Global Perspective

Epidemiological Research at the American Cancer Society

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Introduction

When the ACS2 founded its intramural program of epidemiological research in 1946, lung cancer death rates in men had increased approximately 5-fold since 1930, the first year for which mortality statistics encompassed most of the United States (1). Death rates from what had been the two leading fatal cancers in women, uterine (cervix and corpus combined) and stomach cancer, were decreasing, although lung cancer rates were just beginning to climb. Connecticut operated the only population-based tumor registry. Two activities that helped to ground the new program were collaborative efforts to improve the quality and availability of cancer surveillance data and the involvement of ACS volunteers in assembling large prospective cohort studies that could provide insights about cancer etiology.

E. Cuyler Hammond, who first directed the program, saw in the rapidly expanding network of ACS volunteers an extraordinary human resource that could enroll and help to follow large prospective epidemiological cohorts.

More than 50 years later, intramural epidemiological research at ACS remains the most active epidemiological program based in a private, voluntary health organization. Cohort studies and cancer surveillance continue to be central to the program. This article will describe the mission and research activities of the current Department of Epidemiology and Surveillance Research. It will also direct readers toward a variety of publications and Web-based resources and describe opportunities and guidelines for training and/or collaborative research.

Mission

The overall mission of intramural epidemiological research at ACS is to conduct and publish original epidemiological research to advance our understanding of the occurrence, causes, and prevention of cancer. The two arms of the department, Surveillance Research and Analytic Epidemiology, also provide “service” to other parts of ACS and to the public. For example, Surveillance Research compiles and disseminates population-based statistics on cancer occurrence and prevention that are increasingly used to plan and evaluate state cancer control programs as well as for public education and advocacy. Because ACS is a voluntary, community-based organization, staff epidemiologists frequently translate epidemiological findings to nonepidemiological audiences including the media, cancer patients and their families, clinicians, basic researchers, volunteers, and other diverse constituencies. This important service, together with original research conducted by the department, helps to clarify exactly what research on disease patterns in human populations contributes to the understanding and control of cancer.

Roles of Surveillance Research

Currently, surveillance activities at ACS address three aspects of cancer: (a) occurrence (incidence, mortality, and survival); (b) prevention (prevalence statistics on risk factors and screening examinations); and (c) cancer patient care. The first two activities produce ACS educational publications, most of which are available electronically on the ACS website1 as well as from the divisional and national ACS offices. Surveillance Research publishes original studies that highlight disparities in cancer occurrence, risk factors, and prevention. These studies potentially speed the translation of existing knowledge into practice. The newest surveillance activity at ACS involves exploratory studies examining data needs and resources for monitoring of cancer patient care.

Cancer Occurrence. ACS has published Cancer Facts and Figures annually since 1952. A similar document, Cancer Statistics, published yearly since 1970 in CA—A Cancer Journal for Clinicians, reaches a broader clinical audience and can be cited in scientific papers (2). These reports disseminate population-based data on cancer occurrence to the media, clinicians, cancer researchers, and the public. Mortality statistics in these publications are derived from state and national vital statistics (1), from incidence and survival rates from the NCI Surveillance, Epidemiology, and End Results program (3), increasingly from state tumor registries, and from population denominators from the United States Census. Unique to these publications are ACS projections of the number of cancer cases and deaths expected in each state and in the nation in the current year (4). These projections are widely cited because they are current, readily understood by the public, and reasonably accurate when compared with the actual counts of cancer deaths tabulated several years later. However, they represent projections rather than actual counts. More detailed data on certain cancer sites are published periodically in Breast Cancer Facts and Figures or in expanded “banner” sections that discuss colorectal, prostate, and childhood cancers in Cancer Facts and Figures. Most of these are available through the ACS website under “statistics archives.”

Increasingly, ACS surveillance publications highlight inequities in the burden of cancer across socioeconomic, racial, and ethnic subgroups. Cancer Facts and Figures for African Americans (1998–1999) and a banner section on Racial and Ethnic Patterns published in 1997 describe the higher cancer

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2 The abbreviations used are: ACS, American Cancer Society; NCI, National Cancer Institute; CDC, Centers for Disease Control and Prevention; CPS, Cancer Prevention Study.

Internet address: http://www.cancer.org.

5 Internet address: http://www.cancer.org.
occurrence rate and poorer survival rate in certain populations. These disparities have stimulated research on the interplay between socioeconomic and cultural factors, education, access to screening and health care, nutrition, and tobacco use.

Since 1998, ACS Surveillance Research has collaborated with the CDC, NCI, and the North American Association of Central Cancer Registries to publish an annual report on progress against cancer in the United States. These reports (5–7) characterize the decrease in incidence and mortality rates that has occurred for all cancers combined and for many specific cancer sites from 1990 through 1997. They also emphasize tobacco control and colorectal cancer screening as priority areas for cancer control. In 1998, ACS proposed challenge goals to the nation intended to stimulate additional actions to reduce cancer incidence and mortality and to improve the quality of life for cancer patients by the year 2015 (8). Similar to the government’s Healthy People 2010 goals, these objectives aim to motivate progress in key areas of cancer prevention, early detection, and treatment.

Cancer Risk Factors and Screening. In 1992, ACS began to compile and publish population-based prevalence data on cancer risk factors and utilization of screening tests to support state and national cancer control efforts. Two resources are available for cancer control advocates and planners: Cancer Prevention and Early Detection Facts and Figures is published annually and archived data that can be formatted for state-specific presentations are available on the ACS website. These resources allow for comparisons of tobacco use, nutrition (consumption of fruits and vegetables), physical activity, obesity, and the utilization of screening tests for cancers of the female breast, uterine cervix, and colorectum across states and over time. Monitoring trends in youth and adult smoking, physical inactivity, obesity, and under utilization of mammography, Pap, and colorectal cancer screening provides immediate, objective feedback about factors that affect cancer occurrence and/or progression.

Recognizing the need to address sun exposure behaviors among youth—a high-risk group for melanoma—ACS conducted a population-based survey of youth and their parents in 1998. This survey will provide national baseline measure of sun protection and sun exposure behaviors.

Surveillance of Cancer Patient Care. As an organization, ACS has long sought to improve the quality and accessibility of cancer patient care. The Department of Epidemiology and Surveillance Research began to grapple with the difficult challenges of cancer patient care surveillance in 1996. The Institute of Medicine has underscored the need for reliable, population-based data on the diagnostic and treatment services provided to cancer patients. This need is accentuated by the rapid changes in medical delivery systems, increasing health care costs, aging of the population, disparities in access to quality health care, and uncertainties about whether research advances are translated into practice. Equally daunting, however, are the obstacles to collecting such information. These include the multiplicity of providers, the cost of actively collecting data from many sources, organizational jurisdiction, issues of patient confidentiality, and the need to interview patients directly to verify that recommended treatment was received. In 1999, Surveillance Research collaborated with three state cancer registries and the American College of Surgeons to examine the feasibility of conducting population-based patterns of care studies and to estimate the proportion of patients who received the recommended treatment for colon cancer. Groups that are collaborating to develop cancer patient care surveillance include the ACS, the American College of Surgeons, the CDC, the NCI, and the North American Association of Central Cancer Registries.

Roles of Analytic Epidemiology
Since the 1950s, the intramural epidemiology program at ACS has assembled and followed very large cohorts to provide insight about cancer etiology and prevention. The three main cohorts, Hammond-Horn and the CPS-I and CPS-II described below, feature prominently in many Surgeon General Reports on tobacco (10–13). The traditional prospective cohort studies remain the foundation of analytic epidemiological research at ACS; methods are being updated to include the collection of biological samples and enhanced information on lifestyle, medical, nutritional, and other environmental factors that may interact with familial or acquired genetic susceptibility. This section will describe: (a) the original ACS cohorts initiated before 1990; (b) two new resources, the CPS-II Nutrition and LifeLink cohorts, which will soon provide biological samples, more extensive questionnaire information, and ascertainment of incident cancers as well as deaths; and (c) past and current examples of collaborative research.

ACS Cohorts Before 1990. The first ACS cohort study was Hammond-Horn (Table 1), initiated in 1952 to measure death rates from lung cancer, heart disease, and other conditions in relation to tobacco smoking among almost 188,000 white men, ages 50–69 years, residing in nine states (14–16). Together with E. Cuyler Hammond, Daniel Horn, and other ACS staff, 22,000 community volunteers recruited their male acquaintances to complete a confidential, short questionnaire. Each year during the 44 months of follow-up, the volunteers recontacted the people they had enrolled to determine vital status. Aspects of Hammond-Horn became the prototype for subsequent ACS cohorts, with large numbers of community volunteers recruiting study participants and then helping to identify deaths during follow-up.

At the outset, both Hammond and Horn, themselves smokers, were skeptical of earlier case-control studies (17–20) that implicated cigarette smoking as the major cause of lung cancer. They believed it equally plausible that automotive exhaust, dust from tarred roads, and/or air pollution from coal and oil furnaces were partly or wholly responsible (14). However, after 44 months of follow-up, the increase in death rates from lung cancer, coronary heart disease, and all causes in cigarette smokers compared with lifelong nonsmokers (15, 16) persuaded Hammond and Horn to stop smoking and to focus ACS attention on tobacco. Strong and consistent evidence from subsequent ACS cohort studies has sustained the organization’s 50-year commitment to tobacco control.

The next two CPSs, CPS-I and CPS-II, followed the general Hammond-Horn model but were over five times larger, included women as well as men, encompassed more states, and extended the duration of follow-up (Table 1). CPS-I included approximately one million men and women recruited in 1959 by 68,000 volunteers in 25 states (21, 22). The entire CPS-I cohort was followed for 12 years, through 1972, with longer follow-up of subcohorts from California and long-term survivors (the latter are not shown in Table 1). CPS-II began in 1982 under the direction of Larry Garfinkel and encompassed nearly 1.2 million subjects recruited by 77,000 volunteers in 50 states,

Increased risk of various cancers include diabetes [pancreas and increasing with age (44). Medical conditions associated with body mass index remains constant throughout life, rather than among both men and women in CPS-II, the optimal range of therapy and mortality among elderly United States women. Am. J. Epidemiol., in press, 2000.

The effect of body mass on the association between estrogen replacement and hormones, reproductive factors, and familial and personal style factors such as obesity, alcohol consumption, medications and hormones, reproductive factors, and familial and personal medical conditions affect cancer and other chronic diseases. CPS-II cohort has provided important insights about how life-styles such as obesity, alcohol consumption, medications and hormones, reproductive factors, and familial and personal medical conditions affect cancer and other chronic diseases. CPS-II data attracted widespread research attention and funding.

Besides contributing to tobacco research, the baseline CPS-II cohort has provided important insights about how lifestyle factors such as obesity, alcohol consumption, medications and hormones, reproductive factors, and familial and personal medical conditions affect cancer and other chronic diseases. CPS-II data attracted widespread research attention and funding to the potential of aspirin-like drugs to inhibit colorectal cancer (34, 35). Approximately nine publications from CPS-II have examined the relationship between hormones in women and mortality from cancers of the colon, breast, and ovary (36–43). A publication on obesity and mortality showed that among both men and women in CPS-II, the optimal range of body mass index remains constant throughout life, rather than increasing with age (44). Medical conditions associated with increased risk of various cancers include diabetes [pancreas and colon cancer (45)], infertility [ovarian cancer (46)], nonmelanoma skin cancer [other fatal cancers (47)], and hypertension or antihypertensive medications [renal cell carcinoma (48)] but not spontaneous abortion [breast cancer (49)]. A 1995 analysis of air pollution and mortality found increased death rates among CPS-II participants living in cities with higher particulate air pollution (50). Together with the Harvard Six Cities Study (51), CPS-II findings (50) motivated the Environmental Protection Agency to propose more stringent limits on particulate air pollution. A complete list of publications from CPS-II and other ACS cohorts will soon be available on the ACS website.

The potential contribution of large cohort studies to the fields of molecular and genetic cancer research can be illustrated by two particular insights from CPS-II. Table 2 shows that with respect to death from lung cancer, women are not more likely than men to die from lung cancer after equivalent cigarette smoking. Within narrow strata of age, years of smoking, and cigarettes per day, women have similar or lower death rates from lung cancer than men. This is consistent with several other large prospective studies that show no sex difference in the risk of lung cancer from smoking (52–54). The higher relative risk estimates among women than men reported by other large prospective studies are more likely to reflect biased estimates of exposure in case-control studies, as well as possibly the lower background lung cancer risk in older women than in men who have never smoked actively (54–57). Better evidence is needed to establish the hypothesis of greater risk in women before biochemical and mechanistic studies examine why it occurs (58).

A second insight from Table 2 is that lung cancer death rates among smokers increase so rapidly with the duration of smoking that studies examining genetic polymorphisms must control more rigorously for smoking parameters than simply considering smoking status (current, former, or never) or pack-years. In CPS-II, as in the British Doctors Study (59), lung cancer mortality increases with the fourth or fifth power of the duration of smoking and with approximately the second power

<table>
<thead>
<tr>
<th>Study design</th>
<th>Hammond-Horn</th>
<th>CPS-I baseline</th>
<th>CPS-II</th>
<th>Baseline</th>
<th>Nutrition</th>
<th>LifeLinka</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study participants</td>
<td>187,783</td>
<td>1,051,038</td>
<td>1,185,106</td>
<td>184,194</td>
<td>40,000</td>
<td></td>
</tr>
<tr>
<td>Volunteer recruiters</td>
<td>22,000</td>
<td>68,000</td>
<td>77,000</td>
<td>7,000</td>
<td>2,000</td>
<td></td>
</tr>
<tr>
<td>Number of States</td>
<td>9</td>
<td>25</td>
<td>50</td>
<td>21</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Outcome of interest</td>
<td>Mortality</td>
<td>Mortality</td>
<td>Mortality</td>
<td>Incidence &amp; mortality</td>
<td>Incidence &amp; mortality</td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women (%)</td>
<td>0</td>
<td>57</td>
<td>57</td>
<td>53</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>White (%)</td>
<td>100</td>
<td>97</td>
<td>93</td>
<td>97</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>Black (%)</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Married (%)</td>
<td>?</td>
<td>85</td>
<td>83</td>
<td>88</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>College graduate (%)</td>
<td>?</td>
<td>17</td>
<td>30</td>
<td>38</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Age at entry (median) (yrs)</td>
<td>?</td>
<td>52</td>
<td>57</td>
<td>63</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Age range (yrs)</td>
<td>50–69</td>
<td>30–108</td>
<td>30–111</td>
<td>40–92</td>
<td>48–95</td>
<td></td>
</tr>
<tr>
<td>Current cigarette smokers (%)</td>
<td>57</td>
<td>29</td>
<td>20</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

Table I: Characteristics of ACS cohorts

a Specimen collection is ongoing, the number of participants is estimated, and the demographic characteristics pertain to persons enrolled by October 1999.


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of the number of cigarettes smoked per day. Molecular studies that do not stratify finely on years of smoking and cigarettes per day (60–62) are vulnerable to residual confounding.

**CPS-II Nutrition Cohort.** The CPS-II Nutrition Cohort was established as a subgroup of the larger CPS-II (Table 1) in 1992–1993, several years after the ACS Home Office moved from New York to Atlanta, and Dr. Clark Heath succeeded Larry Garfinkel as department head. The two objectives of the Nutrition Survey were (a) to obtain current, more detailed information on diet, physical activity, adiposity, and other factors that were either inadequately measured or subject to change since 1982 and (b) to initiate prospective follow-up of incident cancers as well as deaths. A self-administered, 10-page questionnaire was mailed to approximately 516,000 CPS-II men and women, ages 50–74 years, who resided in 21 states with population-based state cancer registries. These states included California, Connecticut, Florida, Georgia, Illinois, Iowa, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Missouri, New Mexico, New Jersey, New York, North Carolina, Pennsylvania, Utah, Virginia, Washington, and Wisconsin. This target population was originally chosen to enable follow-up of cancer incidence using computerized linkage with state cancer registries.

Characteristics of the 184,194 men and women who completed the 1992/1993 Nutrition Survey and were thus enrolled in the CPS-II Nutrition Cohort are shown in Table 1. Respondents include a smaller percentage of non-whites, current smokers, and persons with less than a college education than the baseline CPS-II cohort. Additional questionnaires were mailed to the Nutrition subgroup in 1997/1998 and 1999/2000 and will continue biennially to update information on self-reported cancer and to obtain additional exposure data. Because of the age of the cohort, new cancer cases accrue rapidly: 10,775 new cases were reported in the interval between 1992/1993 and 1997/1998 (Table 3). A pilot linkage study with 11 cancer registries verified self-reported cancer of all sites combined and a low percentage of false positives [specificity 0.99 (63)]. Based on this pilot work, we now identify incident cancers by contacting participants who report a new cancer on the biennial questionnaire and by requesting permission to verify and augment the diagnostic information with medical records. Computerized linkage with state cancer registries is used as needed to supplement verification of self-reported incident cancers.

The dietary instrument used in 1992/1993 was the 60-item Health Habits and History Questionnaire developed by Block et al. (64) at the NCI. Supplemental questions inquired about red meat consumption (frequency and degree of cooking), changes in diet since 1982, consumption of restaurant foods and selected low-fat products, and use of vitamin and mineral supplements. Other questions addressed changes in smoking, weight, physical activity, medical history and medication use, occupational history, and, for women, breast and cervical cancer screening, hormone replacement therapy, and family history of breast cancer. Responses to the 1992/1993 food frequency questionnaire were validated against four 24-h dietary recalls by telephone in a stratified random sample of 600 men and women (65). More recently, the 1999/2000 questionnaire included an updated and more detailed dietary assessment, based on the 130-item questionnaire developed by Rimm et al. (66).

### Table 2 Lung cancer death rates among current smokers by age, sex, cigarettes/day, and years of smoking at baseline, CPS-II

<table>
<thead>
<tr>
<th>Age</th>
<th>Lifelong nonsmokers</th>
<th>20 cigarettes/day</th>
<th>40 cigarettes/day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>50–54</td>
<td>5.5</td>
<td>5.8</td>
<td>100.0</td>
</tr>
<tr>
<td>55–59</td>
<td>5.3</td>
<td>7.2</td>
<td>101.4</td>
</tr>
<tr>
<td>60–64</td>
<td>11.6</td>
<td>12.3</td>
<td>189.0</td>
</tr>
<tr>
<td>65–69</td>
<td>21.5</td>
<td>16.7</td>
<td>583.7</td>
</tr>
<tr>
<td>70–74</td>
<td>34.9</td>
<td>30.5</td>
<td>722.9</td>
</tr>
<tr>
<td>75–79</td>
<td>52.0</td>
<td>32.5</td>
<td>2,225.5</td>
</tr>
<tr>
<td>80–84</td>
<td>89.2</td>
<td>57.6</td>
<td>1,764.6</td>
</tr>
<tr>
<td>85+</td>
<td>86.8</td>
<td>60.6</td>
<td></td>
</tr>
</tbody>
</table>

*Death rates per 100,000 person-years pertain to the first 6 years of follow-up (1982–1988) and are shown only for strata with ≥5 lung cancer deaths (30).

### Table 3 Number of self-reported incident cancers by site, CPS II Nutrition Cohort, 1992/1993 to 1997/1998

<table>
<thead>
<tr>
<th>Site</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>3,359</td>
<td>3,359</td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td>594</td>
<td>423</td>
<td>1,017</td>
</tr>
<tr>
<td>Lung</td>
<td>287</td>
<td>232</td>
<td>519</td>
</tr>
<tr>
<td>Breast</td>
<td>16</td>
<td>1,837</td>
<td>1,853</td>
</tr>
<tr>
<td>Uterus</td>
<td>414</td>
<td>414</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>190</td>
<td>190</td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>390</td>
<td>114</td>
<td>504</td>
</tr>
<tr>
<td>Melanoma</td>
<td>920</td>
<td>526</td>
<td>1,446</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>165</td>
<td>132</td>
<td>297</td>
</tr>
<tr>
<td>Other</td>
<td>597</td>
<td>579</td>
<td>1,176</td>
</tr>
<tr>
<td>Total incident cancers</td>
<td>6,328</td>
<td>4,447</td>
<td>10,775</td>
</tr>
</tbody>
</table>

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pooled blood from healthy volunteers are interspersed with the participant samples for use in future quality control assessment. We expect blood collection and storage to be completed in early 2001. A second proposal is under review to collect buccal cell DNA from mouthwash samples from at least 50,000 Nutrition Cohort members who did not give blood.

**Use of the Biorepository.** LifeLink was established to create an archive of serum, plasma, RBCs, and DNA, future analyses of which could be combined with the prospectively collected exposure and outcome data in the CPS-II Nutrition Cohort. The age of the cohort makes LifeLink particularly valuable for studying how hormonal, nutritional, genetic, and other factors measured in blood in middle age relate to the subsequent occurrence and/or progression of cancer. Based on Surveillance, Epidemiology, and End Results incidence rates and excluding persons with prevalent cancer, we expect approximately 420 incident cases of female breast cancer, 685 incident cases of colorectal cancer, 1165 incident cases of prostate cancer, and 700 incident cases of lung cancer during the first 5 years after blood collection. Future nested case-control studies using the archived specimens will be initiated as soon as sufficient numbers of specific cancers are identified. The maturity of the cohort and the availability of questionnaire information that predates blood collection and tumor diagnosis by 15 years will allow rapid testing of hypotheses.

To oversee this valuable resource, ACS will form a standing review panel comprised of intra- and extramural scientists, epidemiologists familiar with large cohort studies, and laboratory and other researchers who collaborate on studies that integrate cancer epidemiology, biology, genetics, and laboratory research. The precise questions to be addressed in LifeLink will depend on the scientific issues that are most relevant at the time, improvements in laboratory technology to study these issues, and the proposals that are judged to have the greatest scientific merit and largest implications for cancer research and/or control. Priority will be given to study proposals of high scientific merit that are best addressed prospectively and that test promising hypotheses rather than generate them. Approved proposals will be further developed and submitted as grant applications to the NIH or other funding agencies.

**Collaborative Research.** Historically, ACS intramural epidemiology research has greatly expanded its scientific contributions through multidisciplinary extramural collaborations. One series of collaborations involved autopsy studies, unrelated to CPS-I or CPS-II, with Dr. Oscar Auerbach, a research pathologist in New Jersey (67–74). These studies helped to demystify the carcinogenic effects of tobacco by demonstrating widespread phenotypic changes (also called a “field” effect) and a continuum of injury from precancerous changes to invasive cancers in the lung (67) and other organs (67–74), correlating closely with the amount and duration of smoking. This spectrum of injury was seen in tissues exposed directly [larynx, bronchi, and lung (68–72)] or indirectly (bladder, esophagus, and pancreas) to carcinogens in tobacco smoke (73, 74). Some 2000 tissue specimens (paraffin blocks) from over 1300 patients in the Auerbach studies have been saved in an archive that is still available for collaborative studies (75). Another historic collaboration with Dr. Irving Selikoff involved studies of lung cancer in asbestos-exposed insulation workers (76).

Currently, ACS epidemiologists collaborate extensively with extramural researchers. Ongoing collaborative studies with researchers at the CDC involve studies of tobacco, nutrition, obesity, and diabetes in relation to specific cancers. Collaborative studies with university researchers include ongoing studies of tobacco and hormones with Oxford University, studies of nutrition and air pollution with Harvard University, and studies of the economic implications of tobacco control policies with Duke University and Massachusetts Institute of Technology.

ACS is also participating in a NCI initiative to form a Consortium of Cohort Studies sufficiently large to address interactions between genetic factors and environmental expo-

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**Fig. 1.** Diagram of the LifeLink aliquoting scheme.
ures. Typically, several thousand cases are needed to provide statistically stable estimates of gene-environment or gene-gene-environment interactions. The current ACS proposal to collect buccal cell DNA from participants who have not already given blood in the CPS-II Nutrition Survey is motivated by the very large sample size needed to study interactions between environmental factors and genetic susceptibility.

Proposals to collaborate using the currently available questionnaire data are evaluated with regard to their scientific merit, timeliness, relevance to cancer, the suitability of ACS data to address the research question, and the likely productivity and collegiality of the working relationship. The mutual benefit of such collaborations is enhanced when the researchers can complete much of the research at the ACS Home Office in Atlanta and/or bring expertise that would otherwise not be available to the department. Funding for collaborative projects is generally sought either through external grants or by ACS fellowship support for visiting scientists. The department also provides several opportunities for training, career development, and/or sabbaticals through its fellowship program. Further information can be obtained by contacting Dr. Michael J. Thun, who succeeded Dr. Clark Heath as department head in 1998.

Research Opportunities

A major strength of the ACS cohort studies, historically, has been their size. Size remains critical for providing stable risk estimates in important subgroups of the CPS-II population such as the more than 480,000 lifelong nonsmokers and 52,000 African Americans. Size is also critical in measuring dose-response gradients over a wide range of exposure and in studying cancer end points of intermediate frequency. The age distribution of CPS-I and CPS-II allows certain cancer hypotheses to be tested more rapidly with greater statistical precision than is possible in younger, smaller cohorts. Participants are also more heterogeneous with regard to education and socioeconomic status than are health professionals in the Harvard cohort studies. Parallel analyses of certain hypotheses can be conducted in men and women, in African Americans and whites, and in various educational and occupational subgroups.

Another strength of the ACS cohorts is that comparisons between CPS-I and CPS-II provide an unusual longitudinal perspective on how mortality from tobacco smoking has changed over the last half-century in the United States. Valid comparisons are possible because both cohort studies used similar methods of selection, exposure ascertainment, and follow-up to measure tobacco smoking and mortality over several generations. The potential for longitudinal comparisons has been extended in the CPS-II Nutrition Survey, which collects more detailed and periodically updated information on nutrition, physical activity, weight and weight change, and medical screening. Future cohort studies can examine how ongoing changes in nutrition, other health-related behaviors, tobacco use, and medical care influence subsequent patterns of morbidity and mortality.

Conclusions

Over the last 50 years, the extraordinary progress in understanding cancer biology and in identifying many of the important “environmental” causes of cancer has often outstripped our ability to implement this knowledge equitably and effectively in controlling cancer. At the same time, advances in molecular biology and genetics are providing powerful new tools with which to understand the progressive development of cancer and the interplay between “environmental” causes of cancer and genetic factors that affect individual susceptibility. The Epidemiology and Surveillance Research program at ACS has a remarkable opportunity to address both of these challenges. By monitoring the occurrence of cancer and temporal trends in risk factors, social policies, and medical practices that affect cancer, Surveillance Research can accelerate the application of existing knowledge into practice. Analytic Epidemiology, in turn, can develop the potential of cohort studies to measure “environmental” exposures, to understand the interplay between these and genetic factors that affect individual susceptibility, and to translate this knowledge into applications that improve public health.

Acknowledgments

We acknowledge the hundreds of thousands of ACS volunteers whose trust and goodwill make epidemiological research at ACS possible, and who provide much of the satisfaction and focus to the work. We also thank the Illinois Division for generous support of the CPS-II Nutrition and LifeLink Cohorts.

References


