Meeting Report

Eighteenth Annual Meeting of the American Society of Preventive Oncology

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The 18th Annual Meeting of the American Society of Preventive Oncology (ASPO) was held March 6–9, 1994, in Bethesda, MD. President Ellen R. Gritz (University of Texas M. D. Anderson Cancer Center, Houston, TX) presided and Margaret R. Spitz (M. D. Anderson Cancer Center) chaired the 1993 Program Committee.

Three affiliated workshops preceded the annual meeting. Alfred Neugut (Columbia University School of Public Health, New York, NY) chaired a New Investigator Workshop; concurrently a Joint Meeting of National Cancer Institute Cancer Prevention Fellows and Preventive Oncology Awardees was held. Caryn Lerman and Bruce Trock (Lombardi Cancer Prevention Center, Georgetown University, Washington DC) developed and cochaired a special genetics workshop, "Introduction to Molecular Genetics: From the Laboratory to Prevention." The workshop was well attended with more than 120 participants, and included presentations by Kenneth D. Tartof (Fox Chase Cancer Center, Philadelphia, PA), Alfred Knudson (Fox Chase Cancer Center) and Terri Beaty (Johns Hopkins University, Baltimore, MD), as well as Drs. Lerman and Trock.

Throughout the meeting, study groups met at breakfast sessions. The Chemoprevention Study Group focused on a discussion of the monitoring and evaluation side effects of chemotherapeutic agents led by Gary Goodman (Swedish Hospital Tumor Institute, Seattle, WA) and recruitment strategies for large scale trials led by Mary Daly (Fox Chase Cancer Center). Goodman stressed the need for standard questions to assess symptoms, a standard physical exam, and a standard grading scale for symptoms and physical findings. Daly discussed both standard and alternative communication strategies in participant recruitment, as well as drop off in response to negative publicity.

The Women's Cancers Study Group, organized by Kathy Helzlsouer (Johns Hopkins University) addressed the issue of quality control in breast cancer screening. Florence Houn (Food and Drug Administration) discussed the Food and Drug Administration's role in the certification of mammography facilities: it develops standards, trains inspectors, and evaluates performance needed for certification, which will become mandatory in October 1994. Robert Brown (National Cancer Institute) presented the results of a survey of more than 1000 mammography facilities in the United States, as well as a more detailed analysis of a sample of 50 facilities in which an investigation of quality control of technical and medical physics aspects yielded satisfactory results. Recommendations for repeated mammography were followed in 70% of the cases, for needle aspiration in 100%, and for biopsies in 75%. Carol A. Chrvala (Colorado Department of Health) reported on the Colorado statewide surveillance of screening mammography program, a voluntary coalition of 50 centers. The coalition includes active educational and follow-up efforts. Of a total of 136,316 mammographies, 0.6% resulted in a diagnosis of suspected carcinoma.

The Diet Study Group, chaired by Larry Kushi (University of Minnesota, Minneapolis MN) and Gladys Block (University of California-Berkeley) heard a presentation by Mark Messina (Washington DC) on soy as an agent in cancer prevention. Several compounds in soybeans have demonstrated anticancer activity, including protease inhibitors, phytosterols, saponins, inositol, and isoflavones. Soy-derived isoflavones, principally genistein, may act through one or more documented mechanisms: as a steroid agonist; as an antioxidant; as a kinase inhibitor; and/or as an inhibitor of angiogenesis at very high doses. He discussed both the experimental and epidemiological evidence which highlight the potential for dietary chemoprevention with soy-based foods and genistein.

The Tobacco Study Group Breakfast, chaired by Michael Fiore (University of Wisconsin, Madison WI), reviewed the California experience in tobacco control. Charles L. Gruder (Tobacco Related Disease Research Program) discussed the structure, function, and activities of a tobacco tax-funded research grant program. John Pierce (University of California-San Diego) presented data from an unreleased report evaluating the California tobacco program. Encouraging gains have been made in the reduction of household and worksite environmental tobacco smoke exposure, smoking prevalence, and per capita consumption in adults. However, no such reduction in tobacco use by children and adolescents has been achieved to date. Targeted advertising by tobacco companies has nullified the success of the program in underage smokers.

Five symposia were included in the meeting program. Frank Meyskens, Jr. (University of California-Irvine) chaired the first symposium, "Retinoids in Chemprevention Trials: An update." Reuben Lotan (M. D. Anderson Cancer Center) discussed the mechanisms of action of retinoids and presented data on the regulation of gene expression by retinoids from studies of premalignant lesions of oral mucosa. Normal stem cells in the oral cavity express RARβ,[2] and

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[2] The abbreviations used are: RARβ, retinoic acid receptor β; CIN, cervical intraepithelial neoplasia; CML, chronic myelogenous leukemia; ASPO, American Society of Preventive Oncology; NHANES, National Health and Nutrition Examination Survey.

its expression is gradually lost during the carcinogenic process. Expression of RARβ is restored in premalignant oral lesions treated with 13-*cis*-retinoic acid; 39% of lesions are RARβ positive before treatment *versus* 92% after treatment. Scott Lippman (M. D. Anderson Cancer Center) followed with a presentation on retinoids in the prevention of upper aerodigestive tract and lung cancers. In these cancers, the rationale for chemoprevention is based on cancer as a multistep process and the concept of field carcinogenesis, which is especially relevant in tobacco-related cancers. He presented results of completed trials using high-dose and low-dose 13-*cis*-retinoic acid with a variety of study outcomes (disease recurrence, survival, occurrence of second primaries). A total of 6 trials (5 Phase IIb and 1 Phase III) have been completed with 13-*cis*-retinoic acid at 0.5 mg/kg/day with positive results. Other trials in progress include combinations of drugs (β-carotene and 13-*cis*-retinoic acid) to halt progression of bronchial squamous metaplasia, and a multicenter trial of stage 1 non-small cell lung cancer. John DiGiovanna (NIH, Dermatology Branch, Bethesda, MD) reviewed the history of chemoprevention of skin cancer with isotretinoins in patients with xeroderma pigmentosum. Studies of these patients, who have extraordinary rates of skin cancer as a result of abnormal repair of UV light-induced DNA damage, have provided clear evidence of the effectiveness of isotretinoin; however, the lowest effective dose with the least toxicity shows large interpatient variability and high rates of recurrence after drug withdrawal. Frank Meyskens then presented data on retinoids in two different cancers, CIN and CML. Phase II trials of retinoic acid indicated that 50% of CIN patients had a complete histological response. Phase III trials are especially important with this lesion because of the high proportion of spontaneous regressions of CIN. Phase III trials indicate no effect of retinoic acid in regression of severe dysplasia and some regression of mild and moderate dysplasia compared to placebo. Meyskens then discussed oral vitamin A as adjuvant therapy with busulfan in the treatment of CML. Improved survival has been demonstrated in patients who received adjuvant vitamin A. An on-going randomized trial will evaluate the effectiveness of *trans*-retinoic acid plus interferon compared to *trans*-retinoic acid plus hydroxyurea in prolonging survival with CML.

Ellen Gritz chaired a symposium on behavioral science interventions in cancer prevention and screening trials. Susan Curry (Group Health Cooperative, Seattle, WA) described The Eating Pattern Study, a randomized controlled dietary intervention trial which included 28 physician's practices with 75 patients/practice. The intervention group received a self-help booklet and had access to a nutritionist by phone, and the goal was to reduce fat and increase fiber intake. At base line, both treatment and control groups reported 37% of calories from fat. At 3 and 12 months, the intervention group had a small but significant reduction in the percentage of calories from fat. Those who read and used the self-help materials showed the greatest reduction. The effect of intervention on fiber intake was puzzling. Both groups reduced rather than increased fiber intake; however, the intervention group had less of a reduction. David Abrams (Brown University, Providence, RI) described the utility of multiple risk factor interventions, rather than single risk factor intervention at the worksite, using the stage of change paradigm. As individuals change, so does the group, in this case the workforce. A program with a large reach and moderate efficacy will have a greater impact than one with high efficacy which reaches few. The Working Well Trial is a multicenter trial randomized at the worksite level which focuses on motivation to change over time and builds on cumulative effect. The interventions tested included smoking cessation and dietary change. Mario Orlandi (American Health Foundation, New York, NY) presented an overview of The Harlem Health Connection Study which seeks to reduce smoking rates in an urban, underserved population. There are few available data on effective smoking control approaches in underserved populations. This study in Harlem recruited 3000 eligible smokers via sign-up cards, and 1280 self-selected participants were randomly assigned to intervention or control groups. Preliminary data indicate a 7.5% quit rate in the intervention group and 2.2% rate in the control group. This program was delivered as part of a community health network and materials (printed and video) were from an Afrocentric perspective. Roshan Bastani (University of California-Los Angeles) discussed her work in a risk notification intervention for women at high risk of breast cancer. Breast cancer patients were randomly selected from the California Tumor Registry, contacted after physician notification, and asked to provide information on first degree female relatives. The relatives were then randomly allocated to intervention (personalized risk assessment, brochures, etc. encouraging mammography) or control groups. Participants were later recontacted by mail or telephone. In the 12 months between intervention and posttest, a significantly higher proportion of women in the intervention group had a mammogram (69% *versus* 61% in control group). Bastani noted, however, that the letter used in the program produced fear and anxiety in 40% of the intervention subjects.

The third symposium, "Biologic Specimen Banking: An Investment for our Future," was chaired by Barbara Hulka (University of North Carolina-Chapel Hill). Three invited speakers from the NHANES program discussed issues related to specimen banking from practical to ethical and legal. Elaine Gunter (NHANES Laboratory, Centers for Disease Control, Atlanta, GA) presented an overview of specimen collection and bank operation. She noted that consideration about banking begins at study design and continues through collection, storage, and utilization. The major anticipated uses of the bank should be delineated *a priori*; the anticipated yield of information over time should be evaluated; legal and ethical issues should be addressed; the types of samples and the best storage for the specimens should be determined; all procedures used should be documented to minimize bias; and specimen use should be tracked in the computer system (freeze-thaw history, etc.). She recommended serum aliquots of 0.5 ml in small containers to minimize waste of materials and space. Gunter announced that the Centers for Disease Control is building a new state-of-the-art specimen banking facility. Robert Murphy (National Center for Health Statistics, Hyattsville, MD) described aspects of NHANES III. He emphasized the need for a standardized protocol to minimize site-specific differences in data collection. He provided information on specific types of specimens and their unique considerations and cautioned that, when in doubt, researchers should ask the lab. Diane Wagner (National Center for Health Statistics) provided a discussion of the ethical and legal issues in specimen banking. A consideration of information sharing after specimen analysis includes such issues as when to inform, whom to inform, how to inform, and maintaining confidentiality. The use of banked samples requires consid-

eration of quality control, informed consent for unanticipated uses, access to identifiers, a hierarchy for the selection of requests for specimen batches, and the obligation for future testing (retests for verification and interpretation, tests for different risk factors, and follow-up).

Frederica Perera (Columbia University) chaired a symposium on biomarkers of exposure, response, and susceptibility. Peter Shields (National Cancer Institute) spoke on biomarkers of cancer susceptibility, including inherited and acquired predisposition, and focused on P-450 metabolic polymorphisms and lung cancer. Noninvasive determination of phenotype is possible using several methods, including metabolism of debrisoquine. He illustrated an interaction between debrisoquine phenotype and occupational exposure to asbestos or polycyclic aromatic hydrocarbons. Extensive metabolizers with one of these exposure had a markedly higher risk of lung cancer than poor metabolizers with exposure or extensive metabolizers with no exposure. 7-alkyl Gp adducts are markers of exposure to tobacco-specific *N*-nitrosamines. Extensive metabolizers have significantly higher adduct levels than poor metabolizers. Phenotype is most important for light smokers and persons with passive exposure and is less of a determinant of risk among heavy smokers where dose overwhelms phenotype. John Groopman (Johns Hopkins University) next presented data on aflatoxin adducts and *p53* mutations in hepatocellular cancer in China. Aflatoxin is a potent and ubiquitous carcinogen with huge differences in exposure dose worldwide. The biomarker of aflatoxin exposure most highly correlated with dietary intake is the aflatoxin B_1-N7 guanine adduct. Hepatitis B virus surface antigen acts as a cell proliferation agent in liver and increases risk of hepatocellular carcinoma. Groopman reported results of a nested case-control study from a cohort of 18,244 adult men aged 45–64 in Shanghai which measured both of these exposure biomarkers. Relative to hepatitis B virus surface antigen-negative persons with no aflatoxin detected in urine, a 59-fold increased risk of hepatocellular carcinoma was found for men positive for both markers. George Lucier (National Institute of Environmental Health Sciences, Research Triangle Park, NC) considered gene-environmental interactions. Biomarkers offer promise in reducing some of the uncertainty in risk assessment. Data are generally available for plotting dose-response relationships at high doses, but the shape of the curve has historically been estimated for the low-dose region. Dioxin and its analogues act as potent and persistent environmental hormones. Dioxin interacts with DNA bound to its receptor. The amount of receptor is highly variable among individuals and may indicate differences in risk from dioxin exposure. Risk assessment will be further refined when individual variation is better understood and included in assessment. Perera discussed the use of biomarkers in risk assessment and gave the example of carcinogen-DNA adducts which can provide comparative molecular dosimetry data in humans and laboratory animals at low levels of exposure. She also showed polycyclic aromatic hydrocarbon-DNA data from four different studies that demonstrated a nonthreshold dose-response. She discussed biomarkers as a handle on interindividual variability in biological response to carcinogens. The National Academy of Sciences has recently underscored the need for explicit consideration of this variable in risk assessment.

The final symposium, chaired by William Blot (National Cancer Institute), focused on esophageal adenocarcinoma. Susan Devesa (National Cancer Institute) presented esophageal cancer time trends and international variation in overall rates. Historically, most esophageal cancers have been squamous cell. The proportion of cases which are adenocarcinoma range from 3.6% to 29.9% in men and 2.2% to 27% in women in a comparison of rates from several European countries, although the actual rates of adenocarcinoma are considerably less variable (0.6–1.4/100,000). However, rates of adenocarcinomas of the esophagus and gastric cardia have both increased in recent time periods, and both are higher in white males than in black males. The increases in incidence rates in the Surveillance, Epidemiology, and End Results program average 10.3%/year in men and 8.8%/year in women from 1976–1978 to 1988–1990. Adenocarcinoma is now more common than squamous cell cancers of the esophagus among white males. Stuart Spechler (Harvard University) reviewed the role of antecedent Barrett's esophagus in esophageal adenocarcinoma. Barrett's esophagus results when metaplastic glandular epithelium replaces the normal epithelium of the distal esophagus. This lesion is found in 10–15% of patients with esophageal reflux, but autopsy data suggest that clinic data greatly underestimate the prevalence of Barrett's: 376/100,000 at autopsy *versus* 23/100,000 in a clinic series at the Mayo Clinic. Present estimates suggest that 1 in 125 patients/year with Barrett's esophagus develops cancer; however, the cost of surveillance with annual endoscopy is quite high ($62,000/cancer detected). Although surveillance results in earlier detection and improved 5-year survival, as yet no data indicate that early detection reduces mortality. A recent endoscopy-based study highlighted an entity which may contribute to the recent rise in esophageal adenocarcinoma. Of 139 patients with no Barrett's visualized, 25 (18%) were found to have "short segment Barrett's" at histological evaluation. Environmental and host risk factors for esophageal adenocarcinoma were reviewed in the final presentation by Thomas Vaughan (University of Washington, Seattle, WA). Risk factors can be broadly classified into those which promote reflux (dietary fat, obesity, alcohol, tobacco, hiatal hernia, selected medications) and those which irritate directly (alcohol, tobacco, nonsteroidal antiinflammatory drugs). On the basis of results of three case-control studies, alcohol and tobacco appear to be associated with increased risk of esophageal adenocarcinoma, but the magnitude of the association is much smaller than that for squamous cell carcinoma. Fruits and vegetables exert protective effects whereas dairy products and a high fat diet are associated with increased risk. A possible link between colorectal cancer and adenocarcinoma of the esophagus has been noted in men, but not women, and requires further evaluation. Future research directions should also include the role of medications (nonsteroidal antiinflammatory drugs, H2-blockers, and others), predictors of metaplasia in patients with reflux symptoms, and the role of genetic susceptibility.

Five presented paper sessions were held and included two sessions on breast cancer, as well as sessions on molecular epidemiology, biomarkers, and a miscellaneous topics session Abstracts for papers presented in these sessions were published in the March, 1994, issue of Cancer Epidemiology, Biomarkers and Prevention. An evening poster session included a total of 50 posters. The Best Poster Award was presented to Jonine Bernstein for her poster on

the absolute risk of developing a second primary breast cancer.

The Joseph Cullen Memorial Award was presented this year to C. Tracy Orleans (Fox Chase Cancer Center). Her address was directed to self-help tobacco cessation methods. She noted that self-help is the preferred approach as the paradigm shifts from a clinical to a public health model and that it is relatively effective. Over 90% of 40 million ex-smokers quit on their own, and only 1.5% ever used formal cessation programs. She reviewed five objectives for cessation programs developed by an National Cancer Institute-convened expert panel, added two additional objectives, and presented intervention opportunities and a research agenda for each objective. The objectives are to: broaden delivery mode; target the program to all stages of smoking cessation; include critical information and strategies in self-guided programs; target programs to high risk populations; consider adjuncts to boost success rates; link self-help treatment and public policy initiatives; and capitalize on health care reform and the growth in managed care.

Anthony B. Miller (University of Toronto, Ontario, Canada) received the 1994 Distinguished Achievement Award. In his address he posed the question, "Is it time for a paradigm shift in screening for cancer?" He challenged the assumption that early detection through screening is always beneficial. This lecture will be published in Cancer Epidemiology, Biomarkers and Prevention.

Devra Lee Davis (Assistant Secretary, United States Department of Health and Human Services) gave the keynote address, an overview of cancer prevention: what we know; what we don't know; and what we need to know. She discussed cancer patterns observed in two recently published articles which she coauthored, and highlighted the excesses of several types of cancer in farmers, as well as the newly-initiated Long Island Breast Cancer Study.

Richard Love (University of Wisconsin) was presented the ASPO Distinguished Service Award for his pivotal contributions to the ASPO throughout his tenure as Secretary-Treasurer. As President-Elect (1995–1997), he will no doubt continue to provide leadership and dedication as he has for many years. Alfred Neugut was elected to serve as Secretary-Treasurer of the ASPO. The 1995 annual meeting will be held in Houston, TX.

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