blanket use and breast cancer risk among younger women. *Am J Epidemiol* 1998;148:556-563)

Risk of Maternal Breast Cancer in Relation to Pregnancy Characteristics

A large population-based case-control study assessed the relation of several pregnancy characteristics to risk of breast cancer. Information on pregnancies were obtained from 1,239 cases and 1,166 parous women under the age of 45. Women who reported nausea or vomiting in their first pregnancy had a slightly lower risk of breast cancer. No strong or consistent associations for increased risk were related to gestational length, pregnancy weight gain, gestational diabetes, pregnancy hypertension, or gender of the offspring. There was some evidence of protective effects for toxemia and specific aspects of twinning. These estimates were unaffected by adjustment for age at first birth, number of pregnancies, or other established breast cancer risk factors. These data provide little support for the hypothesis that pregnancy hormone levels, which affect some of the variables studied, are associated with subsequent maternal risk of breast cancer before age 45. (Troisi R, Weiss HA, Hoover RN, Potischman N, Swanson CA, Brogan DR, Coates RJ, Gammon MD, Malone KE, Daling JR, Brinton LA. Pregnancy characteristics and maternal risk of breast cancer. *Epidemiology* 1998;9:641-647)

Serum Levels of Organochlorine Pesticides and Polychlorinated Biphenyls and Risk of Breast Cancer

A nested case-control study was conducted to prospectively evaluate the relation of serum levels of organochlorine pesticides and polychlorinated biphenyls (PCBs) with risk of breast cancer. Women with hexachlorobenzene levels in the upper three quartiles had twice the risk of breast cancer compared with those in the lowest quartile. However, there was no evidence for a dose-response relationship, and the association was limited to women whose blood was collected close to the time of diagnosis. Women with higher serum levels of other organochlorine pesticides and PCBs showed no increased risk of breast cancer overall, although positive associations were suggested for PCB-118 and PCB-138 when blood was collected close to the time of diagnosis. Results of this study do not support a role for organochlorine pesticides and PCBs in the etiology of breast cancer. (Dorgan JF, Brock JW, Rothman N, Needham LL, Miller R, Stephenson HE, Schissler N, Taylor PR. Serum organochlorine pesticides and PCBs and breast cancer risk: Results from a prospective analysis. *Cancer Causes Control*, in press)

Serum Concentrations of Organochlorine Compounds and Risk of Endometrial Cancer

Serum concentrations of organochlorine compounds, which have estrogenic properties, were measured from a multicenter case-control study of endometrial cancer. The adjusted relative risk of endometrial cancer in the highest quartile of exposure compared with women in the lowest quartile was 0.7 for *p,p*-DDE and 0.9 for total polychlorinated biphenyls. These findings do not support an association between exposure to organochlorine compounds and risk of endometrial cancer. (Sturgeon SR, Brock JW, Potischman N, Needham LL, Rothman N, Brinton LA, Hoover RN. Serum concentrations of organochlorine compounds and endometrial cancer risk (United States). *Cancer Causes Control* 1998;9:417-424)

Human Leukocyte Antigen and Risk of Cervical Neoplasia

The host immune response to infection by human papillomavirus (HPV) is believed to be an important determinant of progression of HPV-associated cervical neoplasia. Human leukocyte antigen (HLA) is important in the presentation of foreign antigens to the immune system. A nested case-control study within a 24,000-woman cohort study in the United States was conducted to evaluate the association of HLA class I and class II alleles and risk of cervical neoplasia. Of 711 women studied, 141 were diagnosed with high-grade squamous intraepithelial lesions of the cervix, 202 were diagnosed with low-grade intraepithelial lesions, 166 had no history of cervical neoplasia but showed evidence of HPV-16

infection, and 202 had no history of cervical abnormalities and were HPV negative. DNA extracted from cervicovaginal lavage samples was used for HLA genotyping. The results support previous findings that *HLA B7* and *DQB1*0302* are positively associated with cervical neoplasia, and are consistent with studies suggesting that *DRB1*13* is negatively associated with disease, but do not confirm previous assertions that *DRB1*1501-DQB1*0602* increases the risk of cervical cancer. (Hildesheim A, Schiffman M, Scott DR, Marti D, Kissner T, Sherman ME, Glass AG, Manos MM, Lorincz AT, Kurman RJ, Buckland J, Rush BB, Carrington M. Human leukocyte antigen class I/II alleles and development of human papillomavirus-related cervical neoplasia: Results from a case-control study conducted in the United States. *Cancer Epidemiol Biomark Prev* 1998;7:1035-1041) ■

Genetic Epidemiology Branch

Risk of Breast Cancer in Carriers of a BRCA2 Mutation

Using the Icelandic Cancer Registry, a population-based study of 575 breast cancer patients (541 women and 34 men) was conducted to estimate the risk of cancer by comparing the cancer history of first-degree relatives having a common founder mutation *(999del5)* in the *BRCA2* gene with noncarriers. Ten percent of the women and 38 percent of the men were mutation carriers. The estimated risk of breast cancer for female carriers was 17 percent at age 50 and 37 percent at age 70. These results indicate that the mean risk of breast cancer in *BRCA2 999del5* carriers is lower than previously suggested from studies of high-risk families, and even from the Washington, DC, population survey of Ashkenazi Jews. Individual risk assessments need to consider family history and other risk factors in addition to mutation carrier status. (Thorlacius S, Struewing JP, Hartge P, Olafsdottir GH, Sigvalsdason, Tryggvadottir L, Wacholder S, Tulinius H, Eyfjörd, JE. Population-based study of risk of breast cancer in carriers of *BRCA2* mutation. *Lancet* 1998;352:1337-1339)

Von Hippel-Lindau Disease Germline Mutations among Affected Families

Von Hippel-Lindau disease (VHL) is a dominantly inherited disorder characterized by predisposition to clear cell renal cell carcinoma, pheochromocytoma, pancreatic neuroendocrine tumor, hemangioblastoma of brain and spine, retinal angiomas, endolymphatic sac tumor, and epididymal and broad ligament cystadenoma. After the VHL tumor suppressor gene was reported on chromosome *3p25-26* in 1993, germline mutations were detected in 39 to 75 percent of families affected by VHL. Using an expanded panel of tests, including additional combinations of enzymatic digests, it is now possible to identify germline mutations in virtually all families with VHL. This advance will significantly impact clinical management and counseling of families, and has implications for ongoing studies of molecular pathways in search of treatment and prevention modalities. (Stolle C, Glenn G, Zbar B, Humphrey JS, Choyke P, Walther M, Pack S, Hurley K, Andrey C, Klausner R, Linehan WM. Improved detection of germline mutations in the von Hippel-Lindau disease tumor suppressor gene. *Hum Mutat* 1998;12:417-423)

Familial Eosinophilia Maps to the Cytokine Gene Cluster

Familial eosinophilia is an autosomal dominant disorder with idiopathic hypereosinophilia with or without organ involvement. A genome-wide search of one large family provided evidence for linkage on chromosome *5q31-q33*. This region contains the cytokine gene cluster, including genes for interleukin 3, interleukin 5, and granulocyte/macrophage colony-stimulating factor, whose products play important roles in the development and proliferation of eosinophils. However, no mutations or polymorphisms were found in these cytokine genes, suggesting that the primary defect is caused by another gene locus in the area. (Rioux JD, Stone VA, Daly MJ, Cargill M, Green T, Nguyen H, Nutman T, Zimmerman PA, Tucker MA, Hudson T, Goldstein AM, Lander E, Lin AY. Familial eosinophilia maps to the cytokine gene cluster on human chromosomal region *5q31-q33. Am J Hum Genet* 1998;63:1086-1094) ■

Occupational Epidemiology Branch

Diet and Risk of Pancreatic Cancer

Despite numerous epidemiologic studies, the relation between diet and risk of pancreatic cancer remains unclear. On the basis of dietary histories and other interview data from 436 pancreatic cancer patients and 2,003 control subjects, obesity was associated with a 50 to 60 percent statistically significant increase in risk. Caloric intake also showed a statistically significant association with increased risk. Although the relative risk did not differ between white and black subjects, the greater prevalence of

obesity among blacks may explain their higher incidence of pancreatic cancer. The study also revealed a 50 percent decreased risk of pancreatic cancer associated with frequent consumption of cruciferous vegetables. (Silverman DT, Swanson CA, Gridley G, Wacholder S, Greenberg RS, Brown LM, Hayes RB, Swanson GM, Schoenberg JB, Pottern LM, Schwartz AG, Fraumeni JF Jr, Hoover RN. Dietary and nutritional factors and pancreatic cancer: A case-control study based on direct interviews. *J Natl Cancer Inst* 1998;90: 1710-1719)

Occupational Risk Factors of Breast Cancer

Using the Shanghai Cancer Registry and the Chinese Third National Census, a record-linkage study was carried out to explore the risk of breast cancer that may result from exposure to occupational and environmental factors. The study found elevated risk of breast cancer among women in several occupations, including those employed as rubber workers, exposed to organic solvents in general, or exposed to benzene. These findings suggest the need for further study of the role of environmental chemicals. (Petralia SA, Chow WH, McLaughlin J, Jin F, Gao YT, Dosemeci M. Occupational risk factors for breast cancer among women in Shanghai. *Am J Ind Med* 1998;34:477-483) ■

Radiation Epidemiology Branch

Rates of Thyroid Cancer and Nuclear Bomb Tests

With the use of incidence and mortality data for thyroid cancer in selected areas of the country, as well as recent information on the levels of I-131 exposure by county across the United States from the Nevada nuclear bomb tests, risks were not found to increase with cumulative dose received at ages 1 to 15 years. Associations were suggested for persons exposed when under 1 year of age and for those in the 1950–59 birth cohort. However, the number of cases is small and no causal relation could be inferred from these ecological data. (Gilbert ES, Tarone R, Bouville A, Ron E. Thyroid cancer rates and I-131 doses from Nevada atmospheric nuclear bomb tests. *J Natl Cancer Inst* 1998;90:1654-1660)

Chernobyl-related Thyroid Cancer among Children from Belarus

In 1986, the Chernobyl nuclear power plant accident released I-131 and other radioiodines that contaminated southern Belarus. This case-control study assessed the risk of thyroid cancer in children from exposure to these radioisotopes. Two sets of matched controls were used: one on the pathway for diagnosis and the other based on an area of heavy fallout. I-131 exposure to the thyroid was estimated from various sources, including ground deposition of Cs-137 and I-131 and data from thyroid radiation measurements made in 1986. Highly significant differences were observed between cases and both sets of controls with respect to estimated thyroid dose of I-131, providing strong evidence for the relation between increased risk of thyroid cancer in children from radioactive fallout from the Chernobyl accident. (Astakhova LN, Anspaugh LR, Beebe GW, Bouville A, Drozdovitch VV, Garber V, Gavrilin YI, Khrouch VT, Kuvshinnikov AV, Kuzmenkov YN, Minenko VP, Moschik KV, Nalivko AS, Robbins J, Shemiakina EV, Shinkarev S, Tochitskaya SI, Waclawiw MA. Chernobyl-related thyroid cancer in children of Belarus: A case-control study. *Radiat Res* 1998;150:349-356)

Risk of Skin Tumor among Atomic Bomb Survivors

Melanoma and nonmelanoma skin cancers in 80,000 atomic bomb survivors were studied to determine the effects of radiation on histologic types of skin cancer and to better describe the dose-response relationship. A clear excess of basal cell carcinoma was observed, with the risk decreasing as age at exposure increased. The risk was highest in parts of the body not generally exposed to ultraviolet radiation. There was no clear excess risk of other skin tumors associated with radiation exposure. These results suggest that the basal layer of the epidermis is quite sensitive to radiation carcinogenesis, particularly at a young age, but that the suprabasal layer is more resistant. (Ron E, Preston DL, Kishikawa M, Kobuke T, Iseki M, Tokuoka S, Tokunaga M, Mabuchi K. Skin tumor risk among atomic-bomb survivors in Japan. *Cancer Causes Control* 1998;9:393-401)

Risk of Childhood Leukemia and Use of Electrical Appliances

As part of a comprehensive study of residential magnetic field exposure in nine midwestern and mid-Atlantic states, 640 patients aged 14 and younger with acute lymphoblastic leukemia and 640 matched controls were evaluated. Each mother was interviewed regarding use of electrical appliances

during her pregnancy and by the child. The risk of acute lymphoblastic leukemia was elevated in children whose mothers reported use of an electric blanket or mattress pad during pregnancy and in children who used these appliances. The risk also rose with increasing number of hours per day children spent watching television. However, the inconsistency in dose-response patterns, the reporting and selection bias, and the lack of an effect for measured 60-Hertz magnetic fields or wire codes must be considered before ascribing these associations to exposures from magnetic fields. (Hatch EE, Linet MS, Kleinerman RA, Tarone RE, Severson RK, Hartsock CT, Haines C, Kaune WT, Friedman D, Robison LL, Wacholder S. Association between childhood acute lymphoblastic leukemia and use of electrical appliances during pregnancy and childhood. *Epidemiology* 1998;9:234-245)

Risk of Leukemia after Platinum-based Chemotherapy for Ovarian Cancer

Platinum compounds serve as the cornerstone of modern treatment for ovarian, testicular, and some other cancers, but few investigations have quantified late sequelae of the treatment. A case-control study of secondary leukemia was conducted within a population-based cohort of 28,971 women diagnosed with invasive ovarian cancer between 1980 and 1993. The 96 women who developed acute or myeloid leukemia were matched to 272 control patients and compared with regard to chemotherapy and radiation dose delivered to the bone marrow. Platinum-based combination chemotherapy was linked to a high risk of leukemia (relative risk [RR] 4.0), while chemotherapy with carboplatin (RR 6.5) or cisplatin (RR 3.3) was associated with significant excesses of leukemia. Dose-response risks reached sevenfold to eightfold at 1,000 mg or more of platinum (P trend = 0.0007). These findings suggest that of 10,000 ovarian cancer patients treated for 6 months with cumulative doses of cisplatin between 500 and 1,000 mg or 1,000 mg and greater and followed for one decade, an excess of 21 and 71 leukemias, respectively, might be anticipated. Nevertheless, the significant improvement in clinical response afforded by platinum-based treatment for advanced ovarian cancer, with 5-year survival rates of up to 20 to 30 percent, outweighs the relatively small excess risk of leukemia. (Travis LB, Holowaty EJ, Bergfeldt K, Lynch CF, Kohler BA, Wiklund T, Storm H, Curtis RE, Clarke A, Hall P, Andersson M, Gospodarowicz M, Pukkala E, Boice JD, Sturgeon J, Stovall M. Dose-dependent risk of leukemia following platinum-based chemotherapy for ovarian cancer. *N Engl J Med,* in press) ■

Viral Epidemiology Branch

Cancer in HIV-infected Children

Although HIV-associated malignancies have been well described in adults, relatively little is known about cancer in HIV-infected children. The Children's Cancer Group and the NCI Pediatric Oncology Branch were surveyed to define the spectrum of malignancies in HIV-infected children and to determine differences in cancer types between adults and children with HIV infection. Of 65 tumors reported among the children, 42 were non-Hodgkin's lymphoma (65 percent) and 11 were leiomyosarcomas (17 percent). Unlike the children, no increase in incidence of leiomyosarcoma has been observed in adults with HIV infection. Other malignancies included acute leukemia (5 cases), Kaposi's sarcoma (3 cases), and Hodgkin's disease (2 cases). (Granovsky MO, Mueller BU, Nicholson HAS, Rosenberg PS, Rabkin CS. Cancer in human immunodeficiency virus-infected children: A case series from the Children's Cancer Group and the National Cancer Institute. *J Clin Oncol* 1998;16:1729-1735)

Human Papillomavirus 16 Antibodies and Risk of Epithelial Cancers

Human papillomavirus (HPV), particularly HPV-16, is causally linked to the development of cervical cancer and other anogenital tumors, but the role of this virus in other cancers is unclear. In a serosurvey of 905 patients with 21 types of tumors and a group of noncancer subjects, immunoglobulin G to HPV-16 virus-like particles (VLPs) was measured to assess exposure to HPV-16. HPV-16 VLP antibody seroprevalence was highest in patients with cancers of the cervix, vulva, vagina, and penis. The seroprevalence was much lower in the noncancer group and all other cancer patients. The results confirm the strong relation of HPV with several lower anogenital tract tumors, but do not identify additional epithelial tumors associated with high seroprevalence of HPV-16 VLP antibodies. (Strickler HD, Schiffman MH, Shah KV, Rabkin CS, Schiller JT, Wacholder S, Clayman B, Viscidi RP. A survey of human papilomavirus 16 antibodies in patients with epithelial cancers. *Eur J Cancer Prev* 1998;7:305-313) ■

FELLOWS REPORT

Survival Skills Seminars Returned this Fall!

The monthly "Survival Skills" seminar series for fellows, sponsored by the NIH Fellows Committee, started September 28 with "Job Hunting, Part One." Dr. Michael Zigmond of the University of Pittsburgh began his presentation by asserting that only one of five current postdoctoral fellows will ever find a research-oriented, tenure-track position in a university or research institution. The remainder will have to find another way to make a living, hopefully without completely abandoning the scientific realm. According to Dr. Zigmond, job searching begins with soul searching—assessing wants and needs, strengths and weaknesses, preferences and constraints. He suggested open-mindedness when pondering career opportunities and emphasized the importance of networking, since most jobs are not advertised. "Don't expect to get a job offer just because you sent out a few letters!" he advised. Dr. Zigmond recommended that fellows sign up for the NIH Writing Skills and Speaking Skills Seminars, since communication skills are essential in any scientific or technical career.

The seminar concluded with a panel discussion featuring three former postdocs who have achieved success in divergent career paths: Dr. Michael Kerchner, Director of the Graduate School and the Undergraduate Neuroscience Program at Washington College in Chestertown, Maryland; Dr. Susan Old, Health Scientist Administrator at the National Heart, Lung, and Blood Institute; and Dr. Ellis Rubinstein, Editor of *Science* magazine. Dr. Zigmond closed the seminar with a quote from President Franklin Delano Roosevelt: "The only limit to our realization of today will be our doubts of tomorrow."

Topics and tentative dates for the remaining seminars in 1999 are as follows:

- January 11: Oral Presentations
- February 8: Writing Research Articles
- March 8: Grantspersonship
- May 5: Personnel Skills ■

Frank Groves

DCEG Cancer Genetics and Epidemiology Fellows

DCEG's Cancer Genetics and Epidemiology Fellowship Program celebrated its first year by holding a special meeting of the Genetic Epidemiology Branch at which first-year fellows presented overviews of their research activities. The talks were excellent and were complemented by exciting computer-aided visual effects. The diversity of topics was remarkable, and the talks demonstrated the fellows' great capabilities and enthusiasm for research in cancer genetics. The presentations are listed below:

Genes affecting susceptibility to smoking and lung cancer (Andrew Bergen, Ph.D.)

Family history as a risk factor for melanoma and other cancers (Christina Bromley, Ph.D.)

Uptake and impact of genetic testing in hereditary breast and ovarian cancer families (Naoko Ishibe, Sc.D.)

The face of hypereosinophila syndrome (Mary Lou McMaster, M.D.)

Familial chronic lymphocytic leukemia (Maria Sgambati, M.D.)

We plan to make these research presentations an annual event of the fellowship program. ■

Dilys Parry

Workshops on Epidemiologic Studies

All DCEG fellows are invited to attend three workshops on conducting epidemiologic studies at NCI. The workshops will cover issues related to requirements for conducting research, study design, and implementation. The workshops will be held in EPN/H from 10:00 am to 12:00 pm on the below dates:

- December 14: Epidemiology at NCI: From the Idea to the Field (Jim Sontag, Lois Travis, and Joanne Colt)
- January 4: Multi-Center Cohort Studies: Design, Field Methods, and Analysis (Michael Alavanja)
- January 11: Multi-Center Case-Control Studies: Design, Field Methods, and Analysis (Jay Lubin and Ruth Kleinerman) ■

Shelia Zahm

NEWS FROM THE TRENCHES

Biostatistics Branch

Ms. Linda Morris Brown was elected to the National Board of the Commissioned Officers Association of the U.S. Public Health Service. Her term runs from July 1998 through June 2001.

In September, Ms. Gloria Gridley and Dr. Ann Hsing visited Shanghai to meet with collaborators at the Shanghai Cancer Institute (SCI) to review the progress of the case-control study of biliary tract cancer. Collaborators at SCI demonstrated a new data processing system for this study, and Ms. Gridley visited two bacteriology labs to discuss issues related to bile specimen culture.

Dr. Wei-Cheng You and Dr. Susan Devesa traveled to China in October to meet with scientific collaborators. Dr. You visited the Beijing Institute for Cancer Research and field personnel in Linqu County to discuss preparations for an endoscopic examination scheduled to begin in March 1999 as part of the Shandong Intervention Trial. Dr. You and Dr. Devesa met with researchers at the Cancer Institute in Beijing to discuss collaborative analyses of cancer mortality in China and with collaborators at the SCI to discuss expanded analyses of cancer incidence patterns in urban Shanghai. ■

Environmental Epidemiology Branch

Dr. Montserrat Garcia-Closas presented a paper, entitled "Genetic susceptibility to heterocyclic amines in foods," at a meeting on carcinogenic/anti-carcinogenic factors in food in October at the University of Kaiserslautern, Germany. The meeting was organized by the Deutsche Forschungsgemeinschaft Senate Commission on Food Safety.

Dr. Louise Brinton gave a presentation on risk factors associated with endometrial cancer at the Breast Cancer Prevention Workshop on Tamoxifen, which was held in July in Chantilly, Virginia. Also in July, she presented an update on NCI's follow-up study of women with augmentation mammoplasty at a meeting on breast implants at the Institute of Medicine, National Academy of Sciences. In August, Dr. Brinton gave an overview of breast cancer epidemiology at the Fourth Annual Perspective in Breast Cancer meeting in Atlanta, Georgia. At the September meeting of the Federal Coordinating Committee on Breast Cancer, held in Washington, DC, she discussed the Physical Activity and Breast Cancer Conference (Brinton LA, Bernstein L, Colditz GA. Summary of the workshop on physical activity and breast cancer, November 13–14, 1997. *Cancer* 1998;83(Suppl):595-599) as an example of an effective partnering experience.

In September, Dr. Catherine Schairer participated in the National Coalition of Breast Cancer's Environmental Summit on Breast Cancer, which was held in Washington, DC. The purpose of the meeting was to formulate the Coalition's policies on the environment and breast cancer. ■

Genetic Epidemiology Branch

In September, Drs. Lynn Goldin, Alisa Goldstein, and Andrew Bergen attended the Genetic Analysis Workshop, then the Seventh Annual Meeting of the International Genetic Epidemiology Society (IGES) in Arcachon, France. The workshop focused on comparing methods for analyzing complex diseases. Participants analyzed either simulated datasets of a complex disease with genetic, environmental, and interaction effects or data from a large, multicenter, ongoing family study of alcoholism and related traits. Both analyses included a genome scan. Dr. Goldin and Dr. Goldstein are editors of the workshop's proceedings.

Dr. Goldin is President-elect of the IGES, and will serve during the year 2000. The IGES was formed in 1991 to foster the development of methodology for the study of health and disease in a way that integrates host and environmental factors and the application of these approaches to human populations. Further information about IGES can be accessed on the internet at *http://darwin.cwru.edu/iges.html.* ■

Nutritional Epidemiology Branch

Dr. Rashmi Sinha delivered a presentation entitled "Role of well done, grilled meat, and heterocyclic amines (Hcas) in the etiology of human cancer risk" at the 7th International Conference of Carcinogenic/Mutagenic *N*-Substituted Aryl Compounds in Nagoya, Japan, in November. ■

Occupational Epidemiology Branch

Drs. Dalsu Baris and Martha Linet (Radiation Epidemiology Branch) were invited to participate in the International Workshop on Exposure Metrics and Dosimetry for Electromagnetic Field (EMF) Epidemiology. The workshop was organized by the National Radiological Protection Board and was held this September in Chilton, England.

Dr. Kenneth Cantor has been appointed a member of the Subcommittee on Arsenic and Drinking Water, Committee of Toxicology, National Resource Council. The Safe Drinking Water Act Amendments of 1996 require the U.S. Environmental Protection Agency (EPA) to propose a standard for arsenic by January 2000 and to promulgate a final standard by the following year. The mandate of the subcommittee is to review the arsenic toxicity database and evaluate the scientific validity of EPA's 1998 risk assessment for arsenic in drinking water.

Dr. Wong-Ho Chow was invited to the 2nd International Scientific Symposium on Tea and Human Health, held in September in Washington, DC. Dr. Chow provided an overview of the epidemiological evidence relating tea drinking to risk of cancer.

Dr. Mary Ward traveled to Mexico in October to chair a session on environmental health policy at the International Symposium on Environmental Engineering and Health Sciences: A Joint Effort for the 21st Century. She also presented a paper, "Estimating environmental exposure to agricultural pesticides using remote sensing and a geographic information system: Results from a feasibility study."

Dr. Aaron Blair gave a plenary presentation on "Cancer and agricultural exposures," and Dr. Dalsu Baris spoke on "Agricultural use of DDT and risk of non-Hodgkin's lymphoma" at the Fourth International Symposium on Rural Health and Safety in a Changing World, which was held in October in Saskatoon, Canada. The NCI cosponsored this conference. ■

Radiation Epidemiology Branch

Dr. Elaine Ron was a speaker at the American Thyroid Association meeting, held in September in Portland, Oregon. Her presentation was entitled "Epidemiology of thyroid cancer."

Ms. Ruth Kleinerman represented the NCI's Children's Cancer Group study of childhood leukemia at the Electromagnetic Field and Childhood Cancer Meta-analysis Meeting, which was sponsored by the European Community in November in Padua, Italy.

Drs. Charles Land, Elaine Ron, and Ethel Gilbert attended the meeting "Cancer Risks among Individuals Exposed to Ionizing Radiation in the Newly Independent States," which focused on methodological considerations and developments in radiation studies conducted in the former Soviet Union. The meeting was held in November in Munich, Germany. ■

DCEG PEOPLE IN THE NEWS

Dr. Michael Alavanja, Occupational Epidemiology Branch, received the Commendation Medal at the NCI Awards Ceremony for outstanding research contributions to lung cancer etiology in women.

Dr. Dalsu Baris, Occupational Epidemiology Branch, has been appointed a Staff Scientist under the expanded Title 42 authority. She is involved in a large, interdisciplinary case-control study of bladder cancer in high-risk areas in the northeastern United States. Dr. Baris received her M.D. degree from the faculty of Medicine, Hacettepe University, Ankara, Turkey, and her Ph.D. in occupational health from McGill University, Montreal, Canada. From 1992 to 1996, she worked as an epidemiologist for the Atomic Energy Control Board of Canada, and has been a member of the Branch since 1996. Dr. Baris has published several papers on health risks related to occupational and environmental exposures.

Ms. Joanne Colt has been appointed as the Assistant to the Chief of the Occupational Epidemiology Branch. Ms. Colt is an epidemiologist with a background in environmental hygiene, and is a collaborator in DCEG's case-control study of non-Hodgkin's lymphoma.

Ms. Michele Doody, Radiation Epidemiology Branch, was a finalist for the Russell Hibbs Award in the Clinical Science Category at the Scoliosis Research Society annual meeting held recently in New York. Her paper was entitled "Breast cancer following diagnostic x-rays among women with scoliosis."

Mr. Dan Grauman, Biostatistics Branch, received the NIH Director's Award at the NIH Awards Ceremony for his outstanding performance in creating the "Atlas of U.S. Cancer Mortality" and for its distribution through the internet.

Ms. Gloria Gridley, Biostatistics Branch, received the NIH Merit Award for developing analytic tools and data resources to study medical conditions and diet as risk factors of cancer.

Dr. Charles Land, Radiation Epidemiology Branch, received the PHS Citation at the NCI Awards Ceremony for his role in the development of NCI statements to the press and the public describing the NCI report on the nationwide study of radioactive fallout from nuclear tests, and for providing invaluable information on risk of thyroid cancer.

Dr. Robert Miller, NIH Scientist Emeritus in the Genetic Epidemiology Branch, was awarded the American Academy of Pediatrics' President's Certificate for Outstanding Service at the group's annual meeting in October. The award was given for his work as the Academy's Chair of the Committee on Environmental Hazards, whose goal was to place pediatricians on national committees that influence health policy. The current emphasis on children's health and the environment at the NIH, the Environmental Protection Agency, and the Centers for Disease Control and Prevention is largely due to his efforts in this area.

Dr. Philip Rosenberg, Biostatistics Branch, received the NIH Merit Award at the NCI Awards Ceremony for developing statistical methods to monitor the AIDS epidemic and for major contributions to understanding the epidemic trends and natural history of HIV disease.

Ms. Diana Schneider, a predoctoral Cancer Research Training Award fellow in the Environmental Epidemiology Branch, received an award for the Best Overall Prize Paper at the 1998 biennial meeting of the American Society for Colposcopy and Cervical Pathology. Her paper described a collaborative study evaluating cervicography, a visual screening method for cervical cancer, conducted in Guanacaste, Costa Rica. The findings suggest that cervicography to detect invasive cancer performs well, but has a lower sensitivity than the conventional Pap smear in detecting high-grade lesions. Ms. Schneider also received an award from Delta Omega, the Public Health Honorary Society, for this work.

Dr. James Sontag, Ms. Catherine McClave, and **Ms. Michelle Renehan**, Office of Division Operations and Analysis, received the NIH Merit Award at the NCI Awards Ceremony for their group achievement in redesigning and implementing an expanded DCEG Research Inventory Processing System (RIPS) database.

Dr. Patricia Stewart, Occupational Epidemiology Branch, was awarded an NCI Federal Technology Transfer Act Cash Award for developing occupational questionnaires for use in case-control studies. The questionnaires were designed to evaluate exposure to a wide variety of substances, including pesticides, solvents, metals, asbestos, and dust. They were used in the DCEG's case-control study of brain cancer and will be used in case-control studies of bladder cancer in Spain and breast cancer in Poland.

Dr. Howard Strickler, Viral Epidemiology Branch, received the Commendation Medal at the NCI Awards Ceremony for his research on the role of papovaviruses, specifically human papillomavirus and SV40, in the development of cancers.

Dr. Jeffery Struewing, Laboratory of Population Genetics, was awarded the Sir Henry Wellcome Medal and Prize, an award given to a Federal health care professional who authored a peer-reviewed article contributing to biomedical research and development. His winning article was entitled "Risk of cancer associated with specific mutations of *BRCA1* and *BRCA2* among Ashkenazi Jews." The award was presented at the annual dinner of the Association of Military Surgeons of the United States in November.

Dr. Sholom Wacholder, Biostatistics Branch, received the NIH Director's Award at the NIH Awards Ceremony for his fundamental contributions to statistical methods and for outstanding collaboration and consultation within DCEG. ■

ADMINISTRATIVE UPDATES

Administrative Resource Center

After 15 months of planning, DCEG will be moving to the seventh and eighth floors of Executive Plaza South beginning in January.

The NCI Alternative Work Site Program (AWSP) policy, based on the NIH Flexible Workplace Program, makes it possible for certain employees to work at home under an approved tour of duty for an established time. Participation by an employee in AWSP is voluntary; it is not an employee benefit, but a management option. AWSP will be approved only if it enhances the work of the office and the performance of the employee's responsibilities. More detailed information on AWSP can be accessed at *http://virtual.nci.nih.gov/odep.*

The Administrative Directory, NCI's on-line Yellow Pages, is an active and up-to-date resource with the latest contact information on all administrative subjects. The Directory site can be accessed at *http://camp.nci.nih.gov/admin/directory/index.html.*

The *NCI Administrative Newsletter* is a publication of the Office of Management. The newsletter details current administrative items of interest. The newsletter can be accessed at *http://spot.nci.nih.gov/new/intranet/index.htm.*

The NIH IntraMall, an electronic shopping center, is now a first-stop location to find and buy needed supplies and equipment. There are already over 60 vendor stores available on the IntraMall. If the products you are buying from your preferred vendor are on the IntraMall, use it to place the order and charge them to your IMPAC purchase cards instead of telephoning or faxing the vendor. The IntraMall can be accessed at *http://intramall.nih.gov.* ■

Mary Jude Jacobs

Acquisition Management Branch (Previously Research Contracts Branch)

President Clinton's Management Council is strongly encouraging all Federal agencies to use a new type of contract called "Performance-Based Service Contracts." NIH was recently criticized for its lack of support in awarding this contract type. The foundation of performance-based contracts is the statement-of-work, which describes the requirement in terms of objective, measurable performance standards such as what, when, where, how much of, and how well the work is to be performed. A quality assurance plan, which directly corresponds to the performance standards and measures contractor performance, must be written by the project officer to determine whether the contractor's services and support meet statement-of-work requirements. Positive or negative performance incentives, based on the quality assurance plan measurements, must be included in the contract. This type of contract should help correct problems commonly associated with services and support contracts, particularly cost overruns, schedule delays, and failure to achieve specified results. Although it may take more time for project officers and contract specialists to write performance-based requirements and to monitor them, the payoff should be better contractor performance for less money.

Classes on performance-based service contracts are available. Project officers interested in taking a class or in awarding a performance-based contract should call Ms. Sharon Miller at (301) 435-3783. ■

Sharon Miller

REMINDERS

Travel deadlines:

- Domestic travel is due to the Administrative Resource Center (ARC) 7 working days before the travel date;
- Foreign travel is due to the ARC 4 weeks before the travel date;
- Local travel should be submitted to the ARC each month; and
- Sponsored travel is due to the ARC 4 weeks before the travel date.

Performance appraisals:

- Now is the time to complete 1998 Employee Performance Management Plans and to establish new ones for 1999.

COMINGS . . . GOINGS . . .

Dr. Paolo Boffetta, Chief of the Unit of Environmental Cancer Epidemiology, International Agency for Research on Cancer, is spending a 6-month sabbatical with the Occupational Epidemiology Branch. Dr. Boffetta will be reviewing the relation of various occupational exposures to risk of cancer.

Ms. Jennifer Donaldson transferred from the Biostatistics Branch to the Radiation Epidemiology Branch in August. She has already proven to be an invaluable member of the Branch by setting up tracking systems and by assisting in preparations for the budget and site visits.

Dr. Lea Harty has accepted a position as a Clinical Research Investigator at Pfizer Central Research in Groton, Connecticut, beginning in December. She will provide a genetic epidemiologic perspective to Pfizer's initiative to incorporate biomarkers into the investigation of pharmaceutical agents being developed to treat cancer, immunologic diseases, and infectious diseases. During her 5 years in the Genetic Epidemiology Branch, Dr. Harty worked on studies of oral cancer, Hodgkin's disease, von Hippel-Lindau disease, and buccal cell collection techniques. She hopes to continue to interact scientifically with DCEG staff.

Dr. Ellen Heineman, formerly a tenure-track investigator in the Occupational Epidemiology Branch, has joined the Epidemiology and Genetics Program, Division of Cancer Control and Population Sciences. She is working with Dr. Iris Obrams' group on the Long Island case-control study of breast cancer. Dr. Heineman is located in EPN/218 and can be reached at (301) 435-6614.

Dr. Kiyohiko Mabuchi, Chief of the Epidemiology Department, Radiation Effects Research Foundation, Hiroshima, Japan, recently joined the Radiation Epidemiology Branch as an exchange scientist for 1 year. He is collaborating with Drs. Elaine Ron, Gilbert Beebe, and Charles Land on investigations of radiation-related cancers of the thyroid, central nervous system, and liver among atomic bomb survivors as well as cancer mortality among populations exposed to radiation from the Mayak nuclear facility in the former Soviet Union. His office is located in 6110 Executive Boulevard, room 7B05, and he can be reached at (301) 496-5064.

Dr. Katherine McGlynn has joined the Environmental Epidemiology Branch as a tenure-track investigator. She received an M.P.H. from Tulane University and a Ph.D. from the University of Pennsylvania. Before coming to DCEG, she was an associate member in the Division of Population Science at Fox Chase Cancer Center in Philadelphia. Dr. McGlynn's research interests include genes in the homocysteine-methionine pathway and lipotrope/alcohol intake, genes involved in vitamin D metabolism and vitamin D/calcium intake, and genes related to iron metabolism. She has been involved with case-control studies of breast, prostate, and colon cancers and of adenomatous polyps and with cohort studies of primary liver cancer. Dr. McGlynn is located in EPN/531 and can be reached at (301) 435-4918.

Dr. Nancy Potischman, a tenure-track investigator in the Nutrition Epidemiology Branch, has accepted an associate professor appointment in the Department of Epidemiology and Biostatistics, School of Public Health and Health Sciences, University of Massachusetts, Amherst. She has been a member of DCEG since 1989, and will be leaving for her new position at the end of January.

Ms. Rebecca Schiller has joined the Nutritional Epidemiology Branch as a predoctoral fellow. She received an M.S. in nutrition from Bastyr University in Seattle, Washington. Prior to her appointment at NCI, Ms. Schiller worked at Fred Hutchinson Cancer Research Center as an assistant researcher. Her research interests focus on the role of individual fatty acids in the development of breast and prostate cancers. She will analyze plasma samples obtained from the case-control study of tumors that occur in excess among blacks and from the case-control study of breast cancer among Asian Americans. Ms. Schiller is also participating in a project to evaluate the feasibility of developing a nationwide database of nutrient supplements and botanicals for use in epidemiologic research. Ms. Schiller is located in EPN/431 and can be reached at (301) 496-4155.

Ms. Tammy Shields has joined the Environmental Epidemiology Branch as a Cancer Research Training Award predoctoral fellow. She is a doctoral candidate at the University of Washington, where she recently completed her M.P.H. Ms. Shields' thesis focused on the risk of endometrial cancer associated with unopposed estrogen use among women with

other risk factors. She plans to extend her research interests to other female reproductive cancers. Ms. Shields is located in EPN/443 and can be reached at (301) 435-3975.

Dr. Christine Swanson has accepted a position in the NIH Office of Dietary Supplements (ODS), Office of the Director. The ODS conducts and coordinates scientific research on dietary supplements and serves as the principal advisor to Federal agencies on issues related to supplements. Dr. Swanson has been a member of DCEG since 1990. Much of her research has focused on anthropometric variables as indices of nutritional status and in terms of their relation to cancer etiology, particularly cancers of the breast and endometrium. More recently, she initiated several studies to examine the role of alcohol in carcinogenesis. Dr. Swanson thanks the DCEG staff and administration for the opportunity to learn cancer epidemiology in a research environment filled with extraordinary talent.

Ms. Michelle Wethje recently joined the Environmental Epidemiology Branch as an Office Automation Clerk under the Student Temporary Employment Program. Ms. Wethje is a senior at Covenant Life High School. Next year, she plans to enroll in the nursing program at Montgomery College. ■

MIDDLE EAST CANCER CONSORTIUM

The Middle East Cancer Consortium (MECC) was established about 2 years ago to facilitate cancer research and decrease the burden of cancer in the Middle East through multilateral cooperation. There are five member countries (Israel, Jordan, Cyprus, Egypt, and Palestine) and one associate member (Turkey). Ajoint cancer registration project is building on existing structures to establish a population-based cancer registry covering a designated area in each MECC member country. These areas have a combined population of approximately 20 million people.

One aim of the MECC is to stimulate joint research in cancer epidemiology among member countries, using cancer registry data as a starting point. If anyone has suggestions for interesting projects or would like to get involved in a MECC collaborative study, please contact Dr. Elaine Ron, Chief of the Radiation Epidemiology Branch, at *rone@epndce.nci.nih.gov.*

CALENDAR OF EVENTS

Following is a schedule of upcoming events of particular interest to DCEG.

Date	Event
January 7–8	NCI Combined Intramural Retreat
February 4	DCEG Senior Advisory Group EPN/H: 1–4 pm
February 8–10	National Cancer Advisory Board
March 4	DCEG Senior Advisory Group EPN/G: 1–4 pm
March 8	NCI Board of Scientific Counselors Subcommittee A

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