



CANCER EPIDEMIOLOGY PROGRAM AT NCCC/STANFORD

February 13, 2008

Volume II Number 1

In this issue

Introduction	
Cancer and Infectious Agents	1
Surveillance Research	3
Cancer Registries Threatened	4
2007 Population Sciences Seed Grants	5
Save the Date!	7
~Important Web Links~	7

Contact us

Editors

Esther M. John, PhD, ejohn@nccc.org

Alice S. Whittemore, PhD, alicesw@stanford.edu

Editorial Assistant

Jackie Koechlin, koechlin@stanford.edu

Introduction

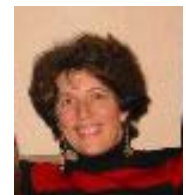
In this issue, we feature epidemiologic research on the relationships between cancer risk and infectious agents such as viruses and bacteria. We also describe the Greater Bay Area Cancer Registry (GBACR) at the Northern California Cancer Center (NCCC), and the surveillance research program at NCCC that uses the GBACR.

A particular threat to the GBACR and to all US cancer registries is the recent decision by the US Veterans Affairs (VA) Department to restrict the registries' access to cancer data of patients at VA hospitals. We discuss this decision and report on its impact on the quality of cancer registry data and the consequences for surveillance research.

We conclude with a description of the 2007 Population Sciences Seed Grants.

Cancer and Infectious Agents

We know little about the cumulative effects of lifetime exposures to microbial agents on risk of cancer and other chronic disease later in life. *Cancer Epidemiology Program (CEP)* member Julie Parsonnet plans to assess serological antibodies to specific agents in relation to incidence of site-specific cancers and other chronic diseases associated with aging.



While we now know that some infectious agents increase the risk of certain cancers, others may reduce risk and some may have opposing effects on different cancers. The conjecture that some microbial exposures are needed for immune and maintenance system development has been well studied in relation to immunologic dysfunctions, but has had relatively little attention in relation to cancer. Family size, early childhood infections, and other markers of microbial exposures have been associated with risk of Hodgkin lymphoma and childhood leukemias. *CEP* members Christina Clarke, Sally Glaser, Ellen Chang and

Theresa Keegan at NCCC are working to better understand these and similar factors in the etiologies of Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) using several data resources. Clarke is also exploring the hypothesis in relation to breast cancer risk in ongoing population-based case-control studies, and in relation to risk of breast cancer, lymphoma and melanoma in the California Teachers Study cohort.

Viruses

Ellen Chang, Christina Clarke, Sally Glaser and Theresa Keegan are studying the etiologic and prognostic roles of the Epstein-Barr virus (EBV) in Hodgkin lymphoma (HL). Their work concerns how risk factors and survival differ between HL patients with tumors containing EBV proteins and nucleic acids and those whose tumors lack the virus. Glaser and Keegan evaluated the presence of EBV DNA in a population-based series of HL patients in northern California. Among both men and women diagnosed at older ages, they found poorer relative survival in those with EBV-positive HL than in those with EBV-negative HL. Working with colleagues at the Harvard School of Public Health and the Karolinska Institute, Chang found that some etiologic factors – such as socioeconomic status – vary between EBV-positive and EBV-negative HL, whereas others – such as preschool attendance – are similarly related to both types of HL.

To address the observed inter-study variability in EBV prevalence among HL tumors, Glaser and colleagues also studied the reliability of the most widely used assays for EBV detection in HL, documenting inter- and intra-observer variation in assay application and interpretation. They have generated interpretation guidelines designed to minimize this variation

CEP investigators also are investigating the roles of EBV in other cancers. Glaser conducted a population-based case-control study of breast cancer that applied a widely used EBV detection assay to the sera of women at diverse risk of breast cancer; no association was found. She also applied a comprehensive battery of EBV assays to a representative group of breast cancers, demonstrating that EBV was present in breast tumors only at low levels. However the epidemiological characteristics of patients with EBV-positive tumors differed from those of patients whose tumors showed no evidence of EBV. As part of this work, she and her colleagues have developed a comprehensive panel of novel EBV detection assays for breast cancer.

While less thoroughly studied than EBV, other viruses have received some attention for their roles in cancer. Glaser and Clarke have examined the impact of human-immunodeficiency virus (HIV) infection on HL risk, documenting its effects on incidence trends in California both before and after the introduction of Highly Active Antiretroviral Therapy (HAART). In addition, Chang is working with Samuel So, *Cancer Prevention and Control Program* member, and colleagues at the Asian Liver Center at Stanford on several projects related to chronic hepatitis B virus (HBV) infection and hepatocellular carcinoma. Most recently, they have been funded to launch a program to prevent perinatal HBV transmission and promote medical follow-up of HBV-positive mothers and infants in Santa Clara and Alameda Counties. They also received a separate grant to support the San Francisco: Hep B Free campaign, a program to provide routine HBV testing for all Asians and Pacific Islanders in San Francisco, vaccination of unprotected individuals, medical management of chronically infected individuals, and HBV-related education for health care providers throughout the city. In addition, Chang, So, and Research Scientist Mei-Sze Chua are working together to identify novel biomarkers for hepatocellular carcinoma using DNA microarrays, with the ultimate goal of developing a new screening test for early cancer detection.

Bacteria

The role of *Helicobacter pylori* infection in gastric and esophageal cancer has been studied extensively by Julie Parsonnet. She was one of the first to demonstrate a causal relationship between *H. pylori* infection and gastric adenocarcinoma, the leading cause of death in developing countries. Paradoxically, her research suggests that this bacterium reduces risk of esophageal cancer. Parsonnet also has published groundbreaking research on the cost-effectiveness of *H. pylori* screening to prevent gastric adenocarcinoma, and has conducted an important community-based trial of *H. pylori* eradication in Chiapas, Mexico.

Chang and colleagues at the Karolinska Institute have studied the impact of infection with the bacterium *Borrelia burgdorferi* on risk of subtypes of NHL.

Surveillance Research

The CEP includes a major center for local, national, and international cancer surveillance research—the Greater Bay Area Cancer Registry (GBACR) of the NCCC. Cancer surveillance research, defined as the use of systematically collected cancer patient data to test hypotheses about cancer predictors, incidence and outcomes, is an important part of cancer epidemiology. Cancer surveillance data includes cancer registry case counts and a wide variety of other population-based and routinely collected survey data. These resources allow researchers to examine patterns of cancer incidence, mortality, survivorship, secondary health outcomes, risk factors, screening, treatment, and prevention—usually with sample sizes and population diversity superlative to those of any other resource.

Since 1973, the GBACR has collected information on over 700,000 cancers diagnosed or treated in its nine-county catchment area (Alameda, Contra Costa, Marin, Monterey, San Benito, San Francisco, San Mateo, Santa Clara and Santa Cruz counties). Funding for this work comes from the National Cancer Institute (NCI), the Centers for Disease Control, and the state of California since the 1986 enactment of a state cancer reporting law. GBACR data are abstracted from medical records by certified tumor registrars at hospitals and other medical facilities; for each tumor, routinely collected information includes cancer site and histology, extent of disease, first course of treatment, and patient demographics such as age, sex, and race/ethnicity. Confirmation of case completeness in the GBACR comes from systematic review of death certificates and, increasingly, electronic pathology reports. In addition, all patients are followed for life for subsequent cancers, survival time, and cause of death. GBACR data are contributed regularly to the NCI's Surveillance, Epidemiology, and End Results (SEER) program, the statewide California Cancer Registry, the North American Association of Cancer Center Registries (NAACCR) and the International Association for Research on Cancer at the World Health Organization.

At NCCC, these data are analyzed extensively by the Surveillance Research team, established by Sally Glaser, Director of the GBACR, and also including Scarlett Lin Gomez, Christina Clarke, Ellen Chang, Theresa Keegan, Rudy Rull, Pamela Horn-Ross and Dee West. Together, the team has published over 75 peer-reviewed papers describing cancer occurrence and survival in the Greater Bay Area, state, nation, and world, as well as methods to improve the data quality and use. See <http://www.nccc.org> for a complete listing of papers and topic areas. Notable recent research findings include the following areas:

- *Understanding unprecedented decline in breast cancer incidence*
- *Understanding cancer trends in Asian populations*
- *Understanding lung cancer in nonsmokers*
- *Understanding increasing melanoma rates*

Several efforts are ongoing to facilitate new collaborations involving the GBACR data and Cancer Center investigators. Those with research hypotheses that may benefit from GBACR or other surveillance data who would like more information on collaborating with members of the surveillance research team should contact Christina Clarke, Associate Director of Surveillance Research: tina@nccc.org

Cancer Registries Threatened

The Veterans Affairs Department has issued a national directive setting conditions for using personal information from cancer patients and will not provide data for these patients to state cancer registries until the state registries sign it. In an article in *The New York Times*, Joel Kupersmith of the VA research and development office was quoted as saying: The paramount issue for us is the protection of patient privacy and the protection of patient information. He added that the agency is particularly sensitive to privacy issues because of incidents like the theft last year of a laptop containing personal information of 26.5 million veterans.

So far, only a few states have signed the directive. The states that have not--including California, whose population includes more veterans than any other state--say the VA's conditions for cancer data security and use are nearly impossible to meet and, moreover, ignore the effective data security and privacy protections already present in state cancer registry regulations. Some of the conditions in the VA directive are requirements for researchers to obtain permission from the VA's under secretary of health, or find an agency researcher to collaborate with and get permission from the hospitals ethics board. Dee West, who directed the GBACR from 1987 to 2006 and who now chairs the National Coordinating Council for Cancer Surveillance, is concerned because the VA directive requires cancer registries to maintain patient information in an encoded form in a separate location from other cancer registry data to prevent unauthorized people from reading it. The registries may not even share the data with state departments of Vital Statistics to identify deaths among cancer cases. The restrictions obstruct the registries' task of merging patient information from multiple hospitals (an estimated 40% of VA patients are seen both at VA and other hospitals). In addition, the GBACR often links records to external sources, such as Medicare records, to add value to cancer surveillance studies and to establish if patients have died, which may not be possible under this directive.

Because veterans are an important part of the population, cancer patterns and trends, as well as research studies into the causes and outcomes of specific cancers, will not be accurate if veterans are excluded. Consequently, it is critical that they be included in these efforts. However, cancer researchers note that it will be difficult to meet the directive's conditions to make this possible. For example, it is not easy to find a VA collaborator. As noted by Christina Clarke, it means the VA collaborator has to have the time and interest to work with you on your research question. As for the ethics board, Clarke said it could take a year or more to get the required permissions from a local board, the registry's board and, now, the VA's board. Any time a board wants a change that the others did not approve, the proposal would have to go back to the others. Privacy concerns are serious, Clarke said. But at the same time, this is a baby with the bath water problem.

Brenda Edwards, associate director of the National Cancer Institute's surveillance research program, notes that cancer research will be impacted severely by the VA's directive. Surveillance research will be particularly hard hit since it is now difficult to compile national statistics and interpret them with incomplete veteran's data.

Because California has not signed the directive, transmission of VA cancer data to its cancer registry has virtually ceased, and its cancer surveillance database has not included VA data since October, 2005. CEP member Philip Lavori, former Acting Chief of Clinical Trials Research for the VA, notes: "Research on cancer in general, and the cancer registry in particular, exist and operate for the benefit of current and future patients with cancer, and those who are at risk of cancer. To serve the best interests of their patients, administrators at the VA should choose the real benefits of registry-based research that accrue to veteran patients, over an entirely hypothetical privacy risk."

2007 Population Science Seed Grant Awards

The following is a brief description of each of the five 2007 awards. The first three awards are for projects led by *CEP* members, and the remaining two awards concern projects led by members of the *Cancer Prevention and Control Program*.

Broadening the Spectrum of Cancer Risk Reduction Research in the California Teachers Cohort

CEP member Christina Clarke and investigators from the Stanford Prevention Research Center and the California Teachers Study (CTS) will plan the creation of a new infrastructure for recruiting California teachers into intervention studies that test the means by which cancer risk factors can be best mitigated.

The CTS includes 130,000-plus female California teachers and school administrators who joined the cohort in 1995. The group is well characterized with respect to cancer risks (including breast cancer rates that are over 50 percent higher than expected) and risk factors, making these women ideal as a base population for future interventional studies.

The researchers hope that by broadening the spectrum of cancer risk reduction research from an existing cohort study, they will speed the translation of epidemiologic research findings into workable strategies for promoting individual behaviors, as well as societal or environmental conditions that will reduce population levels of cancer.

Co-investigators on this study include *CEP* members Pamela Horn-Ross and Peggy Reynolds, and *Cancer Prevention and Control Program* members Abby King, Randall Stafford, and Marcia Stefanick.

Cancer Risk Reduction Strategies for Those at High Risk

More than 250,000 women in the United States carry an inherited mutation in the *BRCA1* or *BRCA2* cancer susceptibility genes, which convey lifetime risks of 45 to 65 percent for breast, and 11 to 39 percent for ovarian cancer. Given these elevated risks, management strategies require earlier, more frequent and more invasive interventions than in the general population.

Currently, the only alternatives for breast cancer risk reduction are preventive mastectomy or intensive breast screening including magnetic resonance imaging. These approaches yield very different outcomes and side effects. Stanford researchers believe that clinical decision support tools could provide individualized estimates of patient outcomes, and may yield particular benefit when patient preference dictates the choice between medical acceptable alternatives.

CEP members Sylvia Plevritis and Allison Kurian have received a seed grant to develop a clinical decision support tool that offers individualized assessments of cancer risk-reduction strategies to female *BRCA1* or *BRCA2* carriers and their physicians. The study will include adapting a previously developed computer simulation model of breast and ovarian cancer in *BRCA1* or *BRCA2* mutation carriers. It is hoped that results of this study will have an immediate and direct impact on the cancer risk-reduction decisions and clinical care of high-risk women.

A Risk Assessment Tool for Childhood Brain Tumors

Little is known about the causes of childhood brain tumors, which constitute the second most common malignancy in children. There has been much interest in the degree to which various birth characteristics, such as birth weight and birth order, might be indicators of risk for the development of childhood brain tumors, but few studies have been large enough to be able to account for the enormous differences in brain tumors in children. *CEP* members Peggy Reynolds from NCCC and Paul Fisher from Stanford, and Julie Von Behren and Michael Lavefsky from NCCC will analyze data from 3,000 newly diagnosed cases of

childhood brain tumors, the largest case-control study of its kind conducted to date. The researchers will assess the risk for childhood brain tumors by demographic factors and birth characteristics, including high birth weight, birth order, race, ethnicity and parental age. Results of the study will provide a valuable resource for future studies of childhood brain tumors, as well as serve as an important complement to prospective studies proposed to the National Cancer Institute, for which the NCCC and Stanford are collaborating institutions.

Physical Activity in Cancer Survivors

While a physically active lifestyle is known to have a significant positive impact on cancer prevention and improves our quality of life, there are few data concerning its impact on survival and quality of life among cancer patients. Abby King, a member of the *Cancer Prevention and Control Program*, and colleagues will assess the initial and longer-term impact of physical activity on cancer patients' strength, fitness and quality of life. Data will be derived from the Center's "Living Strong, Living Well" (LSLW) program for cancer patients, which is administered at eight YMCAs throughout the San Francisco Bay area. The multidisciplinary research group includes experts in exercise, behavioral science, physiology, epidemiology, oncology and statistical analysis.

The scientists will analyze 12-week and six- and 12-month outcome and process data that have been collected, but not yet examined, from the 626 cancer patients who have already completed the LSLW program. The study will include conducting exit interviews with participants; evaluating recruitment, assessment and intervention delivery and quality control practices to inform a larger-scale study; and identifying additional YMCAs in underserved Bay Area communities as a means to broaden the ethnic and economic diversity of patients targeted in a larger scale study.

King's collaborators include *Cancer Prevention and Control Program* members Ingrid Oakley-Girvan and Marcia Stefanick, *Lymphoma Program* member Sandra Horning, as well as David Ahn, Julie Anderson, and Joyce Hanna.

Is Bone Health Being Neglected among Breast Cancer Survivors? - A Web-based Pilot Study

There are currently an estimated 2.4 million breast cancer survivors in the United States. As women continue to use early detection methods, treatment effectiveness will improve, deaths from simultaneously occurring conditions will decrease and the number of breast cancer survivors will grow.

There are many important questions related to the impact of treatment decisions on long-term health and subsequent development of co-morbid chronic conditions such as osteoporosis, a condition that causes low bone mass and increased susceptibility to fractures.

Because of chemotherapy or surgery, many breast cancer survivors experience a loss of ovarian function, and, consequently, a drop in bone-protecting estrogen. While the impact of osteoporosis is significant in the general population (1.5 million fractures annually), the risk in breast cancer patients exposed to chemotherapy and radiotherapy may be even greater.

A multidisciplinary study headed by *Cancer Prevention and Control Program* member Randall Stafford will attempt to answer these questions, with the ultimate goal of improving bone health and preventing chronic disease in the growing, ethnically diverse population of breast cancer and other cancer survivors.

Investigators from the Stanford Prevention Research Center, the Northern California Cancer Center and the Palo Alto Medical Foundation Research Institute will collaborate on this study.

Save the Date!

2008

March 13

Population Sciences Retreat

10:00 a.m. – 5:00 p.m.

Cordura Hall, on the corner of Campus Drive and Panama Street

April 7

Stanford Cancer Center Members Retreat

Quadrus Center on Sand Hill Road

Overarching topic of the retreat is "New Initiatives of the Stanford Cancer Center."

Keynote speaker is John Niederhuber, MD, Director of the National Cancer Institute.

Members will receive an invitation to the retreat and more information about the agenda by the end of February.

April 9

Population Sciences Surveillance Meeting

9:00 a.m. - 3:00 p.m.

Clark Center auditorium and auditorium lobby

May 19

External Advisory Board Review

~Important Web Links~

Northern California Cancer Center

<http://www.nccc.org>

Stanford Cancer Center

<http://cancer.stanford.edu/>

Population Sciences - *Cancer Epidemiology Program*

<http://cancer.stanford.edu/research/populationsci/>

Cancer Epidemiology Program members' profiles

<http://med.stanford.edu/profiles/cancer/frdActionServlet?choiceId=showFacByDivsion&orgcode=SCC0>