

PROGRAM
and
ABSTRACTS

21st Annual Meeting

*American Society
of
Preventive Oncology*

March 23 - 25, 1997

Royal Sonesta Hotel
New Orleans, Louisiana

Program Chair: **Marcy A. List, PhD**
University of Chicago Cancer Research Center

Sponsored by:
The American Society of Preventive Oncology, Schering Corporation, SmithKline Beecham, and a conference grant from the National Institutes of Health/National Cancer Institute.

American Society of Preventive Oncology

The American Society of Preventive Oncology is an active and growing organization that is striving to: 1) promote the exchange and dissemination of information and ideas relating to cancer prevention and control; 2) identify and stimulate research areas in cancer prevention and control; and 3) foster the implementation of programs in cancer prevention and control.

After attending the **21st Annual Meeting** of the American Society of Preventive Oncology, participants should be better able to:

- * evaluate the effect of managed care on prevention service delivery and research;
- * advise patients and other health care professionals regarding tobacco cessation programs;
- * evaluate the desirability of genetic testing and behaviors it evokes;
- * understand the relationship between diet, life style and chronic disease in the public health arena; and
- * advise health professionals regarding appropriateness of screening procedures in specific areas.

Meetings of the American Society of Preventive Oncology are organized for professionals in clinical, educational or research disciplines who appreciate the challenges of a multidisciplinary scientific forum and who are committed to a comprehensive approach to cancer prevention and control.

ASPO - 1997

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University of Wisconsin School of Medicine
1300 University Avenue, Suite 7-C
Madison, WI 53706
(608) 263-7066

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Alfred I. Neugut, MD, PhD
Columbia University
School of Public Health
600 West 168th Street
New York, NY 10032
(212) 305-9414

Past President

Ellen R. Gritz, PhD
The UT M. D. Anderson Cancer Center
Department of Behavioral Science
1515 Holcombe Blvd., Box 243
Houston, TX 77030
(713) 792-0919

STUDY GROUP CHAIRS

Chemoprevention Co-Chair

Mary Daly, MD
Fox Chase Cancer Center
510 Township Line Road
Cheltenham, PA 19012
(215) 728-2705

Diet & Nutrition

R. Sue McPherson
University of Texas/Public Health
1200 Herman Pressler
Houston, TX 77096
(713) 500-9317

Tobacco Co-Chair

Paul Cinciripini, PhD
The University of Texas
M. D. Anderson Cancer Center
1515 Holcombe Blvd., Box 243
Houston, TX 77030
(713) 792-0919

Tobacco Co-Chair

Susan Curry, PhD
Group Health Cooperative
Center for Health Studies
1730 Minor Ave., Suite 1600
Seattle, WA 98101
(206) 286-2873

Women's Cancers

Kathy Helzlsouer, MD, MHS
Johns Hopkins University
School/Hygiene & Public Health
615 N. Wolfe St., Rm 6029 B
Baltimore, MD 21205
(410) 955-9727

Executive Committee, cont'd.

Chemoprevention Co-Chair

Robert Bostick, MD, MPH
The Bowman Gray School of Medicine
Medical Center Blvd.
Winston-Salem, NC 27157
Seattle, WA 98104
(206) 386-2122

President-Elect

Margaret R. Spitz, MD
The University of Texas
M. D. Anderson Cancer Center
1515 Holcombe Blvd., Box 189
Houston, TX 77030
(713) 792-3020

At-large Executive Committee Members

Pelayo Correa, MD
L S U Medical Center
Department of Pathology
1901 Perdido Street
New Orleans, LA 70112
(504) 568-6035

Robert Hiatt, MD, PhD
Kaiser Permanente
Division of Research
3505 Broadway
Oakland, CA 94611
(510) 450-2109

Elizabeth Holly, PhD, MPH
UC - San Francisco
Department of Epi. & Biostatistics
1388 Sutter Street, Suite 920
San Francisco, CA 94109
(414) 476-3345

Jon Kerner, PhD (Membership)
Georgetown University
Lombardi Cancer Research Cntr
2233 Wisconsin Ave., NW, #535
Washington, DC 20007
(202) 687-0801

Bernard Levin, MD
The University of Texas
M. D. Anderson Cancer Center
1515 Holcombe Blvd., Box 203
Houston, TX 77030
(713) 792-3900

Rodger Winn, MD (Policy)
The University of Texas
M. D. Anderson Cancer Center
1515 Holcombe Blvd., Box 501
Houston, TX 77030
(713) 792-8515

Marcy A. List, PhD
University of Chicago Cancer Research Center
1997 Program Chair, *ex officio* member

1997 Program Committee

Marcy A. List, PhD, Chair
University of Chicago Cancer Research Center

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University of California, San Diego

Jean Richardson, DrPH
U S C School of Medicine

Announcements

MESSAGES

Contact Judy Bowser at the ASPO registration desk if you are expecting a message or wish to leave one for someone.

SPECIAL ACKNOWLEDGEMENTS

The ASPO Executive Committee offers special thanks to Program Chair, Dr. Marcy List for her extraordinary commitment in directing the arrangement and development of the program for this meeting.

The ASPO Executive Committee wishes to thank the co-sponsors of this 21st Annual Meeting. The corporate sponsors have given the Program Committee complete latitude in choosing the speakers and program content which are underwritten by their contributions.

SmithKline Beecham has recently made a commitment to sponsor the Joseph W. Cullen Memorial Award recipient at the ASPO Annual Meetings through the year 2001. The entire ASPO membership is grateful that Dr. Cullen may continue to be remembered in this way. The "Cullen Award" recipient is designated by the Tobacco Study Group.

FOR THE FUTURE. . .

Please take a few minutes at the close of the meeting to complete the questionnaire at the back of the printed program. This will help future Program Committees and conference staff to better meet your professional and logistical needs. If you see any of the following people during the course of the meeting, they will welcome your comments. They constitute the Program Committee for the 1998 Meeting.

Chair: Robin Bostick, MD, The Bowman Gray School of Medicine
Melissa Bondy, PhD, The UT M. D. Anderson Cancer Center
Mary Daly, MD, PhD, Fox Chase Cancer Center
Wendy Demark-Wahnefried, PhD, Duke University Medical Center
Funmi Olopade, MD, University of Chicago Medical Center

American Society of Preventive Oncology

21st Annual Meeting
March 23-25, 1997, New Orleans, Louisiana

SUNDAY, MARCH 23

REGISTRATION -- 12:00 - 5:00 pm

1:00-5:00 pm
Choctau Room

New Investigators Workshop

(Open for participation only to those with accepted proposals)

Organizer: **Alfred I. Neugut, MD, PhD**
Associate Professor
Columbia University

Faculty: **John D. Potter, MD, PhD**
Fred Hutchinson Cancer Research Center

Melissa Bondy, PhD
The UT M. D. Anderson Cancer Center

Thomas A. Sellers, PhD, MPH
University of Minnesota

9:00 am-1:00 pm Joint Meeting of NCI Cancer Prevention Fellows and Preventive
Oncology Awardees

North Ballroom

4:30 - 9:00 pm Meeting of Cancer Center Associate Directors for Prevention &
Tesche/Belle Grove Control -- Working Dinner

6:30-10:00 pm Executive Committee Meeting -- Working Dinner
Oak Alley/Madewood

Notes

ASPO 1997 -- General Session

MONDAY, MARCH 24

REGISTRATION -- 7:00 am - 5:00 pm

7:30-8:45 am Hot topics Breakfast Sessions (Two Concurrent Sessions)

Acadia Suite Screening: Chair: Victor Vogel, MD
University of Pittsburgh

"Screening Women Ages 40-49 with Mammography: Drafting
the ASPO Consensus Statement"

Nutrition: Chair: R. Sue McPherson, PhD
University of Texas, School of Public Health

Presenter: Tom Baranowski, PhD
Dept. of Behavioral Science/Div. Cancer Prevention
The UT M. D. Anderson Cancer Center

"Why Aren't Community Interventions Working as Desired?"

9:00 am
Grand Ballroom

General Session

Welcome

Richard R. Love, MD, MS
ASPO President, University of Wisconsin Medical School

9:15-10:15 am Distinguished Achievement Award and Address

Barbara K. Rimer, DrPH
Duke University Medical Center
Cancer Prevention, Detection & Control Research

*"Breaking Down the Barriers to Informed Decisions and
Behavior of Change"*

Monday, March 24 - cont'd.

10:30-12:30 pm

SYMPOSIUM – *Phoods and Phytochemicals*

Chair: **Cheryl Ritenbaugh, PhD, MPH**
The University of Arizona

"Evolution of Diet and the Rise of Chronic Disease"

George J. Armelagos, PhD
Professor of Anthropology, Emory University

"New Perspectives on the Carotenoids: A Complex Relationship with Cancer Prevention"

Cheryl L. Rock, PhD, RD, FADA
Assistant Professor, Program In Human Nutrition;
The University of Michigan

"Living With a Tyrosine Kinase Inhibitor"

Steve Barnes, PhD, Professor of Pharmacology and
Toxicology, U of Alabama at Birmingham

Discussion to be led by: **Cheryl Ritenbaugh**
(Implications for public health; how will this be translated
into interventions?)

12:30-1:30 pm

Lunch on your own (Poster set-up time)

Posters may be set up in the Evangeline Suite

Notes

Monday, March 24 - cont'd.

1:30-3:00 pm **SYMPOSIUM – *Managed Care: Implications for Prevention***

Chair: **Bernard Levin, MD**
The UT M. D. Anderson Cancer Center

"Prevention Research Opportunities in Managed Care"

Edward H. Wagner, MD, MPH
Director, Center for Health Studies of Group Health Coop.
Professor, University of Washington, Seattle

"How Does Managed Care Effect Preventive Services?"

Robert Kaplan, PhD
University of California School of Medicine
Department of Family & Preventive Medicine

3:00 - 3:15 Break

3:15-3:45 pm Business Meeting

Notes

Monday, March 24 - cont'd.

3:45-5:15 pm

Presented Papers (2 concurrent sessions)

Grand Ballroom

Session A – Cancer Epidemiology

Chair: **Susan Gapstur, PhD**
Northwestern University

3:45 pm

W. Thomas London, MD

Fox Chase Cancer Center

"Epidemiology of Liver Cancer in the Haimen City Cohort"

4:05 pm

Karen J. Goodman, PhD

The UT Houston-School of Public Health

"Feasibility Study: Helicobacter Pylori Transmission Intervention in Colombian Children"

4:25 pm

Shine Chang, PhD

The UT M. D. Anderson Cancer Center

"Trends and Patterns of Inflammatory Breast Cancer by Race: The Experience of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program from 1975 to 1992"

4:45 pm

Habibul Ahsan, MD

Columbia School of Public Health

"Association of Adenocarcinoma and Squamous Cell Carcinoma of the Esophagus with Tobacco-Related and Other Malignancies"

5:05 pm

Steven S. Coughlin, PhD

Tulane School of Public Health

"Predictors of Mortality from Kidney Cancer in 332,547 Men Screened for the MRFIT"

(Abstracts immediately follow on left-hand pages, with space for notes on right-hand pages.)

Notes

Abstracts

Session A: Cancer Epidemiology

3:45 - 5:15 PM

EPIDEMIOLOGY OF LIVER CANCER IN THE HAIMEN CITY COHORT WT London¹, AA Evans¹, G-C Chen², L Shen², W-Y Lin³, P An¹, K McGlynn¹, L-L Gao¹, E Ross¹, A Balshem¹, F-M Shen¹, and the Haimen City Collaborating Group²; Fox Chase Cancer Center¹, Philadelphia, PA; Haimen City Anti-Epidemic Station², Haimen, China; School of Public Health³, Shanghai Medical University, Shanghai, China.

Risk factors for hepatocellular carcinoma (HCC) were studied in a cohort of 60,984 men in Haimen City, Jiangsu Province, China. Blood samples and questionnaire information were collected from all members of the cohort and hepatitis B infection (HBsAg) status determined at study entry. 9630 were HBsAg(+). By 1/1/1996, 193,610 person-years (py) had been accumulated by cohort members. Deaths of 1007 men in the cohort were identified from Death Certificates; 349 (34.7%) were caused by HCC and 11.2% by chronic liver disease (CLD). Examination of deaths by HBsAg status at enrollment revealed an age-adjusted all-cause mortality of 1241 per 10⁵ py among the HBsAg(+) men compared with 311/10⁵ py for the HBsAg(-) men (RR=4.0). The increased risk of death among the HBV carriers was accounted for entirely by excess risks of HCC (RR=13.7) and chronic liver disease (RR=15.2).

A nested case-control analysis of the initial questionnaire information was performed on 347 HCC deaths. 5 controls were matched for each case on township of residence, age \pm 2 years, and HBsAg status. Significant factors were: a) occupation, peasants (farmers) were at higher risk than non-peasants (odds ratio, OR=1.8, $p < 0.001$); b) history of clinically diagnosed acute hepatitis (OR=1.8, $p < 0.001$); c) history of cirrhosis (OR=5.1, $p = 0.002$); and d) family history of HCC (OR=2.2, $p < 0.001$); 1st degree relative affected (OR=2.5, $p < 0.001$); 2nd degree relative affected (OR=2.8, $p = 0.01$). Neither cigarette smoking nor alcohol consumption was associated with an increased risk of HCC. Stratifying the entire cohort by HBsAg status, history of acute hepatitis, and family history of HCC revealed an age-adjusted HCC mortality of 2184/10⁵/yr for men positive for all three factors compared with 50/10⁵/yr for those negative for the three factors (RR=43.7). Biomarker analyses will further define this highest risk group, permitting precise targeting of prevention efforts.

Notes

Feasibility Study: *Helicobacter pylori* Transmission Intervention in Colombian Children. Goodman KJ¹; Fontham ETH²; Bravo LE³; Ruiz B²; Correa P². ¹University of Texas-Houston School of Public Health; ²Louisiana State University Medical Center; ³Universidad del Valle, Cali.

Control of *H. pylori* infection has promise for reducing the occurrence of gastric cancer, one of the world's deadliest neoplasms. We conducted a study to assess the feasibility of implementing potential *H. pylori* control measures among children in Pasto, Colombia. 65 children infected with *H. pylori* received standard triple therapy while their families were randomized to one of four interventions: a) concurrent antibiotic treatment of infected family members; b) 14-week water purification regimen; c) a and b; d) treatment of index child only. *H. pylori* status was determined by the 13C-urea breath test at 4 and 12 weeks post-treatment. 79% of the children had negative breath tests at 4-weeks post-treatment, with no clear difference across intervention groups. Preliminary results for 40 index children who were negative for *H. pylori* at 4 weeks show that the 12-week cumulative reinfection was 15%. The family treatment regimen yielded a 12-week risk ratio for reinfection of 0.24 (95% CI. 0.03-1.91), while the water regimen showed no clear effect. The results suggest that 1) standard anti-*H. pylori* therapy is reasonably effective among Andean children; 2) concurrent treatment of infected family members may reduce the risk of reinfection; and 3) the potential for waterborne transmission remains unclear.

TRENDS AND PATTERNS OF INFLAMMATORY BREAST CANCER BY RACE: THE EXPERIENCE OF THE NATIONAL CANCER INSTITUTE'S SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS (SEER) PROGRAM FROM 1975 TO 1992. Chang S¹, Parker SL², Pham T¹, Buzdar A¹, Hursting SD¹. M.D. Anderson Cancer Center, Houston, TX¹ and American Cancer Society, Atlanta, GA². The etiology of inflammatory breast cancer (IBC), a rare and aggressive form of breast cancer, is poorly understood. We present trends and patterns for IBC by race using SEER program data from 1975 to 1992. We calculated age-adjusted and age-specific incidence rates for IBC using all cases diagnosed among whites and African American women (ICD-O-2 code 8530/3). For contrast, we compared IBC rates to those calculated for all other invasive breast cancers combined. From 1975 to 1992, incidence rates for African Americans were 29% greater than those for whites (0.62 per 100,000 vs. 0.48 per 100,000). Comparison of age-specific rates suggested that African Americans had a higher risk of IBC than whites from ages 35 to 64 years, in contrast to the increased risk of other breast cancers observed for African Americans (relative to whites) under 40 years. Between 1975-76 and 1991-92, the overall incidence of IBC increased two-fold for African Americans from 0.65 to 1.25 cases per 100,000 and for whites from 0.35 to 0.70 cases per 100,000. This increase was much higher than the percentage increases observed for other breast cancers by race during the same time period. Our results confirm and extend the only previous report of IBC patterns based on 1975-1981 SEER data (Levine et al. 1985), and reveal important racial variations in risk and age at diagnosis of IBC. Furthermore, differences between IBC and other invasive breast cancers may suggest divergent etiological pathways.

*Supported by Program in Cancer Prevention NCI-R-25-CA57730.

Notes

Association of Adenocarcinoma and Squamous Cell Carcinoma of the Esophagus with Tobacco-Related and Other Malignancies

Ahsan H¹, Neugut AI^{1,2}, Gammon MD¹. From the ¹Division of Epidemiology, School of Public Health, and ²Division of Oncology, Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York.

To explore the etiology of esophageal and gastric cardia adenocarcinoma (EGA), one of the fastest rising cancers in the developed world, we conducted a retrospective cohort analysis utilizing data from the Surveillance, Epidemiology and End Results (SEER) Program to calculate the age-, sex- and period-adjusted standardized incidence ratio as an estimate of the relative risk (RR) of developing esophageal adenocarcinoma (EGA) or squamous cell carcinoma (ESC) following cancers of other sites. We found a significantly elevated risk of EGA following cancers of the lung (RR 1.9 in men and RR 2.0 in women), and head and neck (RR 2.1 in men and RR 6.3 in women) and a stronger elevated risk of ESC following cancers of the lung (RR 2.8 in men and RR 5.1 in women) and head and neck (RR 9.6 in men and RR 38.8 in women). A significantly elevated risk following breast cancer in women was observed for both EGA (RR 2.6, 95% CI 1.8-3.7) and ESC (RR 1.4, 95% CI 1.1-1.9). We also found significantly elevated risk of EGA following bladder (RR 2.0), colorectal (RR 1.7) and prostate (RR 1.4) cancer in men and of ESC following colorectal cancer (RR 1.7) in women. The association with tobacco-related malignancies in this study reinforces the role of tobacco in the etiology of esophageal cancers which appears stronger for squamous cell carcinoma than adenocarcinoma, and in women than men. The study also provides new evidence about the association of both adenocarcinoma and squamous cell carcinoma of the esophagus with breast cancer in women.

Predictors of Mortality from Kidney Cancer in 332,547 Men Screened for the MRFIT. Coughlin S, Neaton J, Randall B, Sengupta A. Tulane University School of Public Health and Tropical Medicine, New Orleans, LA

We examined predictors of mortality from kidney cancer in 332,547 men who were screened as part of the Multiple Risk Factor Intervention Trial (MRFIT). The vital status of each member of this cohort was ascertained through 1990. Death certificates were obtained from state health departments and coded by a trained nosologist. Three hundred and ninety eight deaths due to kidney cancer occurred in the cohort of 332,547 men after an average of 16 years of follow-up. The age-specific rates of mortality from kidney cancer increased from 0.34 per 10,000 person-years among men aged 35-39 to 1.34 per 10,000 person-years among men aged 55-57. We used the proportional hazards model to study the joint association of age, race, income, blood pressure, cigarette smoking, and use of medication for diabetes on risk of death from kidney cancer. We observed independent associations with age, cigarette smoking status (RR = 2.02, 95% CI 1.65-2.48), and systolic blood pressure (RR = 1.12 for 10 mmHg higher systolic blood pressure level, 95% CI 1.06-1.18). We obtained similar results when deaths occurring during the first 5 years were excluded. We observed no important associations with black race, serum cholesterol level, or use of diabetes medication. These findings add to the increasing body of evidence that cigarette smoking and blood pressure are mutable risk factors for kidney cancer in men.

Notes

Monday, March 24 - cont'd.

Acadia Suite

Session B – Cancer Screening

Chair: **Kurt C. Stange, MD, PhD**
Case Western Reserve University

3:45 pm **Ann G. Zauber, PhD**
Memorial Sloan-Kettering Cancer Center

*"Can Surveillance Intervals be Lengthened
Following Colonoscopic Polypectomy?"*

4:05 pm **Electra D. Paskett, PhD**
Bowman Gray School of Medicine

*"Do Community-Based Interventions Work?
Results of the FoCaS Project"*

4:25 pm **Linda P. Engelstad, MD**
Northern California Cancer Center

*"Follow-Up for Abnormal Pap Smears in a
High Risk Population"*

4:45 pm **Fabio Sabogal, PhD**
California Medical Review

*"Pathways to Early Cancer Detection for
Latinas: En Accion Contra el Cancer"*

5:05 pm **Joyce A. Bird, PhD**
Northern California Cancer Center

*"Promotion of Breast and Cervical Cancer
Screening Among Vietnamese Women"*

(Abstracts immediately follow on left-hand pages, with space for notes on right-hand pages.)

Notes

Abstracts

Session B: Cancer Screening

3:45 - 5:15 PM

Can Surveillance Intervals Be Lengthened Following Colonoscopic Polypectomy?

Zauber AG, Winawer SJ, and the National Polyp Study Workgroup

Purpose: Six-year follow-up surveillance data from the National Polyp Study (NPS) was used to assess which newly diagnosed adenoma patients were at higher or lower risk for adenomas at follow-up and who can be deferred to longer surveillance intervals. Colonoscopic polypectomy markedly reduces colorectal cancer incidence but continued colonoscopic surveillance is costly and may not be necessary for all.

Methods: Patients were classified by follow-findings over 6 years as adenomas with advanced pathology (aap) (> 1 cm, high grade dysplasia, or infiltrating cancer), other adenoma, or no adenoma. Polychotomous logistic regression was used to assess baseline characteristics as predictors for follow aap or other adenomas.

Results: 337 patients were followed for at least 6 years with colonoscopic surveillance at 1,3 and 6 years or 3 and 6 years as per protocol. 28 (8 %) had aap, 143 (42 %) had other adenomas, and 166 (49 %) had no adenomas detected over the follow-up period with at least 2 follow-up colonoscopies per patient. 15 (20 %) of 74 patients with 3 or more adenomas at baseline colonoscopy had aap at follow-up in comparison to 7 (4 %) of 187 patients with a single adenoma at baseline [OR=15.7; 95 CI (5.5, 44.3)]. The results were similar with adjustment for age at initial adenoma diagnosis and family history of colorectal cancer.

Conclusions: Patients with 3 or more adenomas at initial colonoscopy are at high risk of follow-up aap and should have surveillance colonoscopy at 3 years. Surveillance for patients with a single adenoma at baseline could be extended to 6 years if not longer.

Notes

Do Community-Based Interventions Work?

Results of the FoCaS Project

Paskett E, Tatum C, Rushing J, Velez R, Michielutte R, Dignan M
Bowman Gray School of Medicine, Winston-Salem, NC

The FoCaS (Forsyth County Cancer Screening) Project is one of six projects funded by the NCI "Public Health Approaches to Breast and Cervical Cancer" initiative. The goal of this project is to improve the use of breast and cervical cancer screening among low-income, predominately African-American, women aged 40 and older. Strategies implemented in the intervention community included public health clinic in-reach strategies (chart reminders, exam room prompts, in-service meetings, and patient-directed literature) and community out-reach strategies (educational sessions, literature distribution, community events, media, and church programs). Baseline and follow-up data from cohort and independent cross-sectional samples in both the intervention and comparison communities were used to evaluate the effects of the intervention program. The proportion of women reporting regular use of mammography increased in both the cohort (40% to 56%; $p = .04$) and the cross-sectional (31% to 56%; $p < .001$) samples in the intervention community. In the comparison community, a non-significant increased trend (46% to 54% and 33% to 40%, cohort and cross-sectional samples, respectively) in mammography utilization was observed. Pap smear screening rates improved only among the cross-sectional sample in the intervention community (73% to 87%; $p = .003$). The effect of the intervention will be described in terms of which women benefited from the program. These results have important implications for community-based research and efforts in underserved populations.

FOLLOW-UP FOR ABNORMAL PAP SMEARS IN A HIGH-RISK POPULATION

Engelstad LP, Bedeian K, Stewart SL

Purpose: This study evaluates an intervention aimed at improving rates of follow-up for abnormal Pap smears in a multiethnic, low-income population of women screened in a public hospital emergency department (ED). **Methods:** Women who were undergoing a diagnostic pelvic examination in the emergency department at Highland General Hospital in Oakland, CA were offered a screening Pap smear. After notification of an abnormal result, women were randomly assigned to either 1) the intervention group in which they were tracked by a nurse follow-up coordinator assisted by a computerized database, or to 2) the control group which received usual follow-up care by referral to the general gynecology clinic. **Results:** Of the 51 women assigned to the follow-up intervention, 33 (65%) returned for at least one diagnostic examination within 6 months compared with 23 (40%) of the 57 women in the control group ($p=0.013$). By 18 months following the abnormal Pap smear, 27 (53%) women in the intervention group had resolved their abnormality compared with 8 (14%) women in the control group ($P<0.0001$). **Conclusions:** This study demonstrates that in a multiethnic, low-income population of women a significant improvement in follow-up rates for abnormal Pap smears can be achieved through centralized tracking by a follow-up coordinator. Despite intensive follow-up efforts, however, many women still experience unnecessary delays in diagnosis and treatment. Further research needs to focus on ways to improve timely follow-up of abnormal Pap smears in high-risk women.

Notes

PATHWAYS TO EARLY CANCER DETECTION FOR LATINAS: EN ACCION CONTRA EL CANCER

Perez-Stable EJ, Sabogal F, Otero-Sabogal R,
Pasick RJ, Napoles-Springer A, Hiatt RA

En Accion Contra el Cancer is a community intervention that promotes early cancer detection among San Francisco (SF) Latinas compared to three other communities in Northern California. En Accion implemented community mobilization strategies including a network of lay health workers (promotoras) and a Spanish language media campaign to clarify misconceptions and increase awareness about cancer screening. En Accion was evaluated by two cross-sectional population-based surveys (1993 and 1996), conducted among Latinas age 40 to 74 yrs, living in census tracts with $\geq 10\%$ Latinos, to ascertain breast and cervical cancer screening behavior. Among women 50-74 yrs, self-reported mammography in previous two years increased from 70% to 87% ($p < .001$) in SF compared to 67% to 80% ($p < .01$) in the comparison cities; in 1996 rate was significantly higher in SF (87% vs 80%, $p = .03$). Among women 50-74 yrs, self-reported Pap smear use in the previous three years increased from 57% to 79% ($p < .001$) in SF, and from 55% to 71% ($p < .001$) in comparison cities; in 1996 the rate was higher in SF (79% vs 71%, $p = .03$). Among women 40-49 yrs, there were no significant changes in mammography rates by city, and a significant increase in Pap smear use in SF (73% vs 85%, $p < .01$) and other cities (67% vs 75%, $p = .05$). We conclude that a culturally appropriate community-based program to increase use of cancer screening among Latinas is effective.

PROMOTION OF BREAST AND CERVICAL CANCER SCREENING AMONG VIETNAMESE WOMEN

Bird JA, McPhee SJ, Ha N-T, Le B, Jenkins CNH

Purpose: Controlled trial of a community outreach intervention to promote clinical breast examinations (CBE), mammograms and Pap smears among Vietnamese women. **Methods:** Over a 3-year period, lay health workers conducted small-group meetings of Vietnamese women in a low-income district of San Francisco, CA. Women in Sacramento, CA served as controls. Lay workers instructed participants about preventive-care check-ups, breast and cervical cancer risks, and screening. Overall, 56 events reached 256 women on general prevention; there were 86 events reaching 344 women on cervical cancer, and 90 events reached 360 women on breast cancer. To evaluate its impact, at pre-intervention we interviewed 306 women in San Francisco and 339 in Sacramento, and at post-intervention, 346 and 373 women, respectively. **Results:** In the intervention community, recognition of screening tests increased significantly between pre- and post-intervention surveys: CBE, 50% to 85%; mammography, 59% to 79%; and Pap smear, 22% to 78% ($p = .001$ for all). Receipt of screening tests also increased significantly: CBE, 44% to 70% ($p = .001$); mammography, 54% to 69% ($p = .006$), and Pap smear, 46% to 66% ($p = .001$). When adjusted for control group rates and significant demographic and psychosocial variables in logistic regression models, the odds ratios also were statistically significant. **Conclusion:** Trained Vietnamese lay health workers had a strong impact on Vietnamese women's recognition and receipt of breast and

Notes

Monday, March 24 - cont'd.

5:15 - 6:00 pm

Grand Ballroom

"NCI Listens"

The Board of Scientific Advisors (BSA) of the National Cancer Institute (NCI) believes it is important to interact with and receive feedback from the research and clinical practice communities affected by NCI policies. The following NCI Staff and BSA Members invite conference participants to join them for this session. A brief presentation will be given by NCI Staff emphasizing the status of grant funding, the By-Pass budget, and the status of several new initiatives including a review of various Program Review Group reports. The brief presentation will be followed by an open question and answer period. The NCI is committed to providing written feedback to the Society concerning issues raised during the session. The BSA hopes that conference participants will take advantage of this opportunity to make their concerns heard.

Chair: **Virginia L. Ernster, PhD**

Professor, Dept. of Epidemiology & Biostatistics
School of Medicine, U C, San Francisco

Speaker: *An Overview of NCI Programs & Initiatives*

Peter Greenwald, MD

Director, Div. of Cancer Prevention &
Control, National Cancer Institute, NIH

Participants: **Question & Answer Session**

Paulette S. Gray, PhD

Executive Secretary, BSA
Deputy Director, Division of Extramural Affairs
National Cancer Institute, NIH

E. Robert Greenberg, MD

Director, Norris Cotton Cancer Center

Caryn E. Lerman, PhD

Associate Professor of Medicine & Psychiatry
Cancer Prevention & Control
Lombardi Cancer Research Center, Georgetown
University

G. Iris Orams, MD, PhD

Director, Extramural Programs Branch
Division of Cancer Epidemiology & Genetics
National Cancer Institute, NIH

Notes

Monday, March 24 - cont'd.

6:00-8:00 pm Poster Session and Reception
Evangeline Suite

8:00 pm Best Poster Award Presentation

Dinner on your own

TUESDAY, MARCH 25

REGISTRATION -- 7:00 am - 5:00 pm

7:30-8:45 am Hot topics breakfast session – Two Concurrent Breakfast Sessions
Acadia Suite **Chemoprevention:** Co-Chair: **Roberd Bostick, MD**
Bowman Gray School of Medicine

Co-Chair: **Mary Daly, MD, PhD**
Fox Chase Cancer Center

“Issues in Utilizing Intermediate Endpoints in Chemoprevention
Studies”

Tobacco: Co-Chair: **Paul Cinciripini, PhD**
The University of Texas
M. D. Anderson Cancer Center

Co-Chair: **Susan Curry, PhD**
Group Health Cooperative

Specific program details to be announced. Check at Registration

Tuesday, March 25 - cont'd.

9:00 - 11:15 am SYMPOSIUM -- *Updates and Controversies in Cancer Genetics*
Grand Ballroom

9:00 - 10:05 am Chair: **Roberd M. Bostick, MD, MPH**
Associate Professor, Department of Public Health Sciences
The Bowman Gray School of Medicine of
Wake Forest University

"Update and Perspectives on Genetic Measurements for Population-Based Studies"

Mark F. Leppert, PhD, Research Associate Professor
Department of Human Genetics
University of Utah School of Medicine

"Molecular-Genetic Epidemiology: Perils and Pitfalls"

Thomas A. Sellers, PhD, MPH
Associate Professor, Division of Epidemiology
University of Minnesota

"Informed Consent and Other Genetics Research Torments (Challenges)"

Judy Garber, MD, Assistant Professor
Dana-Farber Cancer Institute

10:05 - 10:20 am Break

10:20 - 11:00 am *"Predictive Genetic Testing for Cancer: Ethical, Legal, and Social Challenges"*

Karen H. Rothenberg, JD, MPA
Marjorie Cook Professor of Law
Director, Law and Health Care Program
University of Maryland School of Law

"Genetic Testing: The Ecstasy of Discovery and the Agony of Prevention"

Doug Dolginow, MD
President & CEO
Oncormed, Inc.

11:00 - 11:15 am Symposium Speakers and Audience Discussion
"Are we ready for transferring genetic testing from research to the clinical or public health arenas?"

Notes

Tuesday, March 25 - cont'd.

11:15 am

Presidential Address — *"The Perils of Prevention"*

Richard R. Love, MD, MS

University of Wisconsin School of Medicine

12:15-1:15 pm

Lunch on your own

Notes

Tuesday, March 25 - cont'd.

1:15-2:45 pm

Presented Papers (2 Concurrent Sessions)

Grand Ballroom

Session C: Chemoprevention/Biomarkers/Genetics/Nutrition

Chair: **Anna Giuliano, PhD**

University of Arizona Cancer Center

1:15 pm

Stephen D. Hursting, PhD, MPH

The UT M. D. Anderson Cancer Center

*"The Effects of N-(4-Hydroxyphenyl)
Retinamide on the Growth and Death of
LNCaP Human Prostatic Cancer Cells"*

1:35 pm

Zuo-Feng Zhang, MD, PhD

Memorial Sloan-Kettering Cancer Center

*"Tobacco Smoking and Mutations of the
TP53 Gene in Bladder Cancer"*

1:55 pm

Carol J. Fabian, MD

University of Kansas Medical Center

*"Selection of a Cohort for Breast Cancer
Chemoprevention Trials Using Surrogate
Endpoint Biomarkers"*

2:15 pm

Sara S. Strom, PhD

The UT M. D. Anderson Cancer Center

*"Cytogenetic Markers, Sister Chromatid
Exchange and Chromosome Breaks, as
Predictors of Developing Second Cancers
in Hodgkin's Disease"*

2:35 pm

Nava Siegelmann-Danieli, MD

Fox Chase Cancer Center

*"Constitutional Genetic Variation of the
GSTM1 and NQO1 Detoxification Loci,
and Breast Cancer Development"*

(Abstracts immediately follow on left-hand pages, with space for notes on right-hand pages.)

Notes

Abstracts

Session C: Chemoprevention, Biomarkers, Genetics & Nutrition

1:15 - 2:45 PM

The Effects of N-(4-Hydroxyphenyl)retinamide on the Growth and Death of LNCaP Human Prostatic Cancer Cells. S.D. Hursting, J.C. Shen and T.T. Wang, M.D. Anderson Cancer Center, Houston, TX 77030 and NCI-Frederick Cancer Research Center, Frederick, MD 27712.

To explore the mechanisms underlying the prostate cancer chemopreventive effects of the synthetic retinoid N-(4-Hydroxyphenyl) retinamide (4-HPR), we evaluated the anti-proliferative and apoptosis-inducing effects of 4-HPR in the androgen-sensitive LNCaP human prostate cancer cell line. 4-HPR exerted a dose-dependent (optimal concentration = 2.5 μ M) suppression of LNCaP cell proliferation (measured by the MTT assay) and induction of apoptosis (measured by DNA laddering and an ELISA for cytoplasmic DNA fragments). Northern blot analysis revealed that 4-HPR (2.5 μ M) decreased prostate-specific antigen (PSA) expression (~4-fold) and increased MIC-2 expression (~2-fold), suggesting that 4-HPR induces LNCaP cells to differentiate since both PSA and MIC2 are putative prostatic differentiation markers. 4-HPR also decreased (~45%) *bcl-2* mRNA expression (determined by competitive PCR), indicating that the apoptotic effects of 4-HPR may be mediated, at least in part, by alterations in the *bcl-2*-regulated apoptotic pathway. The presence of N-acetyl cysteine (3 μ M) completely blocked the anti-proliferative and apoptotic-inducing effects of 4-HPR, suggesting an oxidative mechanism may be involved in the chemopreventive effects of 4-HPR. Finally, the anti-proliferative and anti-apoptotic effects of R1881, a non-metabolizable androgen which potently induces LNCaP cell proliferation (maximal stimulation at 100 pM), was completely blocked by 4-HPR (2.5 μ M). We conclude that: i) 4-HPR exerts growth suppressive, apoptotic and differentiative effects on LNCaP cells; ii) the apoptotic effects of 4-HPR may be mediated in part by *bcl-2*; iii) a prooxidant mechanism may contribute to the anti-proliferative and apoptotic-inducing effects of 4-HPR; and iv) 4-HPR can interact with androgen to suppress proliferation and induce apoptosis. Supported by NCI P30 CA16672.

Notes

Tobacco Smoking and Mutations of the TP53 Gene in Bladder Cancer. Zhang Z, Lu M, Cordon-Cardo C, Connolly-Jenks C, Cao P, Shu X, Fair W, Scher H, Reuter V, Begg C. Memorial Sloan-Kettering Cancer Center, New York, NY 10021

Purpose. Bladder cancer has been associated with tobacco and certain occupational exposures. Mutations of the TP53 gene are the most frequent events in bladder cancer. We studied 109 patients with bladder cancer to explore if tobacco smoking is associated with TP53 mutations.

Methods. This study employed a case-case design to examine the correlation between cigarette smoking and TP53 mutations. Information on smoking was obtained by personal interview by a standard questionnaire. We studied TP53 mutations by using immunohistochemistry (IHC), PCR-SSCP and sequencing.

Results. We identified 45 cases (41.3%) with at least one band shift, an indication of potential mutations. Direct sequencing of the TP53 gene identified 40 patients with TP53 mutations. Forty-three percent of patients with TP53 mutation had GC-AT transition, 15% AT-GC, and 10% of patients had transitions at CpG. Ten percent patients had GC-TA transversion, 10% GC-CG, 2.5% AT-CG, and 10% had deletions or insertions. We found a very high correlation between p53 overexpression by IHC and TP53 mutations as measured by PCR-SSCP ($P < 0.0001$). Smoking is significantly related to TP53 mutations with an odds ratio of 3.4 (95%CI: 1.1-10). A dose-response relationship was identified between cigarettes smoked per day and TP53 mutations, with an odds ratio of 1.3 (0.3-5.2) for these smoked less than a pack per day and that of 4.6 (1.4-14.9) for these smoked one pack or more (p for trend: 0.0081).

Conclusions. The study supports that cigarette smoke leads to TP53 mutations and enhances the risk for bladder carcinogenesis.

Selection of a Cohort for Breast Cancer Chemoprevention Trials Using Surrogate Endpoint Biomarkers.

Fabian CJ, Kamel S, Zalles CM, Kimler BF

The purpose of this prospective study was to identify women at high short-term risk for breast cancer through the use of breast tissue biomarkers. We have previously reported that random fine needle aspirate (FNA) evidence of epithelial hyperplasia with atypia and biomarker abnormalities (DNA aneuploidy; overexpression of p53, EGFR and Her-2/neu) is more prevalent in women at increased epidemiologic risk for breast cancer than a group of low risk controls.

Three hundred thirty-five women at increased risk because of a first degree relative with breast cancer (69%), prior precancerous biopsy (28%), prior invasive cancer (16%), or some multiple thereof (12%), have undergone FNA and been followed for subsequent cancer development between August 1989 and May 1996. Eleven women have developed in situ (7) or invasive disease (4) 2-48 months (median 10) after the initial aspiration. Whether or not the three cases of LCIS are excluded, later detection/development of cancer is predicted by FNA hyperplasia with atypia ($p < 0.001$). In turn, hyperplasia with atypia is predicted by the presence of multiple biomarker abnormalities.

FNA evidence of hyperplasia with atypia was present in 18% of this population at increased epidemiologic risk. An additional 13% had evidence of hyperplasia without atypia but with multiple abnormal biomarkers. Thus, in a population at increased epidemiologic risk largely because of positive family history, 31% had random FNA biomarkers associated with a marked short-term risk of breast cancer and are thus good candidates for Phase II chemoprevention trials.

We conclude that breast FNA, with cytologic and biomarker assessment, can be used to identify a cohort of women at extremely high risk of short-term cancer development and thus particularly suitable for testing potential chemopreventive agents using changes in surrogate endpoint biomarkers as indicators of efficacy.

Notes

Cytogenetic markers, sister chromatid exchange and chromosome breaks, as predictors of developing second cancers in Hodgkin's Disease Strom, Sara S., Gu, Y., Sigurdson, A.J., Spitz, M.R., Liang, J.C., University of Texas M. D. Anderson Cancer Center, Houston, Texas, 77030.

Follow-up reports have shown that HD survivors are at increased risk of second cancers after treatment with combination therapy. Thus, biomarkers capable of identifying high risk subgroups of patients have great therapeutic and prognostic relevance. We evaluated cytogenetic biomarkers, sister chromatid exchange (SCE) and chromosome breaks [spontaneous (SCB) and bleomycin-induced (BIB)], as predictors of second cancer risk in a cohort of 105 adult HD patients treated at M. D. Anderson Cancer Center from 1989 to 1992. SCBs, BIBs and SCEs were measured in 50 metaphases from baseline blood. Patients with a break frequency in the highest quartile were considered "high risk". Kaplan Meier survival analysis was used to predict second cancer risk associated with SCEs, SCBs and BIBs. During the follow-up time (Mean: 5 yrs), 7 second cancers occurred [leukemia (1), non-Hodgkin's lymphoma (1), breast (1), metastatic tongue cancer (1), melanoma (1), and non-melanoma skin (2)]. The mean time from diagnosis to second primary was 4.6 years. There was no association between the number of SCBs and BIBs and the development of second primaries. For SCE, there was a statistically significant difference ($p=0.03$) in the cumulative probability of developing a second cancer in the "high risk" group (Mean: 8.19) as compared to the "low risk" group (Mean: 4.85). Multivariate Cox regression analysis identified only high SCEs and age as being predictive of risk of developing a second cancer. The relative risk (RR) associated with high SCE was 11.6, $p=0.02$ and for age the $RR=1.08$, $p=0.01$. Clinical characteristics, such as histology, stage, and treatment (radiotherapy, chemotherapy or both combined), were not associated with elevated risk. In conclusion, our data suggest that baseline SCE could be a biomarker useful in identifying HD patients at risk of second cancers. These interesting results need to be verified in a larger cohort with a longer follow-up time. Supported by NIH grants KO7CA63183 and RO3CA64123.

Constitutional genetic variation at the GSTM1 and NQO1 detoxification loci, and breast cancer development.

N. Siegelmann-Danieli, K.H. Buetow, Fox Chase Cancer Center, Philadelphia, PA.

Phase I and II metabolizing enzymes are multi-gene families of enzymes that participate in both bio-activation and detoxification of various carcinogens and anti-cancer drugs. Constitutional genetic variation affecting enzymatic activity has been previously described for some of these genes, including the glutathione-S-transferase $\mu 1$ (GSTM1) and NAD(P)H:quinone reductase (NQO1) genes.

In the current work we examined the possible relationship between constitutional genetic variation at these detoxification loci and breast cancer development. Genotyping was done on nucleic acids that were extracted from peripheral leukocytes of cases with breast cancer and controls. Tumor characteristics of cases were abstracted from the medical records. Ninety-five percent of cases and all controls were Caucasians, and the analysis was restricted to females aged 27 - 83 years old. Genotyping included 399 cases and 134 controls for GSTM1, and 399 cases and 134 controls for NQO1. Neither the null genotype of GSTM1 nor any specific allele of NQO1 were noted to be associated with the occurrence of breast cancer. GSTM1 null genotype was significantly associated with larger tumors (T1 and 2 versus T3 and 4 according to the TNM classification, $p=0.024$, $\chi^2=5.062$), as well as with the presence of metastases to axillary lymph nodes ($p=0.046$, $\chi^2=3.983$). Homozygous individuals for the active form of NQO1 were over-represented in cases with higher histology grade ($p=0.028$ and $\chi^2=7.157$). Heterozygous cases having one copy of the less active allele of NQO1 were over-represented in cases with lobular carcinoma, while homozygous individuals for the active form were over-represented in cases with ductal carcinoma. This difference was significant at $p=0.002$ and $\chi^2=12.077$.

We concluded that constitutional genetic variations at these detoxification loci were not associated with the development of breast cancer. However, constitutional GSTM1 expression might have a protective role in preventing tumor progression, and is associated with the most important prognostic factors of breast cancer. In addition, different quinone compounds might have a role in the development of ductal and lobular breast neoplasms.

Notes

Tuesday, March 25 - cont'd.

Acadia Suite

Session D — Behavioral Science/Tobacco

Chair: **Suzanne M. Miller, PhD**
Fox Chase Cancer Center

1:15 pm **Kimberly Siejak, MS**
Fox Chase Cancer Center

*"Telephone Counseling Improves Adherence
to Long-Term Follow-Up Screening for
Cervical Abnormalities"*

1:35 pm **Kathryn L. Taylor, PhD**
Georgetown University Medical Center

*"Patient Decision Making in Prostate
Cancer Screening"*

1:55 pm **Ronald E. Myers, PhD**
Thomas Jefferson University Hospital

*"Prostate Cancer Education and Screening
Among African American Men"*

2:15 pm **N. R. Boyd, PhD**
Fox Chase Cancer Center

*"A Cost-Effectiveness Analysis of a Physician
Delivered Smoking Cessation Intervention for
Older Smokers"*

2:35 pm **Kathryn M. Kash, PhD**
Strang Cancer Prevention Center

*"Comparisons of Women at Various Risk
Levels for Breast Cancer on Knowledge,
Interest, and Decision Making About
Genetic Testing"*

Notes

Abstracts

Session D: Behavioral Science & Tobacco

1:15 - 2:45 PM

Telephone Counseling Improves Adherence to Long-Term Follow-Up Screening for Cervical Abnormalities

K. Siejak, S. Miller, C. Schroeder, R. Sipps, C. Lerman, E. Hernandez, W. Helm

We examined the long-term impact of a brief telephone counseling intervention, delivered immediately before an initial diagnostic follow-up for abnormal Pap smear, among low-income inner-city women. A randomized trial design compared telephone counseling (with and without a "booster" counseling telephone call before the six-month repeat colposcopy appointment) to telephone appointment confirmation, and standard care (no telephone contact). The telephone counseling protocols assessed and addressed three barriers to adherence: encoding/expectancy (e.g., understanding cervical cancer risk); affective/emotional (e.g., worry about the condition and its consequences); and self-regulatory/practical (e.g., forgetting). Patients receiving telephone counseling were significantly more likely than telephone confirmation patients to adhere to the six-month follow-up visit, whether or not they received the six-month booster call (61% v. 35.5% adherence; OR = 2.70, 95% CI = 1.15 - 6.51, $p < .04$); adherence rates for patients in the telephone confirmation and standard care groups did not differ significantly (35.5% v. 31.5% adherence). Addressing psychological barriers to adherence in a preventive — as well as cost- and time-effective — manner thus appears to be an effective strategy for enhancing long-term adherence to follow-up cervical screening in a traditionally underserved population. This type of targeted intervention is particularly important for conditions such as precancerous cervical disease, which typically need to be tracked over time.

Notes

Although the utility of prostate cancer screening among asymptomatic men continues to be controversial, the number of men who are screened each year is on the rise. A critical issue is that this increased awareness about prostate cancer has not been associated with increased knowledge about the limitations of screening and treatment. In the present study, we conducted two telephone interviews with 180 men registered for a free prostate cancer screening program, once prior to the screening and once following receipt of the screening results. Information on demographics, prostate cancer knowledge, prostate cancer screening practices, decisional conflict, and decisional satisfaction was collected. Participants were an average of 58 years of age, 71% were married, 87% were insured, 56% had a college degree or better, 45% were African-American, and 20% had a family history of prostate cancer. In the past 1-2 years, 60% had had a rectal exam and 49% had had a PSA blood test. In spite of the relatively high levels of education, positive family history, and participation in past screenings, 55% were unable to name any disadvantages of screening, only 12% mentioned the controversy as a negative aspect of screening, and only 13% were aware of the potential for a false positive result. However, the decisional conflict scale indicated that men: 1) were very certain in their decision to be screened ($X = 4.3$, out of 5.0), 2) believed they were well aware of the limitations of screening ($X = 4.0/5.0$), and were very satisfied with their decision to be screened ($4.77/5.0$). The influence of campaigns encouraging screening was apparent, as the reasons most often mentioned for attending the screening were "wanting peace of mind," that it was free, and that prostate cancer had been in the news lately. These results suggest the importance of the development of standard informed consent procedures and educational programs for the thousands of asymptomatic men participating in free prostate screenings each year, as the decision to be screened is being made without the benefit of a full understanding of the current state of medical knowledge about prostate cancer screening. Until the definitive results of the PLCO Cancer Screening Trial are available, improved patient education is needed to assist men in making screening decisions consistent with their own preferences.

Prostate Cancer Education and Screening Among African American Men. R. Myers, Ph.D., G. McGrory, T. Wolf, D. Burgh, J. Diehl, S. Marcus, Thomas Jefferson University; G. Chodak, M.D., M. Williams, S. Lindsey, University of Chicago.

Thomas Jefferson University and the University of Chicago identified 548 African American male patients at the University of Chicago University Health Service (UHS) for a study of prostate cancer education and screening. The men were 40 to 70 years of age, had no record of prostate cancer, had visited the UHS within two years prior to the study, and had no record of digital rectal examination (DRE) or prostate specific antigen (PSA) testing in the previous year. A total of 413 (75%) men completed a baseline telephone survey. Respondents were randomly assigned to either a control group or treatment group. Control group (CG) men received a letter that encouraged the recipient to schedule a clinic appointment for prostate cancer education and screening and a reminder letter. Treatment group (TG) men were provided an invitation letter, a reminder letter, and an educational intervention (i.e., educational booklet, instruction telephone call, and reminder telephone call).

Overall, 25% of CG and 52% of TG men made an education and screening appointment. Multivariate analyses showed that appointment-making was positively and independently associated with exposure to the intervention, personal history of benign prostatic hyperplasia, perceived screening efficacy, and the belief that a screening exam should be done in the absence of symptoms. 84% of CG and 77% of TG men kept their scheduled appointment. Appointment-keeping was significantly and positively associated only with family influence. Findings show that the educational intervention was effective in encouraging the participation of men in a program of cancer education and screening. Study results highlight the importance of pre-screening education for African American men and their supportive others.

Notes

A COST-EFFECTIVENESS ANALYSIS OF A PHYSICIAN DELIVERED SMOKING CESSATION INTERVENTION FOR OLDER SMOKERS

N Boyd¹, E Noll¹, G Morgan², C Orleans³, B Rimer⁴. Fox Chase Cancer Center¹, Philadelphia, PA; Wyoming Valley Family Practice Residency², Kingston, PA; Robert Wood Johnson Foundation³, Princeton, NJ; Duke Comprehensive Cancer Center⁴, Durham, NC.

Cost-effectiveness analyses of cancer prevention interventions implemented in medical settings are essential in the era of managed care. This paper describes the outcome of a cost-effectiveness analysis of a physician delivered smoking cessation trial for smokers aged 50-74 years. The study compared usual care with a physician delivered intervention, based on the NCI 4 A's model, combining brief MD advice, self-help materials and nicotine gum. Thirty-nine outpatient medical practices (659 smokers) were randomized to one of two study groups. Quit rates at 6 months post intervention were nearly twice as high for patients in practices delivering the physician intervention (15.4%) compared with usual care (8.1%). Cost-effectiveness analysis were conducted to assess the comparative costs and behavioral impact of the two cessation approaches used in the trial: physician vs. usual care. The principal costs included in this analysis were personnel time and materials cost. Intervention development costs, facilities use, and patient time were not used in these estimates. The results indicated that the physician intervention and the usual care component costs were \$131.50 and \$183.66 respectively. Sensitivity analyses were also performed by estimating the costs associated with an intervention effect diminished by 20% (holding the usual care quit rate constant) and increasing personnel time costs by 20%. The cost per quit remained in favor of the physician delivered intervention even with these adjustments.

COMPARISONS OF WOMEN AT VARIOUS RISK LEVELS FOR BREAST CANCER ON KNOWLEDGE, INTEREST, AND DECISION MAKING ABOUT GENETIC TESTING.

Kash KM, Rosenthal G, Dabney MK, Miller DG, Osborne MP.

With the cloning of the BRCA1 and BRCA2 genes, women are requesting genetic testing and many are inappropriate candidates. We queried women as to their knowledge of breast cancer and genetic testing as well as their interest in and potential decision making about testing. Three hundred and ninety four women at increased risk for developing breast cancer (due to family histories) from rural and urban areas of the U.S. completed a questionnaire regarding genetic testing, psychological distress, and health beliefs. They were compared with 385 age matched controls, from the same geographical areas, with no family history of breast cancer in a first degree relative. Mean age was 44 with a range from 20 to 76, primarily white (97%), married (78%), less than a college education (40%), and from cities with populations less than 150,000 (72%). Thirty-one percent of women with family histories thought their chances of being BRCA1 gene mutation carriers were very to extremely likely compared with only 1% of women without family histories ($p < .0001$). Women at high risk reported significantly more breast cancer anxiety, greater knowledge of genetic testing, and more reasons for not undergoing genetic testing than women at average risk (all $p < .0001$). Despite having less knowledge of genetic testing, lower perceived risk of being a carrier, and fewer reasons for not having testing, 42% of average risk women stated that, if a test were available to them now, they would have their blood taken and get the results immediately. A multiple regression analysis revealed that the best predictors of willingness to undergo genetic testing were: greater perception of being a gene mutation carrier, fewer negative and more positive aspects to testing, being at higher risk, and greater breast cancer anxiety (30% of variance). Women at high risk report more reasons against than reasons for genetic testing and may have a better understanding of the implications of both positive and negative results of genetic testing. Of greatest concern is that breast cancer anxiety is high and perception of being a gene carrier is greater than expected in women at high risk, thus influencing decision making. Improved education and access to genetic counselling are essential in order to help all women make appropriate decisions about genetic testing.

Notes

Tuesday, March 25 - cont'd.

3:00-4:00 pm

Cullen Award Presentation and Lecture

Edward Lichtenstein, PhD

Oregon Research Institute

"Sustainable(?) Tobacco Cessation Programs for Health Care Settings"

The Joseph W. Cullen Memorial Award is sponsored by SmithKline Beecham.

Notes

Tuesday, March 25 - cont'd.

4:00-5:30 pm

Grand Ballroom

Session E — Plenary Paper Session (Highest-ranked papers of those submitted for oral presentation)

Chair: **Richard R. Love, MD, MS**
University of Wisconsin School of Medicine

4:00 pm

Norman F. Boyd
Ontario Cancer Institute

"Long Term Effects of a Low-fat High-Carbohydrate Diet on Radiological Features of the Breast"

4:20 pm

Wei Zheng, MD, PhD
University of Minnesota

"Pathologic Features of Initial Adenomas as Predictors for Metachronous Adenomas of the Distal Colon and Rectum"

4:40 pm

Frank L. Meyskens, Jr., MD
University of California, Irvine

"A Randomized Double-Blind Placebo-Controlled Phase IIB Trial of Difluoromethylornithine (DFMO) for Colon Cancer"

5:00 pm

Caryn Lerman, PhD
Georgetown University Medical Center

"A Controlled Trial of Pre-Test Education Approaches to Enhance Informed Decision-Making about BRCA1 Testing"

5:20 pm

Xifeng Wu
The UT M. D. Anderson Cancer Center

"Cytochrome P4502E1 'Dra1' Polymorphisms in a Minority Lung Cancer Study"

(Abstracts follow immediately on left-hand pages, with space for notes on right-hand pages.)

Notes

Abstracts

Session E: Plenary Paper Session

4:00 - 5:30 PM

Long Term Effects of a Low-fat High-carbohydrate Diet on Radiological Features of the Breast.

NF Boyd, G Lockwood, M Yaffe, J Byng, L Little D Tritchler, for the Canadian Diet and Breast Cancer Prevention Study Group. Ontario Cancer Institute, Toronto, Canada

We have assessed the long term effects of a low fat high carbohydrate diet on radiological features of the breast in participants in a randomized trial of dietary intervention. Comparison of mammograms before and after 4 years of dietary intervention was made using digitized mammograms and an image processing system to measure the area of the breast, the area of density, and the percent of the breast area occupied by radiologically dense tissue.

Data are from 436 subjects (193 intervention; 243 controls). The area of density decreased 10.0% in the intervention group compared to a 5.1% reduction in the control group ($p=0.01$). Age at entry ($p=0.001$) and change in menopausal status from baseline to 4 years ($p<0.001$) were associated with change in the area of density, while change in weight was not. After controlling for these variables in multiple regression, dietary group remained significantly associated with reduction in area of density ($p=0.03$). Change in the percent of the breast area occupied by density was strongly significantly different between groups after controlling for changes in weight and menopausal status ($p=0.001$), with a larger reduction in the intervention group. Change in breast size did not differ between intervention and control subjects ($p=0.35$).

These results to date show that the adoption of a low-fat high-carbohydrate pattern of eating reduces the area of mammographic densities in the breast, a strong risk factor for breast cancer. Further observation will be required to determine whether these changes are associated with a reduction in risk of breast cancer.

Notes

Pathologic Features of Initial Adenomas as Predictors for
Metachronous Adenomas of the Distal Colon and Rectum.
Zheng W, Yang G, Sun Q-R, Potter J, Zheng S.

Patients with colorectal adenomas are at an increased risk of cancer because of a high recurrence rate of adenomas. To assess whether the risk of metachronous adenomas could be predicted by pathologic characteristics of the initial adenomas, we conducted a cohort study in Zhejiang, China. The study included 1,490 adenoma patients who were identified in 1977, and were followed endoscopically at years 2, 4, 6, 11, and 16 after their initial polypectomy. New adenomas in the distal colon and rectum were identified in 280 patients in these follow-up examinations. A 2-to 3-fold significantly elevated risk of metachronous adenomas was observed for patients who had >2 initial adenomas, or whose most advanced initial adenoma was >1.0 cm, was of villous/tubulovillous type, or showed severe dysplasia. For advanced metachronous neoplasms, defined as cancer or adenomas with severe dysplasia, the adjusted relative risks associated with size of initial adenoma (>1.0 cm vs. ≤ 0.5), pathologic type (villous/tubulovillous vs. tubular), and dysplasia (severe vs. mild) were 4.2 (95 percent confidence interval, 1.8 to 9.9), 8.1 (4.2 to 15.6), and 14.4 (5.0 to 41.3), respectively. In particular, patients who had a large (>1.0 cm) adenoma with severe dysplasia at baseline, were at a 37-fold significantly elevated risk of developing advanced metachronous neoplasms, compared with those having small adenoma(s) with mild dysplasia. This study indicates that the risk of metachronous adenomas, especially of advanced metachronous neoplasms, is closely related to the pathology of the initial adenomas; this pattern identifies a high-risk group of adenoma patients for close surveillance and chemoprevention after their initial polypectomy.

A Randomized Double-blind Placebo-controlled Phase IIb Trial of Difluoromethylornithine (DFMO) for Colon Cancer Prevention. Meyskens F., Gerner E., Pelot D., Durbin T., Doyle K., Lagerberg W., Emerson S. We previously conducted a phase IIa trial to determine the lowest dose of DFMO that suppressed polyamine levels in rectal mucosa of individuals with a prior history of resected colon polyps. Using a similar at-risk population, 122 participants were randomized to one of four oral daily doses (0, 0.075, 0.20, 0.40 gm/m²) of DFMO for one year. Baseline and serial audiometry, polyamine levels, and extensive symptom monitoring were performed over a 15 month period. There was no apparent difference between the symptoms or audiograms of the 4 groups at any time point. DFMO inhibited putrescine levels in a dose dependent manner, an effect that was evident by 6 months and showed a consistent proportionate decrease with each equal sized dose increment. At a dose of 0.4gm/m² they were decreased to approximately 10% of the placebo group. Similar results were seen in the permidine/spermine ratio. All polyamine levels returned to baseline after discontinuation of DFMO. Continuous dose-related suppression of polyamine levels in the rectal mucosa by very low doses of DFMO and an excellent safety profile suggests that a dose of 0.1 - 0.2 gm/m² should be considered for phase III trials.

Notes

A Controlled Trial of Pre-Test Education Approaches to Enhance Informed Decision-Making About BRCA1 Testing

Lerman C., Biesecker B., Benkendorf J., Kerner J., Gomez-Caminero A., Hughes C., Reed M.

Background: Initial studies indicate high levels of interest in BRCA1 testing in the general public and in high risk populations. However, the optimal strategies to educate and counsel individuals have yet to be determined. **Purpose:** To evaluate the impact of alternate strategies for pre-test education and counseling on decision-making regarding BRCA1 testing among low to moderate risk women with a family history of breast and/or ovarian cancer. **Methods:** A randomized trial design was used to evaluate the effects of education only (educational approach) and education plus counseling (counseling approach), as compared to a waiting list (control) condition (n=400). Study outcomes included changes in: knowledge; perceived risk; perceived benefits, limitations and risks of BRCA1 testing; and testing intentions. Provision of a blood sample for future testing served as a proxy measure of testing decisions (since BRCA1 testing currently is not recommended outside of high risk families). The effects of intervention group on study outcomes were evaluated in hierarchical linear and logistic regression models which controlled for confounder variables. **Results:** The educational and counseling approaches both led to significant increases in knowledge, relative to the control condition ($p<.001$ for both). The counseling approach, but not the educational approach, was superior to the control condition in producing significant *increases* in perceived limitations and risks of BRCA1 testing ($p<.01$) and *decreases* in perceived benefits ($p<.05$). However, neither approach produced changes in intentions to have BRCA1 testing. Both before and after education/counseling, approximately one-half of participants stated that they intended to be tested and 52% provided a blood sample. **Conclusions:** Standard educational approaches may be equally effective as expanded counseling approaches in enhancing knowledge. However, optimal decision-making requires not only knowledge, but a reasoned evaluation of the positive and negative consequences of alternate decisions. The counseling approach is more likely to achieve this goal. Neither education nor counseling appear to diminish interest in testing, even among low to moderate risk women.

Cytochrome P4502E1 *DraI* Polymorphisms in A Minority Lung Cancer Study. Wu XF, Kemp B, Shi H, Jiang H, Hong WK and Spitz MR. The University of Texas M. D. Anderson Cancer Center and School of Public Health, Houston, TX 77030 (Supported by CA55769, CA68437 and CRFA).

Purpose: Cytochrome P4502E1 (*CYP2E1*) is involved in the metabolic activation of carcinogenic *N*-nitrosoamines. This study was conducted to examine whether *CYP2E1 DraI* polymorphism was related to susceptibility to lung cancer. **Methods:** Genotyping of *CYP2E1* was performed using the polymerase chain reaction on peripheral white blood cell DNA from 126 patients with previously untreated lung cancer (85 African American (AA) and 41 Mexican American (MA)) and 193 controls (104 AA and 89 MA). Mutagen sensitivity (MS) was based on an *in vitro* assay quantitating bleomycin-induced chromatid breaks in peripheral blood lymphocyte cultures. **Results:** The *CYP2E1* CC genotype was found in 86.5% of cases overall vs. 74.6% of controls ($P=0.03$); 78.0% of MA cases vs. 69.7% of MA controls ($P=0.70$); and 90.6% of AA cases vs. 78.8% of AA controls ($P=0.05$). The CC genotype was found to be associated with significantly higher risk of LC overall with an odds ratio (OR) (95% confidence interval) of 2.2 (1.3, 8.7). The risks were significantly elevated for men and for ever smokers with ORs of 3.4 (1.3, 8.7) and 2.6 (1.1, 6.0), respectively, but not for females and nonsmokers with ORs of 0.7 (0.1, 3.8) and 0.9 (0.1, 10.6), respectively. Stratified analysis showed a greater than multiplicative interaction between cigarette smoking and *CYP2E1 DraI* CC genotype. The ORs for the *CYP2E1 DraI* CC genotype, cigarette smoking and both risk factors combined were 1.5, 8.5 and 22.7, respectively. The association between *CYP2E1* susceptible genotype and pack-years of smoking followed the same pattern. This interaction was especially strong in heavy smokers (≥ 30 pack years) in whom the OR for the *CYP2E1 DraI* CC genotype was 85.0. **Conclusion:** *CYP2E1 DraI* polymorphisms may play an important role in lung carcinogenesis.

Notes

Tuesday, March 25 - cont'd.

Closing Remarks

Dr. Richard Love

Conclusion of Annual Meeting Program

Poster Abstracts

An Overview of The Canadian Breast Cancer Screening Database

Beauvais J, Pennock J, Levy I

Purpose: To develop a national breast cancer screening surveillance system collating data from Canadian provincial breast cancer screening programs to support program evaluation and monitoring.

Methods: Since 1993, the Canadian Breast Cancer Screening Database has collated information from eight provinces and territories in Canada. Data for this national system is collected according to a core data set, and includes personal and medical risk factors, screening history, screening results, results of diagnostic testing and information about cancers diagnosed. Information is also collected on cancers that are missed in the screening process.

Results: As of October 1995, none of the provincial screening programs were screening the recommended proportion (70%) of the provincial target population, however, results from the recent National Population Health Survey indicate that a large number of women are receiving screening in settings other than the provincially organized screening programs. Retention rates, abnormal screen rates, benign to malignant biopsy ratios, sensitivity and specificity of screening, and interval cancer rates can be calculated using data from the system.

Conclusion: This database will provide national data on program-based breast cancer screening.

2

Mammography Diffusion and Trends in Late-Stage Breast Cancer: Evaluating Outcomes in Populations. SH Taplin.MD,MPH., MT Mandelson, PhD, C Anderman, MPH, E White, PhD, RS Thompson.MD, D Timlin, EH Wagner MD, MPH

Purpose: We assessed whether an organized breast cancer screening program offered to enrollees of a consumer-controlled health care organization ($n \geq 60,000$) contributed to an increased rate of "ever-use" of mammography and decreases in late-stage cancer (tumors ≥ 3 cm.) compared to the surrounding four-county community in Western Washington state ($n = \geq 745,000$). The screening program used automated reminders and 1 to 3 year screening intervals.

Methods: Among women ages ≥ 40 , we conducted time trend analyses with unconditional logistic regression to compare the age-adjusted rate of change in "ever-use" of mammography (1987-1992), and late-stage breast cancer (1983/84-1991/92) among and between the two populations.

Results: Among all GHC women ages 40 to 49, and 50 years of age and older, 67.4% and 82.8% respectively ever-used mammography by 1992, compared to 78% and 84.4% among four-county women. The rate of diffusion was lower among GHC compared to four-county women ages 40 to 49 ($p=0.01$) but the same for women 50 years of age and older ($p=0.14$). The rate of late-stage tumors declined significantly in both populations among women 50 years of age and older ($p<0.001$), but not among women ages 40 to 49. The rate of change was not significantly different between the populations.

Conclusion: The organized program did not exceed the rate of mammography diffusion of the surrounding community, despite successful implementation. Reductions in late-stage disease occur among women ages ≥ 50 , even when "regular" was not synonymous with annual.

4

BARRIERS AND INTERVENTION PREFERENCES REGARDING PROSTATE CANCER SCREENING IN AFRICAN-AMERICAN MEN

Bastani R, Ph.D., Maxwell AE, DrPH, Yancey A, MD, MPH

African-American (AA) men have the highest incidence rates of prostate cancer in the entire world. Since primary prevention is not a realistic option at this time, secondary prevention, albeit controversial, is the only available means for controlling the disease in this high risk population. Yet, very little is known regarding prostate cancer screening related knowledge, attitudes and behavior of AA men. We conducted telephone interviews with 134 AA men, 40+ years, to obtain this information.

Thirty-four percent had ever had a PSA test, 26% in the past year. Eighty-one percent had ever had a rectal exam, 46% in the past year. Fifty-seven percent believed that they were somewhat or very likely to develop prostate cancer in their lifetime. Still, 69% cited currently being healthy as a factor inhibiting participation in screening. Other barriers included not knowing that screening should occur (77%), fear of finding cancer (61%), feeling violated (56% , rectal), not liking needle (25%, PSA), discomfort or pain (51%), and lack of a recommendation from a physician (44%). Physicians (83%), followed by friends and relatives (70%), were cited as being most important in influencing the decision to get screened. Educational videos (51%), T.V. spots (41%), and written appeals (40%) were cited as less influential.

3

BREAST CANCER KNOWLEDGE, ATTITUDES AND BEHAVIORS AMONG FILIPINO WOMEN RESIDING IN LOS ANGELES

Maxwell AE, DrPH, Bastani R, PhD, Warda US, MS

Face-to-face interviews in English or Tagalog were conducted with 218 Filipino-American women 50 years and older to assess knowledge of and adherence to breast cancer screening guidelines and related attitudes and barriers, and to determine intervention preferences.

The mean age of the sample was 65 years, and the majority reported an income of less than \$25,000. Sixty-six percent ever had a mammogram and 56% had obtained a screening mammogram within 2 years prior to the survey. These rates are about 20% lower than those found in the 1994 California Behavioral Risk Factor Survey among non-Asian women. Variables positively related to screening were having health insurance, longer duration of residency in the U.S., a physician's recommendation to obtain a mammogram, group norms that were supportive of screening, social support and the belief that getting a mammogram is worthwhile. Barriers that were negatively related to screening were concern about cost, inconvenience of finding time and transportation to get a mammogram, embarrassment, and being uncomfortable requesting the procedure from a physician. Intervention preferences included receiving information about breast health in Tagalog, discussing these issues with peers, receiving a mammogram from a Filipino health care professional and being able to obtain a mammogram on a weekend.

FACTORS ASSOCIATED WITH THE USE OF FLEXIBLE SIGMOIDOSCOPY IN PRIMARY CARE PHYSICIANS.

Cooper G, Landefeld C, Fortinsky R, Hapke R, Department of Medicine, Case Western Reserve University, Cleveland, OH.

Flexible sigmoidoscopy (FS) is an effective method for prevention of colorectal cancer, but is currently much underutilized. Factors that influence physician performance and patient receipt of the procedure have not been well characterized. Therefore, we surveyed a random sample of 1762 primary care physicians (family practitioners and internists) in 10 states to assess practitioner characteristics associated with the use of FS, as well as reasons cited for not screening. Completed questionnaires were received from 874 physicians (50%). FS was performed by 44%, 46% referred patients for FS, and 10% did not use FS. Although no physician characteristics were associated with the reported use of FS, factors associated ($P < 0.001$) with self-performance of FS were board certification (55% vs. 27%), male gender (54% vs. 19%), and medical school graduation after 1970 (53% vs. 36%). In a multivariable analysis, all three physician characteristics were independently associated ($p < 0.0001$) with self-performance. Major reasons cited for not screening among all respondents were poor patient acceptance (48%), time required (16%), lack of training (16%), and lack of equipment (16%). Poor patient acceptance was the most frequently reported reason among all three groups—physicians not screening, those referring for FS, and those performing FS themselves (47%, 42%, and 54%, respectively). We conclude that although targeting specific groups of primary care physicians for training in FS may enhance the use of the procedure, broad based interventions to improve patient understanding and acceptance are also necessary.

6

PRIOR UTILIZATION, FEAR, AND PERCEIVED VULNERABILITY AS PREDICTORS OF INTENTION TO GET SCREENING MAMMOGRAPHY

W. Haddad, M. Costanza, A. Stoddard, R. Luckmann, M. White, and D. Klaus, University of Massachusetts Medical School, Worcester, MA.

2,507 women members from two HMO's identified as underutilizers of mammography screening, were interviewed to explore the relationship between selected variables: prior mammogram utilization, calculated risk of developing breast cancer (Gail score), attitudes toward breast cancer, sociodemographic factors and the intention to utilize mammography screening in the next 24 months. Underutilizers were also characterized according to the transtheoretical model (stages of change). Bi-variate results supported previous findings that age, education, working status, general health, and prior utilization were associated with intention to get a mammogram. Several variables not previously reported were found to be significantly associated with intention: calculated risk of breast cancer, perceived vulnerability, worry about getting breast cancer, and fear of learning (from a mammogram) that one has breast cancer. In multiple regression analysis, prior utilization, fear of learning one has breast cancer, worry about breast cancer, and perceived vulnerability were significantly associated with intention. These findings suggest focused interventions which address the specific concerns of these "committed" underutilizers.

Factors Associated with Physician Recommendation for Mammography. Tropman S, O'Malley MS, Earp JA. UNC Lineberger Comprehensive Cancer Center.

While studies have consistently found a strong, positive association between mammography use and physician recommendation, less is known about factors associated with recommendation. Using 1993-94 data on 1,920 women (954 Black, 966 White) ages 52 and older from the NC Breast Cancer Screening Program, we examined relations between women's self-reports of physician recommendation and 12 demographic and health characteristics. About half (57%) the women reported mammography in the past two years; 50% reported recommendation in the past year. Women reporting recommendation were more likely to have had mammography (OR: 16.0; 95% CI: 8.82 - 19.5). In multiple logistic regression, having a regular physician and a personal history of breast problems were strongly associated with recommendation ($p < .001$; OR: 4.84, 2.01 respectively). Having health insurance and higher educational attainment were also associated ($p < .05$; OR: 1.91, 1.63 respectively). Recommendation was inversely related to age ($p < .001$) but directly related to the number of medications and distance to the regular health care provider ($p < .05$). In this sample of rural, older women, demographic and health characteristics were associated with physicians' recommendations for mammography. Further research should consider how physicians' and women's characteristics interact to influence recommendation.

Primary Care Physicians' Recommendations for Colorectal Cancer Screening in Women. Richards CL, O'Malley MS. UNC Lineberger Comprehensive Cancer Center. We used a mailed survey of 1,292 randomly selected primary care physicians to examine self-reported recommendations for colorectal cancer screening to women in four different age groups: 30-39, 40-49, 50-69, ≥ 70 . After four mailings and telephone follow-up, 545 physicians responded (42%), with few significant differences in selected characteristics between responders and non-responders. For women ages 50-69, physicians reported 42 combinations of fecal occult blood testing (FOBT), flexible sigmoidoscopy (SIG), and colonoscopy (COL), although 5 combinations accounted for 71% of recommendations. Half (51%) reported recommending FOBT + SIG; 20% reported FOBT only; and 23% reported all three screening tests. Most physicians (82%) reported recommending some screening before age 50; 44% reported screening before age 40. In bivariate analysis, FOBT adoption was associated with older, male physicians ($p < 0.01$). SIG and COL adoption was associated with physician age, specialty, and practice size ($p < 0.01$). Responding primary care physicians varied in self-reported colorectal cancer screening recommendations. Contrary to expert guidelines, the majority believed that some colorectal cancer screening should begin before age 50, although actual performance is certainly lower than self-reported practice.

Opportunistic Preventive Service Delivery and Patient Satisfaction

K. Stange

Purpose: Patient visits to primary care physicians for care of illness represent important missed opportunities for preventive service delivery. This study sought to determine if "opportunistic" delivery of clinical preventive services during illness visits to primary care physicians results in lower patient satisfaction compared to illness visits without preventive service delivery.

Methods: Consecutive patient visits to 138 family physicians were directly observed to determine the reason for visit and the rate of delivery of preventive services recommended by the US Preventive Services Task Force. Patient eligibility for preventive services was determined from medical records and patient exit questionnaires. Patient satisfaction was determined using the MOS 9 item visit rating scale and a single item asking patients if their expectations were met. Using t-tests and regression analyses, patient satisfaction was compared during acute and chronic illness visits during which preventive services were and were not delivered.

Results: During 1243 adult patient visits for acute illness and 644 visits for chronic illness, there was no difference in either patient satisfaction measure for visits during which preventive services were performed, compared to visits during which preventive services were not performed. Separate analyses stratified by type of preventive service (health habit counseling, screening services or immunization) yielded similar results.

Conclusions: Patient satisfaction should not be a barrier to using illness visits to primary care physicians as windows of opportunity to increase delivery of clinical preventive services.

Early Detection of Esophageal Cancer in North-Central China. Wang GO, Qiao YL. Cancer Institute (Hospital), Chinese Academy of Medical Sciences, Beijing, China.

Purpose: The purpose of this evaluation was to summarize experience in the detect and treatment of precancerous esophageal lesions and early stage esophageal cancers. **Methods:** Balloon cytology and occult blood tests were used as initial tools in a mass screening program among farmers in north-central China. Endoscopy and mucosal iodine staining were used as secondary tools to confirm the esophageal lesions in patients who were positive on the initial screening tests. Treatment included esophagectomy, mucosectomy and/or electrocoagulation. **Results:** Over the past two decades (1974-1996), 150,000 farmers were screened, including 681 with early esophageal cancer. A total of 350 patients with early esophageal cancer have received treatment. Post-treatment 5-year survival has been over 90%. **Conclusions:** Balloon cytology and occult blood screening can early detect precancerous esophageal lesions and early esophageal cancer. These screening tests are simple, inexpensive and acceptable to the majority of farmers. Endoscopy with mucosal iodine staining can further improve diagnosis and help in the evaluation of treatment options. Future research should focus on improving endoscopy therapies, such as mucosectomy and electro-coagulation, which are favored by farmers who have mucosal dysplasia or early cancer of the esophagus.

Screening Mammography:

Who Should Make The Recommendation?

DM Daniel, DT Lackland, DR Garr, DW Nixon, LF Baron,

AJ Gross, PH O'Brien, and DG Hoel

Medical University of South Carolina, Charleston, South Carolina

The principal reasons cited by eligible women as to why they have not obtained screening mammograms have been lack of knowledge and clinical recommendation. In response to this information, patients (N=749) at three mammography clinics were surveyed to assess their likelihood of compliance with recommendations from different messengers (i.e. physician, nurse, volunteer and media campaigns). The patient profile of the clinics varied by race and socioeconomic status. While nearly all women reported a high likelihood to get a mammogram if recommended by a physician, significant variation was noted among clinics regarding women's responses to reminders from other messengers.

Likelihood Of Receiving A Mammogram Based On The Messenger And Clinic

Messenger	Overall (%)	Clinic 1 (%)	Clinic 2 (%)	Clinic 3 (%)	p-value
Physician	100	99	100	100	ns
Nurse	82	90	85	79	< 0.05
Volunteer	38	51	49	32	< 0.001
Media Campaign	38	49	40	35	< 0.001
p-value	< 0.001	< 0.001	< 0.001	< 0.001	

These findings indicate that clinic-based intervention should consider the messenger and demographics of patients when estimating potential results.

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Urban American Indian Women and Risk of Cervical Cancer

Risendal, B.; Giuliano, A.; Short, B.; DeZapien, J.; Papenfuss, M.; Arizona Cancer Center, Tucson, Arizona, 85716.

Purpose: Although cervical cancer among American Indians is a well-documented public health concern, most of what is known comes from the Indian Health Service (IHS). The purpose of this study was to gather previously undocumented information regarding the health issues facing American Indian women in an urban setting, a group which accounts for half this special population. **Methods:** A cross-sectional face-to-face survey administered by interviewers to 515 randomly selected households (one woman per household) in the metropolitan Phoenix area. **Results:** Most respondents were under age 40 (76%), and currently married/ cohabitating (45%). The majority of women surveyed had a high school education (29%) or less (38%). Almost all women (97%) indicated IHS insurance coverage. Forty-one (41%) of women reported intercourse prior to age 16. However, only 3.2% had their first Pap Test at this time; most women (30%) reported their first Pap at time of pregnancy. One-third (33%) of women reported 3 or more sexual partners before age 20, and 43% from age 20-current. Many women received a routine check-up within the last year (69.5%), which correlates well with the observed annual Pap Test rate of 60% (73% within the last 3 years). A third (33.5%) of these were asked to return for follow-up, and 81% reported compliance. Only 55% of women surveyed indicated that they had been counseled by a physician or health care provider regarding cervical cancer screening. **Conclusions:** These results confirm the continued importance of outreach and education among American Indian women based on the observed prevalence of risk factors and frequency of screening and referrals for cervical cancer.

Validation of a Model to Predict Enrollment in a Chemoprevention Trial for Breast Cancer

Yeomans Kinney A, Vernon SW, Shui W, Weber D, Schell M, Vogel VG

Purpose: We evaluated the performance of a regression model in predicting enrollment in a chemoprevention trial for breast cancer using a population independent of the one from which the model was derived. **Methods:** Questionnaires were completed by eligible participants following attendance at an informational meeting about the Breast Cancer Prevention Trial (BCPT) with tamoxifen during the second year of recruitment. The original model was derived from data collected during the first year of recruitment and was applied to data collected during the second year of the trial. The recursive partition method was used to create a population split at each step of a regression and a tree diagram was constructed. **Results:** Of the 89 women included in the analysis, 42% enrolled in the trial and 58% did not. Demographic factors such as age, educational status, and breast risk scores differed from the women who completed the questionnaires during the first year of the trial. The respondents were older, had lower breast cancer risk scores, and were less educated than the women surveyed during the first year of enrollment. Variables considered in the modeling procedure were: not being able to take estrogen replacement therapy, concern about the costs associated with the trial, the possibility of getting a placebo, concern about the side effects of tamoxifen, and the absence of concern that significant others would be reassured if the respondent was taking tamoxifen. The two dominant variables predicting nonparticipation were the possibility of getting a placebo ($p=0.001$) and not being able to take estrogen replacement therapy ($p=0.001$). Eighty-nine percent of the 27 respondents who reported these two barriers did not enroll in the BCPT compared to 56% of the remaining 62 respondents who enrolled in the trial. **Conclusions:** Recursive analysis is useful to separate out the strongest variables in a successive manner so that the remaining population can be analyzed for other significant associations. More in-depth studies are needed to explore the interactions between demographic and other factors that influence participation in chemoprevention trials.

A Clinical Trial to Evaluate the Effect of Vitamin C Supplementation on *in vitro* Mutagen Sensitivity

King T.M., Trizna Z., Wu X., Amos C.I., Fueger R.H., Fueger J.J., Fritsche H.A., Hsu T.C., Winn R., Spitz M.R.
The University of Texas M.D. Anderson Cancer Center

We report the results of a randomized clinical trial to determine whether increasing levels of ascorbic acid (AA) would reduce the levels of mutagen sensitivity (MS). Two hundred and twenty-eight smokers from twenty-one centers around the country registered through the Clinical Community Oncology Program were randomly assigned to one of four daily treatment regimens (placebo, 1 gm AA, 2 gms AA or 4 gms AA). Treatments were administered for 16 weeks with assessment of MS at baseline, at week 4, 16 and 20 (4 weeks after cessation of treatment). Serum AA levels were measured at baseline and at week 4 and 16. Demographic and risk factor data were collected at baseline and at each measurement point.

Mutagen Sensitivity over time was analyzed with repeated measures analysis of variance. The data were classified as 1) the 4 trial arms 2) low (placebo and 1 gm) vs. high (2, 4 gram) and 3) placebo vs. treatment (1, 2, and 4 gm). There were no significant differences of MS in the groups in these three classifications. Using the serum AA levels, we investigated the relationship of AA directly with MS at week 4 and week 16 individually. The correlation between MS and serum AA was 0.10 ($p = 0.22$) at week 4 and 0.29 ($p = 0.09$) at week 16. Linear regression modeling indicated that the single most predictive factor of MS at each time point is baseline MS. Smoking and alcohol factors were not significantly associated with MS.

We conclude that this clinical trial fails to demonstrate a modulation effect of AA on MS. The daily biologic threshold of AA may be a factor in the negative findings of this study, which run contradictory to previous laboratory and clinical studies.

EFFECT OF SUPPLEMENTAL BETA-CAROTENE ON PLASMA CONCENTRATIONS OF CAROTENOIDS, RETINOL AND ALPHA-TOCOPHEROL IN HUMANS. S. Mavne, B. Cartmel, F. Silva, B. Fallon, K. Briskin, M. Baum, G. Shor-Posner & W. J. Goodwin, Jr. Yale Univ., New Haven, CT 06520 and Univ. of Miami, Miami, FL 33136.

High-doses of beta-carotene (BC), a lipid-soluble nutrient, could potentially affect the plasma concentrations of other lipid-soluble nutrients. The purpose of this study was to assess the effects of long-term daily supplementation with BC (50 mg/day) on circulating levels of other carotenoids, retinol (A) and alpha-tocopherol (E). Data were available from 261 men and women participating in the Carotene Prevention Trial, a two center chemoprevention trial designed to determine whether or not supplemental BC could prevent second malignant tumors in patients cured of an early stage cancer of the oral cavity, pharynx or larynx. Up to 2 blood samples were obtained before the intervention (before and after a 1-month placebo run-in), with post-randomization samples obtained at 3, 12, 24, 36, 48, and 60 months. Bloods were analyzed by HPLC in 1 laboratory. Median nutrient levels ($\mu\text{g/mL}$) at baseline in the group randomized to receive BC were as follows (placebo group nearly identical): BC 0.12; A 0.48; E 12.2; alpha-carotene 0.024; lycopene 0.28; lutein+zeaxanthin 0.14. Supplementation with BC produced a persistent 9 to 10-fold increase in median plasma BC levels (1.2 $\mu\text{g/mL}$ at 3 months), and a persistent 2-fold increase in median plasma alpha-carotene levels (0.051 $\mu\text{g/mL}$ at 3 months). Concentrations of A, E, lycopene and lutein+zeaxanthin were not affected by supplemental BC. These results indicate that up to 5 years of daily supplementation with BC substantially increases circulating levels of alpha- and beta-carotene, but does not alter levels of lycopene, lutein+zeaxanthin, A, or E. CA-42101; CA 64567.

Effects of Dietary Supplementation of α -tocopherol on Plasma Antibodies against 5-hydroxymethyl-2' deoxyuridine (Hmdu) Hu JJ^{1,2}, Chi CX², Frenkel K², Henfelt J¹, Roush GC², Berwick M³, and Mahabir S³. ¹Georgetown U. Med. Ctr., Washington, DC; ²New York U. Med. Ctr., New York, NY.. ³Memorial Sloan-Kettering Cancer Ctr., New York, NY.

To test the hypothesis that antioxidants can protect cells from oxidative DNA damage, we evaluated the effects of α -tocopherol supplementation on plasma antibodies (Abs) against an oxidized DNA base derivative, 5-hydroxymethyl-2'-deoxyuridine (Hmdu) in a randomized double-blind trial. Levels of vitamin E and the titers of anti-Hmdu Abs were assessed twice before α -tocopherol intervention: on day 1 (visit 1), and day 3 (visit 2) and twice after intervention: on day 17 (visit 3) and day 31 (visit 4). Participants were randomized to receive one of the three doses of α -tocopherol, 15, 60, and 200 mg/day. Data were available on a total of 28 healthy volunteers. At baseline, there was a significant inverse relationship between Hmdu and vitamin E levels ($r = -0.53$; $p = 0.004$). Subjects receiving 60 mg/day of α -tocopherol had a significant decrease in Hmdu level on visits 3 and 4 compared to baseline ($p = 0.049$ and $p = 0.02$, respectively). Subjects receiving the highest dose of α -tocopherol, 200 mg/day, had less consistent results: a significant decrease in Hmdu level was seen on visit 4 ($p = 0.04$) but not on visit 3. No significant change in Hmdu Ab level occurred on either visit 3 or 4 for patients on the lowest dose level (15 mg/day) of α -tocopherol. Results from this study demonstrate an inverse relationship between α -tocopherol and anti-Hmdu Ab; a decrease in anti-Hmdu Ab by dietary α -tocopherol suggests a protective effect of α -tocopherol against oxidative DNA damage.

Patient Recruitment and Reasons for Inactivation in a Chemoprevention Trial in Early Head and Neck Cancer
 Cartmel B, Briskin K, Fallon B, Goodwin WJ Jr. & Mayne S. Yale Univ., New Haven, CT 06520 and Univ. of Miami, Miami, FL, 33136

The Carotene Prevention Trial, a two center double-blind randomized trial, was designed to evaluate the effect of 50 mg of supplemental beta-carotene taken daily on second malignant tumors in patients cured of early stage head and neck squamous cell carcinoma (HNSCC). Interim data from the Connecticut (CT) study site are presented here. Recruitment for the trial in CT was population based; all patients in the State of CT with HNSCC, with the exception of those with obvious nodal involvement, were identified by the Rapid Case Ascertainment Shared Resource of the Yale Cancer Center. Reasons for inactivation, defined as permanently stopping the study capsules, were categorized by the study interviewers.

Of the almost 2000 cases of HNSCC that were evaluated for possible eligibility, 207 were randomized, giving a recruitment rate of approximately 10%. Sixty eight percent of cases were ineligible, most commonly because of the advanced stage of their disease. Of those who were eligible, 53% declined participation and 5% dropped out in the one-month placebo run-in period.

The most common reason for inactivation was the release of the results of the Carotene and Retinol Efficacy Trial (CARET) in January 1996. Seventy two patients (35% of those randomized) gave this as their reason for inactivation. The CARET results suggested that beta-carotene was associated with increased risk of lung cancer and deaths from cardiovascular disease. The other major reasons for inactivation in this population were: loss of interest, perceived toxicity, death, recurrence of cancer or second cancer and other illness.

Recruitment strategies for enrollment of control and high risk subjects for colorectal cancer chemoprevention phase II aspirin trial.

KD Burney, K Krishnan, MT Ruffin, I Shureiqi, DE Brenner.
 Departments of Internal Medicine and Family Practice, University of Michigan Medical School and VA Medical Center, Ann Arbor, MI and James H. Quillen College of Medicine and East Tennessee State University and Johnson City, TN.

Background: Subject recruitment for chemoprevention trials is challenging. We launched a colorectal chemoprevention trial in July, 1995 to recruit high risk and control subjects. The goal of this study is to examine the impact of various recruitment strategies on subject enrollment. **Methods:** Potential subjects were identified by review of medical records at the University and Veteran's Administration Hospital. Information on the trial and prepaid response sheets were mailed to 890 people. Five months following initial recruitment, additional methods were employed. Newspapers were contacted, flyers posted and community groups informed. **Results:** At this stage, 15 months later, we have successfully enrolled 91 of the 100 subjects needed. Of the participating subjects, the primary source of recruitment information was letter 44 (48.4%), newspaper ads 30 (33%), flyers 4 (4.4%), and other sources 12 (13.2%). Reasons for not participating were obtained from 216 people. The most common reasons reported were distance 21 (9.8%), not willing to undergo procedure 17 (7.9%), ineligible 96 (44.7%) and other 28 (13%). **Conclusion:** Recruitment of subjects for cancer prevention and control trials is a challenging task. Our experience has shown that personal letters and newspapers advertisements were the primary source of contact for over 70% of enrolled subjects.

Cancer Awareness and Beliefs in Relation to Age and Migration Time Among Salvadorean women. S. Shankar¹, N. Figueroa-Valles², and EE. Huerta³. ¹ Johns Hopkins School of Public Health, Baltimore, MD. ² National Cancer Institute, Bethesda, MD. Washington Hospital Center, Washington, DC.

The purpose of this study was to determine the relationship between the number of years lived in US and cancer awareness and beliefs among immigrant Salvadorean women (ISW) living in Washington DC metropolitan area. A total of 843 ISW (ages 20-82) were interviewed. The mean age of the sample was 34.5 years. The number of years lived in the US varied from 0.1 to 32 years with a mean of 7.6 years. Time in US was categorized as ≤ 4 , 5-11, and ≥ 12 years. While 45% of ISW in the 5-11 category could identify Pap as an early detection test, only 23% of those with a longer stay could do so. To identify mammography as a detection tool the distribution was similar with 30%, 45% and 25% respectively. ISW were largely unaware of cancer signs and symptoms. However, the distribution of knowledge within each category followed the same pattern as that of the early detection tests. Older ISW were more likely to identify unusual bleeding or discharge as signs of cancer, however, there was no association with the length of stay. ISW are likely to believe that cancer is not preventable; cancer is contagious (37%) bumps on the body cause cancer (64%), cancer is punishment from God (49%). In addition, ISW perceive themselves to be more prone (77%) to get cancer than men. For the cancer knowledge and behaviors reported the age, education, and number of years in the US made no significant difference. We conclude that for the ISW living in DC area age or number of years lived in US are not modifiers for cancer awareness and beliefs.

Risk of adenomatous polyps by selenium supplementation at moderate doses. Martinez ME, Giovannucci E. Stampfer MJ, Colditz GA, Hunter DJ, Willett WC.

We assessed the relation between selenium supplementation among continuous users and the diagnosis of adenomatous polyps of the distal colorectum in 18,917 members of the Nurses' Health Study and 14,238 participants of the Health Professionals Follow-up Study who were free of cancer or polyps at baseline, who underwent endoscopy, and who provided information on use of selenium supplements. Between 1982 and 1992, 705 female cases occurred and between 1986 and 1994, 608 male cases were identified. After adjustment for age at endoscopy, endoscopy prior to baseline, family history of colorectal cancer, cigarette smoking, and aspirin use, the relative risk (RR) for adenomas for users of selenium supplements was 0.94 (95% confidence interval (CI)=0.74-1.32) as compared to non-users. The RR for a selenium supplement dose of 1 to 130 mcg/day was 1.09 (95% CI=0.75-1.36) and for 140+ mcg/day it was 0.64 (95% CI=0.29-2.17). No protection was suggested for continuous use of selenium supplements of 1 to 5 years (RR=1.09; 95% CI=0.72-1.44), while an inverse, non-significant association was observed for use greater than five years (RR=0.75; 95% CI=0.53-1.61). These data suggest that selenium supplementation at moderate doses does not protect against the development of adenomatous polyps. Further follow-up of these cohorts should elucidate the effect of selenium supplementation at higher doses and longer duration on risk of these pre-malignant lesions.

ROLE OF PSYCHOLOGICAL FACTORS IN BRCA1 TESTING DECISIONS AND POST-TEST DEPRESSION

Schwartz M., Hughes C., Main D., Fulmore C., Lin T., Narod S., Lynch H., and Lerman C.

We are conducting a prospective cohort study of BRCA1 gene testing in members of hereditary breast-ovarian cancer families. This paper reports on the relationship of psychological distress to uptake of BRCA1 testing and post-test depressive symptoms among 149 participants. Following a baseline assessment of demographics, objective risk, traumatic stress symptoms (Impact of Event Scale-IFS), and global distress (Center for Epidemiologic Studies Depression Scale-CES-D), study participants were offered genetic counseling and BRCA1 test results. Overall, 58% of study participants requested BRCA1 test results and 42% declined. After controlling for demographic factors and risk status, baseline stress symptoms were significantly and positively related to subsequent BRCA1 test use in a logistic regression model (OR=2.9 for mid/upper tertile vs. lower tertile on IES, CI=1.3, 6.9) while baseline global distress was not. Participants were re-interviewed 1-month later to examine psychosocial effects of BRCA1 testing. Linear regression was used to examine the main and interacting effects of test result (gene carrier vs. non-carrier) and baseline stress symptoms on global distress (depressive symptoms) at 1-month follow-up. After controlling for baseline global distress, a significant interaction between test result and baseline stress symptoms was found ($p<.05$). Among individuals identified as gene carriers, those scoring in the mid-upper tertiles for stress symptoms at baseline exhibited significant increases in depressive symptoms. Baseline levels of global distress did not moderate the effects of test result. Those results suggest that the presence of stress symptoms may motivate individuals to seek BRCA1 testing, and that individuals with such symptoms may be more vulnerable to adverse psychological effects. Psychosocial counseling may be warranted for this subgroup of genetic testing participants.

Distress in Women Seeking Genetic Counseling for Breast-Ovarian Cancer Risk: The Contributions of Personality and Appraisal.

Audrain J, Schwartz M, Hughes C, Peshkin P, Biesecker B, Lerman C.

Purpose: The purpose of the present study was two-fold: (1) to characterize the psychological status of women with a family history of breast or ovarian cancer who self-refer for genetic counseling and BRCA1 testing; and (2) to identify specific demographic, personality, and appraisal factors that contributed to cancer-specific distress and general distress in this group of women. **Methods:** Participants were 256 women ages 18 and older who had at least one first-degree relative with breast and/or ovarian cancer. Participants were recruited through breast cancer clinics and ob-gyn departments at two medical centers by responding to program information described in a brochure. **Results:** The results revealed mild to moderate distress levels in this population. Unmarried women experienced more general distress than married women. Optimism and perceived control over breast cancer were significantly related to general and cancer-specific distress. Hierarchical regression of general distress indicated that women with higher levels of general distress were less optimistic and had heightened breast cancer risk perceptions accompanied by feelings of low perceptions of control over the development of breast cancer. Women with higher levels of cancer-specific distress had low perceptions of control over developing breast cancer. **Conclusions:** These findings suggest that self-referred genetic counseling participants may be psychologically vulnerable and may benefit from interventions designed to decrease distress and the perceived absence of control over developing breast cancer.

Reactions to Biomarker Information of Women at High Risk for Breast Cancer. A Beisecker, D Selenke, J Hayes, M Brecheisen, J Klemp, C Simon & C Fabian. Kansas Cancer Institute, Kansas City, KS.

To determine the emotions, behaviors and experiences of women receiving breast biomarker information through their participation in a high risk breast clinic (HRBC) study involving breast aspirations, we conducted a retrospective study (n=39) followed by a prospective study (n=25). Participants completed telephone interviews to assess information-seeking behaviors, changes in lifestyle, information sharing and reactions of others in response to their receiving biomarker information.

Both studies yielded similar findings. 40% of respondents indicated they had experienced some anxiety participating in the HRBC, although none of the respondents indicated an increase in anxiety as a result of receiving their aspiration results. For 27%, anxiety decreased after learning results. When asked how their reactions to aspiration results differed from their reactions to mammography results, 42% felt there was no difference; of the 36 who indicated a difference, 31 felt the aspiration results were more reliable. 60 of the 64 women told a spouse or significant other about HRBC participation; 54 told this person about the aspiration results. Over half the participants told friends, primary care physicians and other relatives (sister, parent, child) about HRBC participation, and 2/3 also shared aspiration results with these people. Respondents gave various reasons for disclosing the information to others. Only one respondent felt disclosure of biomarker results to another caused problems; all others felt disclosure relieved anxiety and helped them cope.

Findings indicate that neither HRBC participation nor receipt of aspiration results are significant sources of anxiety for participants; many participants have misperceptions concerning the significance of aspiration results compared to mammography; and social support and sharing of information is important in dealing with risk.

Strategies For Recruiting African Americans And Mexican Americans From A Variety Of Sources Into A Lung Cancer Case/Control Study. Honn SE, Spitz MR, Chamberlain RM; The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030

In our case/control study of lung cancer in minority populations, we utilized 58 different community resources to recruit African-American and Mexican-American cases and controls. The cases were newly diagnosed, untreated lung cancer patients from county, community, and veterans hospitals in Houston, Galveston, and San Antonio, Texas. The cancer-free controls were matched to the cases by age, sex, ethnicity, and locale. The controls were recruited from a variety of sources, including, community centers, community organizations, city clinics, churches, YMCA's, YWCA's, and health fairs.

Each of the hospitals and community resources we utilized required tailored mechanisms of recruitment from their institution. Developing and maintaining recruitment logistics with these sources was facile compared to convincing African-Americans and Mexican-Americans to consent to a 45 minute interview and to having blood drawn. We had to understand the needs and beliefs held within these two population groups and then creatively address these issues.

We developed an advisory board and held meetings with local community leaders to help us learn how to best reach our two study populations. Using what we learned, we invited people to participate in the study by handing out brochures and by presenting our project to attendees at each of the community locations. As an incentive, cases and controls were given a \$20 gift voucher for their participation.

Recruitment of minorities into population-based studies is both challenging and necessary. Addressing the special issues associated with recruiting minority populations makes it challenging and the fact that these groups are understudied makes it necessary. When we understand the needs and beliefs of minority populations, we are better equipped to educate and care for individuals within these groups.

Supported by NCI grant CA 55769, Margaret Spitz, M.D., Principal Investigator

Impact of Intrusive And Avoidant Ideation on Immune Responses of Women Undergoing Follow-up Screening For Abnormal Pap Smears

S. Miller, M. Mills, S. Simms, A. O'Leary, B. Cook, R. Sipps, C. Mangan, R. Belch, S. Douglas

According to the Cognitive-Social Health Information Processing (C-Ship) model, individuals vary in terms of how they cognitively and affectively process information about their health risks and options. Those who characteristically respond with heightened intrusive and related avoidant ideation are generally more psychologically vulnerable in the face of such threats. Hence, they may be especially likely to show immune decrements, particularly in the case of immune-related conditions such as pre-cancerous cervical disease. In the first phase of a longitudinal study, we explored the relationship between immune function and intrusive and avoidant ideation, along with the potential buffering role of social support. Participants were 148 low-income, inner-city women referred for colposcopy following an abnormal Pap smear. The results showed that women with lower perceived social support experienced significantly higher levels of intrusive and avoidant ideation. Specifically, women who perceived a lack of support were more likely to ruminate excessively over their Pap smear results and to engage in cognitive-avoidance strategies, including distraction and numbing, to cope with elevated distress. Further, women with higher levels of avoidant ideation had a significantly depressed absolute number of cytotoxic T-cells. These findings suggest that ineffective, avoidant coping may take a toll on immune function. Longitudinal assessments currently underway will determine whether these immune decrements ultimately predispose to greater or more rapid progression of cervical disease.

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Correlates of Performance of Breast Self-Examination Among Low-Income Minority Women

C. Schroeder, S. Miller, K. Siejak, E. Hernandez, W. Helm

According to the Cognitive-Social Health Information Processing (C-SHIP) model, individuals differ in how they cognitively and affectively process information about their health risks and options. We predicted that under-utilization of complex, self-initiated health-protective behaviors such as breast self-examination (BSE) would be related to cognitive variables (i.e., value placed on BSE and other similar self-initiated health-protective behaviors, such as exercise), whereas over-utilization of such behaviors would be related to affective/emotional variables, especially intrusive ideation (a signature response to medical threat). We explored these issues among low-income women referred for colposcopy following receipt of an abnormal Pap smear result ($N = 349$). Multiple regression analyses indicated significant effects for value placed on BSE and exercise, exercise behavior, age, and intrusive ideation. Specifically, under-users (i.e., those performing BSE less than every other month; $n = 170$) believed that BSE ($p < .0001$) and exercise ($p < .01$) were less important to their overall health. They also exercised less often ($p < .01$) than correct-users (i.e., those performing BSE at or near the recommended rate: once a month or every other month; $n = 138$). Under-users were also younger than correct-users ($p < .001$), probably reflecting the perception that BSE is not as valuable for younger (lower-risk) women. Strikingly, over-users (those performing BSE more than once a month; $n = 41$) had higher levels of intrusive ideation ($p < .01$) than correct-users. These results suggest that cognitive variables, especially values, should be addressed in the case of under-utilization. In contrast, affective variables, especially intrusive ideation, should be addressed in the case of over-utilization.

Depression is Associated with Depletion of Helper T-Cells in Low-Income Patients at Risk for Cervical Cancer

Savard, J., Miller, S.M., Mills, M., Jenkins, J., Plourde, C., O'Leary, A., Douglas, S.D., and Mangan, C.E.

Studies have generally indicated that greater levels of depression are linked to immunosuppression. If this relationship also holds for patients with low grade cervical lesions, then depression may ultimately contribute to higher rates of precancerous cervical disease progression. The present study investigated depression-immune linkages in 93 low-income women ($M = 26.8$ years) with low-grade dysplasia undergoing diagnostic follow-up (colposcopy) for an abnormal Pap smear. On the day of the procedure, depression was assessed by the Center for Epidemiological Studies Depression Scale (CES-D); immunity was assessed by the absolute count and percentage of helper T-, cytotoxic T-, natural killer, and B-cells. Hierarchical multiple regression analyses revealed that depression significantly predicted the number of T-helper (CD4) cells, with higher levels of depression associated with lower levels of CD4 cells (Increase in $R^2 = .04$; $p < .05$), after statistically controlling for potentially confounding health behaviors (i.e., smoking status, alcohol, drug and caffeine use, and sleep quality; $R^2 = .30$, $p < .0001$). A trend in the same direction was found for the percentage of CD4 cells ($p < .11$). Additionally, decrements in the number of CD4 cells were associated with the presence of human papilloma virus types 16 and 18, which are considered to have high oncogenic potential for the progression of precancerous cervical disease ($r_s = -.32$, $p < .05$). These results suggest that higher rates of depression may represent a risk factor for the development of cervical cancer in women with low-grade dysplasia, via depletion of helper T-cells.

Effects Associated with Age and Educational Level among African-American Women Undergoing Diagnostic Colposcopy

S. Miller, C. Schroeder, K. Siejak, C. Lerman, E. Hernandez, W. Helm

Age and education have frequently been found to be associated with adherence to diagnostic colposcopy following receipt of an abnormal Pap smear result. We explored the effects of these variables on the cognitive-affective reactions of low-income African-American women ($N = 221$; $M = 24.8$ years) undergoing diagnostic follow-up (colposcopy) for an abnormal Pap smear. With respect to education, high school/trade school graduates (61%) reported lower state anxiety ($p < .04$) and less use of denial ($p < .02$) and mental disengagement ($p < .04$) than those with less than a high school/trade school education. Graduates also reported less concern about embarrassment during the appointment ($p < .03$), less concern about what the doctor would find during the appointment ($p < .02$), less interference with daily activity due to worry about the condition ($p < .05$), and less concern about the effect of the condition on the relationship with their partner ($p < .04$). With respect to age, older patients were less concerned about pain or discomfort during the appointment ($p < .05$), less worried about the effect of their condition on future childbearing ability ($p < .001$), and less worried about what the doctor would do during the appointment ($p < .003$). These results indicate that less educated, as well as younger, women are more likely to misunderstand cancer risk feedback and are more vulnerable to adverse psychological consequences in the face of an abnormal Pap smear result, which may interfere with follow-up adherence. These individuals should thus benefit from preventive protocols which target potentially maladaptive reactions to cancer risk follow-up.

Enhancing Adherence in Longitudinal Research with Traditionally Underserved, Cancer Risk Populations: Implications for Recruitment and Retention in Research Protocols

M. Mills, S. Miller, S. Simms, M. Jenkins, C. Plourde, J. Savard, B. Cook, A. O'Leary

Recent research indicates that poorer, less educated, inner-city populations face a variety of structural and psychosocial barriers that undermine adherence to recommended cancer risk screening and follow-up regimens. This pattern may account for findings showing higher rates of morbidity/mortality among this population, along with greater associated costs of medical care. Further, lack of adherence makes it difficult to accrue and retain high-risk populations into clinical research trials. We are currently conducting a large-scale, longitudinal study of the relationship among psychoneuroimmunologic variables and medical outcomes among low-income, inner-city women referred for colposcopy following an abnormal Pap smear. Guided by the Cognitive-Social Health Information Processing (C-SHIP) model, we have refined traditional recruitment techniques to provide more intensive and effective efforts to comprehensively assess and address cognitive-affective barriers to adherence. These include encoding and expectancy barriers (e.g., lack of knowledge about the medical condition and its management); affective barriers (e.g., fear of cancer); and self-regulatory/practical barriers (e.g., forgetting, lack of transportation or child care). By comprehensively addressing these barriers in a preventive fashion (i.e., before a missed appointment), we have significantly increased adherence to scheduled appointments. These results demonstrate that a dedicated, interdisciplinary team, drawing on current findings and theory, can significantly impact on the effectiveness of follow-up care for a population at high risk for progression of precancerous cervical disease.

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Psychosocial Factors and Breast Cancer Survival: Evidence From the Black/White Cancer Survival Study. Richardson LC, RWJ Clinical Scholars Program, and Jackson JS, PhD, Institute for Survey Research, University of Michigan and National Cancer Institute.

Black women have increased mortality with breast cancer compared to whites. The exact cause of this difference is unknown at this time but may include socioeconomic status, genetic susceptibility, and environmental factors. This analysis examines the impact of psychosocial measures on survival with breast cancer.

The goal of the study was to collect data on prognostic factors felt to be important in explaining mortality differences such as disease characteristics of stage, estrogen receptor, and grade; socioeconomic status, access to health care, quality of treatment, and comorbid conditions. Psychosocial measures of social network size, social support, and coping strategies were also collected. Proportional hazards regression was performed to evaluate the contribution of these factors to the black/white survival difference in breast cancer patients.

After controlling for the traditional prognostic variables above, the hazard ratio for race decreased from 2.05 (95% CI 1.64, 2.55) to 1.40 (95% CI 1.08, 1.83). Social network score, social support, and coping were added to the model producing an increase in the hazard ratio for race to 1.47 (95% CI 1.12, 1.94).

These results suggest a trend that psychosocial factors may contribute to improved survival in black women with breast cancer. Future investigation should evaluate the role of psychosocial measures in improving breast cancer survival.

Psychological Distress and BSE Among Women With a Family History of Breast Cancer. Schwartz, M, Taylor, K, Willard, K, Daly, M, Lamdan, R, Siegel J, & Moran, K.

Recent studies have suggested that general psychological distress may be a barrier to BSE among women with a family history of breast cancer. However, other studies have suggested that breast cancer worries may be associated with increased and perhaps excessive BSE. In the present study we evaluated the role of these variables in distinguishing women who practice monthly BSE from those who under-utilize and those who over-utilize BSE. Women (N=110) with a first degree relative treated for breast cancer at the Lombardi Cancer Center, completed a baseline telephone interview in which sociodemographics, breast cancer surveillance practices, and psychological variables were assessed. We utilized two logistic regression models to identify predictors of under-utilization and over-utilization of BSE. In the first model we sought to identify variables that distinguished women who adhered to BSE recommendations (25% of sample) from those who under-utilized BSE (51%). The following variables predicted adherence (relative to under-utilization) of BSE: breast cancer knowledge (OR=1.6, 95% CI=1.1, 3.5), education (OR=0.23, 95%CI=.1, .8) and general distress (OR=0.5, 95% CI=.3, .9). In the second model, we identified variables that distinguished adherers from over-utilizers (24%). The following variables were related to adherence (relative to over-utilization): breast cancer knowledge (OR=2.0, 95% CI=1.1, 3.9) and breast cancer worries (OR=0.5, 95% CI=.2, .9). These data suggest that among women with a family history of breast cancer, high general distress coupled with low breast cancer knowledge may be associated with under-utilization of BSE, while high levels of breast cancer worries coupled with low knowledge may be associated with excessive BSE.

Breast Cancer Screening Practices in an Immigrant Hispanic Population. N. Figueroa-Valles¹, S. Shankar², EE.Huertas³. ¹National Cancer Institute, Bethesda, MD. ²Johns Hopkins School of Public Health, Baltimore, MD. ³Washington Hospital Center, DC.

Little is known about the cancer screening practices of the more recent Hispanics immigrants. The purpose of this investigation was to assess breast cancer early detection practices and to determine predictors of obtaining a mammogram in a sample of 222 immigrant Salvadorean women aged 40 years and older, living in Washington, D.C. area. Interviews were carried out face to face. Seventy-eight percent of the women claimed knowledge on how to perform breast self examination (BSE) and 62% of them practiced monthly. Breast clinical examination (BCE) was within one year for 63%, and within two years for 84%. BCE was part of routine check up for 75%. Eighty-five percent of the women reported hearing about mammogram, but of these, only 61% ever had one. The most recent mammogram was within one year for 62%, and within two years for 85%; it was part of a routine checkup for 70%. Lack of physician recommendation and cost were the main barriers to obtaining a mammogram. Significant predictors for ever having a mammogram were: ever having BCE (OR=11.5), knowing how to perform BSE (OR=4.5), having BCE within two years (OR=2.4), having BCE at a hospital (OR=5.7), willing to pay for a mammogram (OR=2.6), and worrying about getting breast cancer (OR=2.4). These ORs hold after adjusting for age and length of stay in U.S. Access to care was found significant for having insurance (OR=4.5), and seeing an exclusive physician (OR=2.3). Having a place for regular health care became significant after adjusting for age (OR=3.5) and for time living in US (OR=2.6). Preferences for physicians' gender, race, or language were not significant predictors of mammogram. In addition, access to care, knowledge of signs, symptoms, and screening tests were not barriers.

A comprehensive behaviour change program designed to increase sun-protective behaviour among school students

J B Lowe, K P Balanda, W R Stanton, C Del Mar

Purpose of Study: Queensland, Australia has the highest incidence of both malignant melanoma and non-melanocytic skin cancer in the world. The purpose of the project was to develop an intervention to promote the use of sun protection by students and determine the immediate and short term effect.

Methods: The study was based on a matched case-control design involving 26 state government high schools of which 13 were randomly allocated to an intervention group and 13 to a control group. A total of 3,341 students participated in the study. Schools were matched according to geographic location, size and socioeconomic status. The evaluation format adopted a pre and post test design. Students entering their first year of high school in 1992 constituted the cohort which was tracked to the end of their senior year of high school.

Results: The intervention was well received and statistically significant changes were noted in students' attitudes and knowledge with possible changes in their behaviour towards sun protection. The effects of the intervention on school policies will also be discussed.

Conclusion: This five year study concluded in 1996. The results to date suggest that the intervention was well received and may be effective.

Specific Worry about Breast Cancer Predicts Mammography Use in Women at Risk for Breast and Ovarian Cancer

M. A. Diefenbach, M. B. Daly, S. M. Miller, R. Sipp

Previous research suggests that elevated levels of negative affect (e.g., anxiety and depression) are related to non-adherence to health protective regimens. In contrast, other research has emphasized the motivating role of specific cancer-related worries and concerns in initiating and sustaining health-protective behaviors. The aim of the present study was to distinguish the effects of general anxiety and depression from specific cancer-related worries on future cancer-protective behaviors among women at familial risk for breast and ovarian cancer. Participants were 670 women (mean age 40.0, SD=10.04) undergoing diagnostic assessment and counseling in the Family Risk Assessment Program at Fox Chase Cancer Center. Patients were interviewed prior to program enrollment and at a 12-month follow-up visit. Interviews assessed risk history, psychological variables (i.e., perceived worry about cancer, depressive and anxious mood), and risk behaviors (e.g., mammography use). Logistic regressions indicated that higher levels of cancer specific worries at intake predicted future mammography use $\chi^2(1) = 4.20, p < .04$, controlling for age and family history. In contrast, depressive and anxious mood were not significantly associated with adherence to mammography. Further, correlations among cancer worry and depressive and anxious moods were low ($r = .05$ and $r = .21$, respectively). The results suggest that it may be important to activate cancer specific worries, in combination with specific recommendations for screening behaviors, to effectively enhance cancer prevention and control behaviors in at risk populations.

Eyes and Ears: Sources of Health Information Among Minorities. Strom C, Chamberlain RM, Koehly L, Hudmon KS, Spitz MR; The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030

Health-related messages about cancer prevention are directed to the public through various information pathways, including TV, doctors, brochures, newspapers, radio, and books. Little is known, however, about which sources of health information are most effective in reaching minority populations.

We analyzed data collected as part of a case-control study of lung cancer in Mexican-Americans (MA; $n=206$) and African-Americans (AA; $n=290$) conducted at M. D. Anderson Cancer Center. Data were tabulated from responses to the question, "Where do you get your most useful information about how to prevent illness and improve your health?" (Multiple answers were allowed). AAs reported that their primary sources of health information were: doctors (60%), TV (41%), and brochures/pamphlets (38%). In comparison, MAs reported: TV (56%), doctor (44%), and newspaper (36%). Preliminary analysis showed that more AAs than MAs obtained health information from family and friends ($p=0.02$), brochures/pamphlets ($p=0.002$) and doctors ($p<0.001$). When compared with AAs, a significantly larger proportion of MAs obtained information from newspapers ($p=0.003$) and TV ($p<0.001$). Further analysis involving internal unfolding methods will be performed to determine which demographic profiles (as a function of ethnicity, education, sex, and age) prefer which health information sources. Awareness of differences in source preferences will assist future investigators in designing methods of intervention delivery that will more effectively reach the intended audience.

Supported by NCI grant CA 55769, Margaret Spitz, M.D., Principal Investigator.

Church nurse training program - targeting cancer prevention and early detection programs to minority communities. G. Grana, MD, L. Brown, M.Ed., P. Barse, RN, L. Johnson, BS, R. Poh, Ph.D., J. Modelske, RN, C. Rea, RN, R. Kolmer, O. Grace Cancer continues to exert a disproportionate burden on minority communities. While strategies focusing on cancer prevention and early detection have been targeted to minority communities, many barriers have been identified hindering success of these interventions. The church has been shown to be an entry into many minority communities. Programs focusing on AIDS education, asthma and other health issues have been carried out within the church community. The church "nurses" or "ushers" have long had a tradition of being healers and health advocates within the church community. With this in mind, a program was developed in Camden, New Jersey, with local churches, the three major health providers in Camden, and The University of Medicine and Dentistry of New Jersey School of Medicine and School of Nursing, to train a cadre of health advocates functioning within the structure of the church. In collaboration with members of the ministry and representatives of the community, a curriculum was developed and a pilot project was undertaken. In this pilot project, two sample churches were selected, and with the extensive support of their ministers, five individuals from each church were identified who functioned as church "nurses" or "ushers" within that church community. These individuals participated in a ten-week church health education program encompassing ten modules, each lasting two hours, which were conducted in the evenings by the participating institutions. Pre-and-post-assessment was conducted within each of the modules to assess impact as to the information transmitted, understanding of this information, and the potential impact of this information on the participant and the church community. All participants completed the educational program. Additional churches are now being recruited to disseminate this program throughout the City of Camden. Programs such as this, promoting cancer prevention and control to racial and ethnic minorities, merit evaluation and may be amenable to widespread dissemination.

Coping strategies affect psychological well-being among
first-degree relatives of breast cancer patients
Lipkus, I.M., Rimer, B.K., Audrain, J., & Lerman, C.

We explored how women's concerns with, and perceived risk of getting breast cancer, after having a family member recently diagnosed with breast cancer, interacted with coping strategies to affect psychological well-being. Psychological well-being was assessed by the Profile of Moods States (POMS) at baseline and at 3 months ($n = 312$).

At baseline, the greater use of avoidant coping strategies (e.g., denial, did not think about the issue) predicted poorer psychological well-being. Controlling for baseline POMS scores, greater use of avoidance coping predicted improved psychological well-being at 3 months among women who were concerned with, or perceived a greater risk of breast cancer. The use of avoidant coping predicted poorer psychological well-being among women who were not concerned with or perceived a low risk of breast cancer. There were no significant interactions at baseline or at 3 months for coping by trying to: 1) actively confront the stressors related to the diagnosis (problem-solving coping), and 2) regulate one's emotional reactions to the diagnosis (emotion-focused coping). Being concerned with breast cancer was related to poorer psychological well-being at baseline and at 3 months; higher perceived risk was related to poorer psychological well-being at baseline only.

These results suggest that among women who are concerned with or feel at risk for breast cancer, avoidant rather than problem/emotion focused coping may produce positive short-term improvements in psychological well-being.

Closing an intervention trial early: Experiences from Carotene and Retinol Efficacy Trial K Anderson, C Powell, D Bowen, S Shanabarger, M Thornquist

The decision to end a long-term trial earlier than planned presents many challenges. The Carotene and Retinol Efficacy Trial (CARET), a multi-center chemoprevention trial, was designed to test the efficacy of a combination of beta-carotene and retinyl palmitate in preventing lung cancer. The trial's second interim analysis suggested a potential adverse effect of the intervention agent. After extensive review, the external monitoring committee recommended ending the active intervention. The CARET Steering Committee reviewed unblinded data, concurred, and voted to end intervention ending 21 months early on January 11, 1996. To inform participants first, they were mailed letters from the trial's Principal Investigator within two days informing them of the results and telling them to stop taking the vitamins. Reflecting the trial's multi-site nature, letters from the local Investigator were mailed a week later. This letter unblinded participants, asked them to return the vitamins, and to return for a final visit. Notifying participants and releasing all the decisions and results were coordinated centrally. Study results were communicated to other beta-carotene studies. The Investigators' increased involvement continued with local and national press releases, press conferences, and media interviews. Common data, slides and other presentation and explanatory materials were made available. Because of the sensitive nature of ending the intervention early, the six Institutional Review Boards were kept informed and approved all written materials and data collection procedures. When intervention ended the focus turned to CARET's next phase and the scientific priorities for long-term follow-up. Procedures and policies created during this period will help guide future NCI-funded studies through this difficult time.

The Challenge of Participant Retention When Active Intervention Ends Early: The Carotene and Retinol Efficacy Trial Experience C
Powell, K Anderson, D Bowen, S Shanabarger, M Thornquist

The halting of intervention early in a long-term prevention trial can have unexpected effects on participant retention. CARET, a multicenter lung cancer prevention trial in 18,314 men and women, tested the efficacy of a combination of beta-carotene and retinyl palmitate in preventing lung cancer. Because interim analyses suggested an adverse effect, active intervention was ended 21 months early on January 11, 1996. Before public release of study results, participants were sent two individualized letters informing them of the results of the study and whether they were taking the active agent or placebo. These letters and media coverage of the trial resulted in over 1,400 participant calls and contacts with study center staff within three weeks. To standardize our response, scripts incorporating retention principles aided staff in these contacts. Informational meetings were held in January by study centers. Both study center specific and study-wide newsletters discussing the end of intervention were sent to participants. Study centers followed up within three months with supportive letters and organized participant recognition events. To encourage follow-up, flexible scheduling was implemented for the last study center visit. Attention focused on both participant and staff retention by organizing staff grief and loss or other counseling sessions. The initial feedback from participants was supportive of both the study staff and the trial's scientific goals. As of 9/30/96, 62% of the 13,580 participants taking study vitamins on 1/12/96 have completed a transition contact (81% in person, and 19% by phone); 39% of the 3,173 already inactive and not taking study vitamins have completed a transition contact (23% in person, and 77% by phone). These results indicate participants can be retained through the unexpected and potentially disappointing ending of a prevention trial.

TREATMENT DELAY FACTORS AND IMPLICATIONS FOR
TESTICULAR CANCER PATIENTS

Sigurdson AJ, Amato RJ, Hutchinson LH, Strom SS.
University of Texas M. D. Anderson Cancer Center, (MDACC).

Testicular cancer (TC) patients diagnosed with high volume disease have a worse prognosis than those with low volume disease. Treatment delay (TD) is directly related to disease volume in both the rapidly dividing tumors and also in the slower growing ones. We sought to identify factors that contributed to a TD of one month or longer among men with TC. Information on time between the acknowledgement of symptoms to seeking medical attention, age, race, education, income, cryptorchidism and insurance status were abstracted from medical chart reviews of 120 TC patients registered at MDACC between 1990-96 and from a risk factor questionnaire. Kaplan-Meier and the log rank test were used for analysis. There were 49 patients with a TD time of one month or longer, with a median of 6 weeks (range 4 to 104). In Kaplan-Meier analysis, being under-insured (Medicaid or no insurance) and having a history of cryptorchidism increased TD time, but did not reach statistical significance with log rank testing. These results, although based on a small sample, suggest that lack of adequate health insurance and a knowledge deficit about increased risk of TC with cryptorchidism contribute to TD and a higher volume of disease at diagnosis.

Deletion of Poly (ADP-Ribose) Polymerase Gene (PADPRP)

Genetic Material Predisposes to Lung Cancer. Wu XF, Hsu TC, Liu J, Cao S, Hong WK and Spitz MR. The University of Texas M. D. Anderson Cancer Center and School of Public Health, Houston, TX 77030 (Supported by CA55769, CA68437 and CRFA).

Purpose: The PADPRP gene has been implicated in carcinogenesis through its role in DNA repair, replication and recombination. It has been suggested that B allele, which results from a deletion in the PADPRP gene, predisposes to myeloma in blacks. We assessed the association between PADPRP genotype, mutagen sensitivity (MS) and cigarette smoking in a minority lung cancer (LC) case-control study. **Methods:** PADPRP polymorphism was detected by a PCR-based RFLP analysis. MS was based on an *in vitro* assay quantifying bleomycin-induced chromatid breaks in peripheral blood lymphocyte cultures. There were 121 cases (80 African Americans (AA), 41 Mexican Americans (MA)) with previously untreated LC and 171 matched controls. **Results:** The distribution of PADPRP genotype frequencies was significantly different among MA and AA controls ($P < 0.0001$). The genotype with B allele (AB+BB) was found in 53.7% of MA cases, 32.4% MA controls, 81.3% AA cases and in 77.3% AA controls. The odds ratio (OR) and 95% confidence interval for PADPRP genotypes with B allele were 1.9 (1.1, 3.1), 1.3 (0.6, 2.7) and 2.4 (1.1, 5.3) for overall, AA and MA, respectively. Patients with the susceptible genotypes appeared to have developed cancer at earlier ages and have smoked fewer cigarettes than did patients with the non-susceptible genotype. Only adenocarcinoma was significantly associated with the PADPRP susceptible genotype with an OR of 4.0. MS (≥ 1 break/cell) was associated with an OR of 3.3 (1.6, 6.8). On stratified analysis, interactions which appeared multiplicative were noted for PADPRP susceptible genotypes, MS and smoking status in MA. The ORs for PADPRP with B allele genotypes, MS and both risk factors combined were 1.1, 1.6 and 16.9, respectively. The combined OR for PADPRP B allele genotype and smoking status was 19.3. **Conclusion:** This polymorphism appears to be associated with LC risk. However, it is likely that no single genotype is sufficiently predictive of risk, but a panel of susceptibility markers is needed to define high risk subgroup.

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Correlations between DNA Repair Biomarkers for Cancer Susceptibility in Lung Cancer

Qingyi Wei, Lie Cheng, Donghui Li, Mianying Wang, Jun Gu, Waun Ki Hong, and Margaret Spitz. The U.T. M.D. Anderson Cancer Center, Houston, TX 77030

Smoking is suggested as a major risk factor for lung cancer. Benzo[a]pyrene diol epoxide (BPDE), a chemical carcinogen commonly found in tobacco, is both mutagenic and carcinogenic. In this study, *in vitro* BPDE-induced DNA adducts and chromosomal aberrations and DNA repair capacity were determined in peripheral blood lymphocytes of 21 lung cancer cases and 41 normal controls. The BPDE-adduct levels were measured by the ^{32}P -postlabeling assay and the frequency of chromosomal aberrations by the mutagen sensitivity assay, in which the cells were treated at a dose of 4 μM BPDE for 5 h. DNA repair capacity was measured by the host cell reactivation assay, in which plasmids were treated at a dose of 60 μM BPDE for 3 h before transfection. Cellular ability to repair BPDE-induced DNA damage was found inversely correlated with the levels of BPDE-induced DNA adducts ($n=34$; $r=-0.34$; $p=0.048$) and the levels of BPDE-DNA adducts correlated significantly with the frequency of chromosomal aberrations ($n=62$; $r=0.42$; $p=0.001$). However, cellular ability to repair BPDE-induced DNA damage was not correlated significantly with the frequency of chromosomal aberrations ($n=47$; $r=-0.06$; $p=0.677$). Reduced DNA repair capacity is responsible for increased levels of BPDE-DNA adducts, whose persistent levels are responsible for the increased frequency of chromosomal aberrations. These biomarkers have differing sensitivities in measuring repair of damage induced by chemical carcinogens; therefore, the complementary use of these assays should increase the probability of identifying individuals with susceptibility to smoking-related cancers. (Supported by NIH grants CA55769 and CA68437)

Establishment of Biologic Specimen and Data Banks to Study Early Markers and Etiology of Lung Cancer in Chinese Tin Miners. Taylor PR. Qiao YL. Yao SX. Erozan YS. Luo XC. Barrett MJ. Yan QY. Giffen CA. Huang SQ. Maher MM. Forman MR. Tockman MS. National Cancer Institute, Bethesda, MD, USA; Yunnan Tin Corporation, Gejiu, China; The Johns Hopkins Medical Institutions, Baltimore, MD, USA; Information Management Services, Inc., Silver Spring, MD, USA.

Purpose: This study was conducted to establish biologic specimen and data banks for the study of early markers and etiology of lung cancer. **Methods:** A dynamic cohort was established beginning in 1992 through an ongoing lung cancer screening program that includes multiple sputum and chest xray collections, and a single collection of blood, urine, and toenails. **Results:** From 1992-94, 7873 miners at high risk of lung cancer from exposure to radon, arsenic, and tobacco were enrolled in the cohort and 178 new lung cancer cases were identified, including 46 with sputum from up to 3 years before diagnosis. Although occupational exposures are the predominant risk factors, initial cohort analyses also show that lung cancer is associated with chronic obstructive lung disease and a number of measures of tobacco exposure, including early age of first use, duration, and cumulative exposure. **Conclusion:** This is the first large dynamic cohort established explicitly with a biologic specimen bank to evaluate early markers of lung cancer, and new protein and molecular markers for lung cancer are currently being evaluated. Etiologic factors in lung cancer, including smoking, medical conditions, arsenic and radon exposure, and diet are also being examined.

A Case-Cohort Study of Early Biomarkers of Lung Cancer in a Screening Cohort of Yunnan Tin Miners, China. Qiao YL. Tockman MS. Li L. Erozan YS. Yao SX. Barrett MJ. Zhou WH. Giffen CA. Luo XC. Taylor PR. National Cancer Institute, Bethesda, MD, USA, Yunnan Tin Corporation, Gejiu, China; The Johns Hopkins Medical Institutions, Baltimore, MD, USA; Information Management Services, Inc., Silver Spring, MD, USA.

Purpose: This study compared the accuracy of a new early lung cancer biomarker with routine screening methods for detection of preclinical, localized lung cancer. **Methods:** A case-cohort approach was used to compare the accuracy of lung cancer detection by monoclonal antibody (Mab 703D4) recognition of up-regulation of heterogenous nuclear ribonuclear protein (hnRNP A2/B1) with cytology and radiographic screening of miners highly exposed to tobacco smoke, radon, and arsenic in Southwestern China. **Results:** Mab 703D4 detection of hnRNP expression by sputum epithelial cells was more accurate for detection of early (localized) lung cancer than routine screening methods. Among 57 cases and 76 non-cases at the first screening, Mab detection of hnRNP was more sensitive than standard methods (74% vs. 21-42%) but had lower specificity (70% vs. 90-100%). Recognized hnRNP up-regulation resulted in detection of approximately 1/3 more early cases than the combination of x-ray plus cytology. **Conclusions:** Detection of hnRNP A2/B1 expression appears to be a good initial screening test for lung carcinogenesis, identifying those with high probability of developing subsequent clinical cancer. Patient stratification by Mab detection could initiate a progression of diagnostic tests with greater specificity (which are expressed later in the morphologic progression or gene markers).

Chromosomal breaks (CB), spontaneous and bleomycin induced, and sister chromatid exchange (SCE), in peripheral blood lymphocytes have been shown to be sensitive cytogenetic assays to detect susceptibility to DNA-damaging effects in cancer patients and in healthy controls. However, factors such as age, sex, smoking, and alcohol, must be considered important covariates with bleomycin-induced chromosomal breaks and sister chromatid exchange. In this paper, we propose a statistical method to evaluate the number of chromatid breaks per cell using negative binomial family with unknown shape parameter. The negative binomial distribution is important in modeling data when the variance is greater than the mean, often called "overdispersed Poisson data." To show how well the negative binomial family fits, we use three different cancer data sets. The first was a case-control study of Lung cancer in a minority population (286 cases and 156 controls), the second was 311 Head and Neck cancer patients, and the third was 105 individuals diagnosed with Hodgkin's Disease. The results show that age, sex, smoking, alcohol, and race had no effect on bleomycin-induced chromosomal breaks, and that the negative binomial family represents the CB very well. (This work was supported by the NIH grants RO1-GM52607, RO1-CA55769, RO3-CA64121).

Induction of apoptosis in all-trans retinoic acid (ATRA)-resistant lung cancer cell lines by N-(4-hydroxyphenyl) retinamide (4HPR) CP. Zou, CC. Zou, J. Kurie, D. Lotan, WK. Hong, and R. Lotan.

Retinoids can inhibit the growth and enhance the differentiation of various tumor cell lines. However, the majority of human lung cancer cell lines were found to be either nonresponsive or poorly responsive to RA. Recently, it has been shown that 4-HPR can induce apoptosis in leukemia, neuroblastoma, and head and neck squamous carcinoma cells. Therefore, we compared the effects of 4-HPR and ATRA (both at 10^{-6} and 10^{-5} M) on the growth and apoptosis in 10 human NSCLC, 2 SCLC and NHBE cells. Growth was measured by cell counting and apoptosis by DNA ladder formation and terminal deoxynucleotidyl transferase (TDT) assay. All of the cell lines were sensitive to 4-HPR in that their number at the end of a 5-day treatment was about 10% of the control number whereas ATRA decreased the cell number to 60% of the control in 2 cells and was even less effective in the rest of the cells. Both drugs were able to induce apoptosis in lung cancer cell lines. However, apoptosis could be observed earlier and stronger in 4HPR-treated cells. Expression of p53 and bcl-2 genes which are related to apoptosis could be detected in several NSCLC cells, but there was no difference in response to retinoids between the cells which carried wild type and or mutant gene. Three of the cell lines expressed the nuclear RA receptor (RAR) - β constitutively, RA and 4-HPR did not alter its expression. In summary, ATRA and 4HPR both can induce apoptosis, but 4-HPR is more potent than ATRA in growth inhibition and apoptosis induction in lung cancer cells. ATRA could induced RAR- β expression in one of the NSCLC cells and NHBE cells, but 4-HPR were failed to do so. However, no correlation between RAR- β induction and apoptosis was found. Apoptosis induced by retinoids in these cells are p53 and bcl-2 independent. 4-HPR is a stronger growth inhibitor and potent apoptosis inducer than ATRA. It is, therefore, a potential candidate in clinical trials for prevention or treatment of lung cancer. (CPZ was supported by Training Grant R25 CA57730 from the NCI).

PURPOSE: The purpose of this study is (1) to determine phytoestrogen levels in a variety of foods in the forms in which they are commonly consumed and (2) to develop a nutrient database which can be used in analytic epidemiologic studies to assess the relationship between phytoestrogen exposure and disease risk. **METHODS:** Semistructured interviews were conducted with 118 white, black, and Latina women to assess the consumption of over 65 plant-based foods. Various brands/varieties of each food sample are purchased from multiple sources and prepared as described by study participants. Food samples are analyzed by mass spectrometry analysis to obtain quantitative levels of seven phytoestrogens (i.e., daidzein, formononetin, genistein, biochanin A, coumestrol, secoisolariciresinol and matairesinol). **RESULTS:** Preliminary results suggest that source and preparation practices have little influence on most phytoestrogen levels. Many commonly consumed fruits and vegetables contain no or low levels of phytoestrogens. The largest sources of phytoestrogens identified to-date are garbanzo beans (biochanin A), alfalfa (formononetin) and "regular" bean sprouts (coumestrol), plums (matairesinol), and products containing soy-based ingredients, such as most canned chili (daidzein and genistein). **CONCLUSIONS:** The availability of quantitative estimates of the phytoestrogen content in a wide variety of foods will substantially enhance the scope of epidemiologic studies. Such a database will (1) allow the examination of the effects of specific phytoestrogens, (2) minimize the potential for uncontrolled confounding by unmeasured sources of phytoestrogens, and (3) permit the disentangling of the effects of fiber, antioxidant vitamins, and other components of phytoestrogen-rich foods.

Reduced Rates of Metabolism and Decreased Physical Activity in Breast Cancer Patients Receiving Adjuvant Chemotherapy.
W Demark-Wahnefried, V Hars, M Conaway, K Havlin, BK Rimer, G McElveen and EP Winer. Stedman Center for Nutritional Studies/Duke Comprehensive Cancer Center at Duke University Medical Center, Durham NC 27710

Weight gain is a common side effect among breast cancer patients receiving adjuvant chemotherapy - a side effect which may decrease quality of life and potentially impair survival. Weight gain during treatment is a problem that is clinically well-appreciated and has been studied by a number of investigators. Few controlled studies have been conducted to determine reasons to explain this apparent energy imbalance.

An intensive study of 20 premenopausal, early stage breast cancer patients was undertaken to quantitate changes in energy intake, specific components of energy expenditure [i.e. resting metabolic rate (RMR), diet-induced thermogenesis (DIT) and physical activity] and body composition. Complete data on 18 subjects suggest that RMR and DIT decreased significantly from baseline to midtreatment ($p < 0.05$) and then rebounded to levels similar to baseline upon completion of therapy. Overall, levels of physical activity and energy intake also decreased significantly during treatment when compared to baseline levels ($p = 0.04$ and $p = 0.03$, respectively). A trend toward decreased lean body mass (baseline = $42,121 \pm 3,013$ g; completion = $41,738 \pm 3,329$ g) also was noted ($p = 0.10$). Findings suggest that chemotherapy provokes a number of significant changes in body composition and metabolic needs. Further research in this arena will provide valuable insight into creating optimal interventions to curb weight gain in women with breast cancer.

DETERMINANTS OF SERUM ANTIOXIDANT LEVELS IN A POPULATION AT HIGH RISK FOR GASTRIC CANCER.

Schmidt, B.A., Fontham, E.T.H., Malcom, G.T., Ruiz, B., Bravo, L.E.*, Zsembik, C.J., Gibbs, D.G., Correa, P. (PO1-CA-28842)
Louisiana State University Medical Center, New Orleans, LA
70112 ; * Universidad del Valle, Cali, Colombia

The aim of this study was to determine the demographic, lifestyle and histopathological factors related to serum antioxidant levels in a population at high risk for stomach cancer. Serum levels of retinol, α and γ -tocopherol and carotenoids were measured in 688 women and 531 men screened for inclusion into a chemoprevention trial of precancerous gastric lesions in Narino, Colombia. All associations reported below are statistically significant with p-values < 0.05. Men had lower levels than women of α and β -carotene, cryptoxanthin and lycopene. Older women (> 50 years) had lower levels of α and β -carotene, cryptoxanthin and higher levels of α -tocopherol whereas younger men had higher levels of retinol. High body mass index was associated with higher levels of cryptoxanthin, lycopene, β -carotene and α -tocopherol in men only. Male smokers, but not female smokers, had lower levels of all carotenoids, retinol and α -tocopherol compared to nonsmokers. Severe *H. pylori* infection in men was associated with lower levels of all carotenoids but not retinol, α and γ -tocopherol. In women, severe infection was associated with lower levels of lycopene, α and β -carotene. Dysplasia of the gastric mucosa was associated with lower concentrations of cryptoxanthin in women and lower levels of all carotenoids and α and γ -tocopherol in men. This study confirmed a previously observed unique carotenoid profile in this population with α -carotene levels approximately equal to β -carotene and very low levels of lycopene.

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Wheat Bran Supplementation and Estrogen Metabolites in Postmenopausal African American Women

Stark, A.H., Switzer, B.R., Atwood, J.R., Travis, R.G., and Chiu, Y. Univ. of N. Carolina at Chapel Hill- School of Public Health & Lineberger Comprehensive Cancer Center; College of Nursing & UNMC/Eppley Cancer Center

Purpose: Insoluble dietary fiber is considered a protective agent against colon cancer, but it is not clear if or how increasing fiber intake prevents breast cancer. This study investigated the effects of wheat bran fiber supplementation on estrogen metabolism in a group of postmenopausal African American women participating in a community dietary intervention study. **Subjects:** Eighteen female participants (aged 63.7 ± 1.5) in the NIH funded project "Fiber Adherence and Marker Development in Black Churches" were included in this study. Nutritional assessment, blood and 24 h urine samples were collected before and after 6 weeks of supplementing the daily diet with 35 g wheat bran cereal (11.6 g dietary fiber) spiked with 50 mg of riboflavin (biomarker of supplement intake). **Results:** Nine of the eighteen women were taking some form of estrogen replacement therapy (ERT). Baseline and post-intervention levels of estradiol and sex hormone binding globulin (SHBG) were significantly higher, and androstenedione significantly lower in participants on ERT. In participants not receiving exogenous hormones, wheat bran consumption was not associated with a significant decrease in levels of estradiol (25.7 ± 2.7 vs 31.0 ± 1.9 pg/ml), estrone (38.3 ± 10.1 vs 39.3 ± 10.6 pg/ml), and androstenedione (0.78 ± 0.08 vs 0.68 ± 0.11 ng/ml) or increased SHBG levels (35.2 ± 6.4 vs 34.8 ± 6.5 nmol/L). In addition, the fiber intervention was not related to changes in estrogen metabolite levels in women on ERT. **Conclusion:** In postmenopausal women no connection was observed between wheat bran supplementation and a decrease in circulating estrogen levels, an effect thought to be beneficial in lowering breast cancer incidence. These results do not confirm earlier studies indicating that wheat bran fiber decreases serum estradiol and estrone. Inherent differences in premenopausal and postmenopausal metabolism may account for this discrepancy.

The Role of Obesity, Diet, and Vitamin Supplements in Adenocarcinoma of the Gastroesophageal Junction. M. Mooney, A. Michalek, and C. Mettlin. Roswell Park Cancer Institute, Buffalo, New York

Objective: Although rare, adenocarcinoma of the gastroesophageal (GE) junction has increased dramatically in the United States since the 1970's. Previous research suggests obesity is a risk factor and that fruit and vegetable consumption may decrease risk; however, little prior evidence supports a protective role for vitamin supplements. This study investigates the role of these and other risk factors in the etiology of this disease.

Methods: A case-control study comparing responses from 191 patients at Roswell Park Cancer Institute diagnosed with adenocarcinoma of the GE junction from 1971-95 and 382 healthy, age and sex-matched controls to a standard questionnaire on nutritional and other potential risk factors. Unconditional logistic regression analysis was used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs).

Results: Elevated risks were associated with the highest body mass index (BMI) quartile compared to the lowest (OR = 2.1, CI = 1.2 - 3.7). An inverse association was observed with the highest level vegetable consumption (OR = 0.5, CI = 0.3 - 0.7) compared to the lowest. No significant associations were found with consumption of fruits, cruciferous vegetables, meat, coffee or tea. Although there was no association with intake of multivitamin tablets, there was a significant protective effect associated with vitamin C supplements (OR = 0.4, CI = 0.3 - 0.7). These associations held even when controlled for potential confounders.

Conclusion: This study supports the hypothesis that obesity increases the risk of adenocarcinoma of the GE junction and consumption of vegetables decreases the risk. In addition, a significant and independent protective effect was observed for vitamin C supplements.

ATTITUDES TOWARD BIOMARKER FEEDBACK REGARDING SUSCEPTIBILITY TO TOBACCO-RELATED CANCERS

Ostroff J, Moadel A, Hay J, Garland J, LeGeros R, Bivona P

We examined attitudes towards biomarker feedback of susceptibility to tobacco-related cancers among asymptomatic adult smokers. 73% of participants (N=62, 42% female) expressed interest in biomarker feedback. Many (68%) likened their cancer risk to other smokers' risk; 16% underestimated, and 13% overestimated, their risk as compared to other smokers. Interest was associated with a family history of tobacco-related illness, greater cancer risk perceptions, beliefs that continued smoking would increase lung cancer risk, and readiness to quit ($p < .05$). Intentions to quit immediately in response to two hypothetical feedback conditions (higher vs. average smokers' risk for tobacco-related cancers) were greater following higher risk (44%) than average risk (19%) feedback ($p < .01$). Similarly, 14% (higher risk) vs. 41% (average risk) would not plan to quit ($p < .01$). An interaction between risk condition and cancer worry emerged with high worry related to decreased intentions to quit in the average risk feedback condition ($p < .01$). Findings underscore the potential adverse effect of providing average risk information to smokers highly anxious about developing a tobacco-related cancer. Studies of how to frame personalized risk information so as to increase precautionary health behaviors are needed.

A Population-Based Assessment of Lung Cancer Histologic Patterns in Relationship to Smoking History and Demographic Variables. Johnson CC, Newsome B, Divine G, Demers R, Upfal M.

This population-based study examined the relationship between smoking and tumor histology type using lung cancer cases identified through the three-county Detroit area SEER registry. Eligible subjects included all cases of primary cancer of the lung reported from January 1, 1993 through August 31, 1993 for persons 40 years old or older. Lung tumor histologic categories (squamous cell carcinoma, small cell carcinoma, adenocarcinoma, large cell carcinoma, other) were examined with respect to smoking status, adjusting for gender, race, socioeconomic status (based on zip code of residence), and age. Individuals were defined as smokers if they had smoked more than 100 cigarettes in their lifetime. Overall, there were 30 never smokers and 464 smokers among the sampled individuals. There was no significant difference between smokers and never smokers with respect to race ($p=0.181$), socioeconomic status ($p=0.740$), or age of diagnosis ($p=0.111$). There was also no significant difference between the five tumor histology categories with respect to race ($p=0.274$), socioeconomic status ($p=0.427$), or age of diagnosis ($p=0.399$). Adenocarcinoma was the most common histologic category among never smokers (56.67%) as well as smokers (33.41%). There were no never smokers with small cell carcinoma. Squamous cell carcinoma was the most common histologic type among males (35.9%) and adenocarcinoma was the most common among females (42.4%). When compared to never smokers, smokers were more likely to have small cell carcinoma than any other histologic type.

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A prospective analysis of pulse and cancer risk. Cerhan J, Pavuk M, Wallace R (University of Iowa, Iowa City, IA 52242). Several prior studies have shown a positive association between pulse and cancer mortality in men. The authors evaluated this association with cancer incidence in the Iowa 65+ Rural Health Study, a prospective cohort study of older persons in two rural Iowa counties initiated in 1982. Cancer experience was determined by linkage to the Iowa SEER cancer registry for the years 1973-93. There were 1,050 men and 1,825 women aged 65-102 years with an in-person interview (including resting pulse measurement) in 1982 and with no documented cancer in the 10 years prior to baseline. After 11 years and over 24,000 person-years of follow-up, 509 incident cancers were identified. After adjustment for age, weight, smoking, and physical activity, there was a positive association between pulse (beats/minute; quintile analysis) and cancer incidence in men: compared to men with a pulse <63, men with a pulse of 63-68 (Relative risk (RR); 95% Confidence interval: RR=1.63; 1.03-2.59), 69-74 (RR=1.55; 0.96-2.50), 75-82 (RR=1.62; 1.03-2.55), >82 (RR=1.63; 1.02-2.61) were at elevated risk (p for trend=0.098). This association remained unchanged after further adjustment for other factors including blood pressure, alcohol use, and antihypertensive drugs. Exclusion of cases diagnosed in the first two years of follow-up did not alter the association. There was no association between pulse and cancer incidence in women. Analyses stratified by smoking, physical activity, and weight showed that the pulse and cancer association was only apparent in former or current smokers. Cancer site specific analyses in men showed that the pulse association was specific to smoking-related tumors. These data suggest that men with a low pulse (<63) are at lower risk of developing a smoking-related cancer, and this likely reflects residual confounding by smoking rather than a truly independent association.

In the Family Risk Assessment Program (FRAP) at Fox Chase Cancer Center, we have found that women receiving information about their personal risk for breast and ovarian cancer are often most overwhelmed by the impact this new information has on their family relationships. To date, genetic counselors have not had a tool that enables them to incorporate specific family dynamics into their approach to the client. The genogram is a multigenerational family tree that graphically plots biological relationships, as well as information about relationships and psychosocial issues in the family. The genogram has been used extensively in family therapy practice, providing insight into how the individual functions in the context of the family system, and likewise, how individuals interact as a functional whole. We present a pilot study in which genograms were obtained from individuals in the FRAP as part of their genetic counseling session. Following standard pedigree expansion, a series of questions was asked about the proband's relationship with other family members, communication patterns within the family, attitudes toward genetic testing, family reactions to cancer, roles individuals play in the family and significant historical or anniversary events. Relationships were defined as close, very close, conflictual, close and conflictual, distant, or estranged. The distribution of relationship types in 20 families was close (7), very close (8), conflictual (0), close and conflictual (2), distant (2), and estranged (2). Degree of familial cohesion as measured by this questionnaire correlates positively to scores obtained on the standardized Social Adjustment Scale (SAS).

By providing a concise, easy-to-read, and informative summary of the family dynamics and individual psychosocial issues, the genogram can now be tested in the cancer risk counseling model as a valid instrument to target support interventions to individual as well as family-based needs.

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A Case-Control Study of Diet and Lung Cancer Risk in African Americans and Mexican Americans. P. Pillow, S. Hursting, C. Miller, H. Jiang, S. Honn, and M.R. Spitz. M.D. Anderson Cancer Center, Houston TX 77030.

Previous studies have suggested possible relationships between the intake of certain dietary factors and lung cancer risk. The purpose of this study was to determine if dietary differences underly some of the observed ethnic and gender differences in lung cancer rates. The relationship between diet and lung cancer development was examined in 137 cases (44 Mexican Americans and 93 African Americans) and 187 controls (109 Mexican Americans and 78 African Americans) who successfully completed a modified version of the NCI's Health Habits and History Questionnaire as part of their participation in our molecular epidemiologic study of lung cancer in minority populations. All dietary variables were analyzed per 1000 Kcal to adjust for total energy intake. We found that cases had statistically higher mean total fat intakes (45.7 v. 42.7 g/1000 Kcal; $p<0.001$), while controls had higher mean intakes of dietary fiber (9.1 v. 7.6 g/1000 Kcal; $p<0.001$) and fruits (127.4 v. 107.5 g/1000 Kcal; $p=0.02$). Logistic regression analysis showed that, after adjusting for the effects of smoking, age, gender and ethnicity, high total fat consumption remained a significant positive predictor of case status ($p=0.01$), while fiber consumption remained a significant negative predictor of case status ($p=0.002$). Gender and ethnic differences were also observed, as males had higher mean intakes of total fat (44.6 v. 42.5 g/1000 Kcal; $p=0.007$), while females demonstrated higher consumption of fiber (9.2 v. 8.2 g/1000 Kcal; $p=0.003$), fruits (153 v. 105 g/1000 Kcal; $p<0.001$) and vegetables (118 v. 96.2 g/1000 Kcal; $p=0.004$). Mexican Americans, relative to African Americans, had lower total fat intakes (43.1 v. 45 g/1000 Kcal; $p=0.02$) and higher intakes of fiber (9.8 v. 7.2 g/1000 Kcal; $p<0.001$) and vegetables (109 v. 97 g/1000 Kcal; $p=0.07$). These findings suggest that dietary differences may account for at least some of the ethnic and gender differences observed in lung cancer occurrence. This work was supported by NCI RO1 CA55769.

With the recent discovery of the BRCA1 and BRCA2 genes, a growing number of women are seeking genetic risk information. Previous research has shown that communication of risk information can provoke a negative psychological response and interfere with screening adherence. Under the auspices of the Human Genome Project, the Fox Chase Family Risk Assessment Program has been conducting a study to assess whether education and counseling for genetic risk for breast/ovarian cancer is enhanced by a structured psychological support intervention. Women are randomized to receive stress inoculation training or general health education in conjunction with an education program of screening recommendations and risk and genetics information. Participants complete self-administered psychological measures at three time points (baseline, 1-week, 6-month). 131 women with a family history of breast/ovarian cancer were randomized into intervention (n=58) and control (n=73) groups. Preliminary data suggest that risk perception does not differ significantly between groups, with 63% of the intervention group and 62% of the control group estimating their risk for breast/ovarian cancer to be >50% at baseline. However, risk perception decreased in both groups at 1-week, with more women in the control group perceiving their risk to be 50% or less at this time point (56% vs. 47%), suggesting that the stress inoculation intervention was more likely to maintain a heightened sense of risk. Psychological adjustment as measured with the Coping Strategies Questionnaire indicates that both groups have improved coping immediately following the education sessions, but these effects are not maintained over time. The Beck Depression Inventory (BDI) revealed that 20% of our population was mildly to clinically depressed at baseline with 8% reporting suicidal ideation within the past week. Of the 46 completed follow-ups, 30% have improved BDI scores at 1-week, but these effects are not sustained 6 months later, with no difference between groups. Our preliminary results suggest that education and counseling about genetic risk contributes to decreased risk perception and depression and increased ability to cope within the first weeks following the program in both groups. However, these effects are not sustained over time suggesting the need for intermittent "booster" sessions to reinforce risk information and address concerns.

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Hypomethylation An Early Event In Cervical Carcinogenesis.

Short B, B.S.,[†] Giuliano A, Ph.D.,[†] Piyashilako C, Ph.D.,[‡] Nour M, M.D.,^{*} and Hatch K, M.D.^{*} Arizona Cancer Center[†] and Dept. OB/GYN^{*}, Tucson, AZ; and the UAB Comprehensive Cancer Center, Birmingham, AL.[‡]

Purpose: We have previously shown (Cancer Res., 1994) that DNA hypomethylation is significantly associated with grade of cervical dysplasia (SIL). The objective of this study was to further describe this relationship and to investigate the role of folate in the observed association of DNA hypomethylation and SIL.

Methods: Ninety patients with abnormal PAP smear results were referred to the Cervical Dysplasia Clinic at the University of Arizona for colposcopic examination and biopsy. Patients completed a short ques. and provided a non-fasting serum sample. DNA hypomethylation was assessed by incubating DNA extracted from biopsy samples with [³H]-methyl-S-adenosylmethionine and Sss I methylase. The relationship between endogenous DNA methylation and ³H-methyl incorporation is reciprocal. Folate levels were assessed from the tissue biopsy samples and serum samples using a microbiological assay. All folate levels were log transformed during analysis.

Results: The histologic distribution of the samples was 23(CIN I), 17(CIN II), 12(CIN III), 10(CIS), 7(Cancer), and 5(Adjacent normal). Mean age was 32.6 ± 11.5 yr. DNA hypomethylation characterized by ³H-methyl incorporation was significantly different between the histologic levels (P = 0.0007). Both tissue and serum folate levels were significantly related to methylation level (P = 0.0191 and P = 0.0437 respectively).

Conclusions: These data show DNA hypomethylation to be an early event in cervical carcinogenesis and that folate is significantly related to DNA hypomethylation. Further investigation of DNA hypomethylation as a potential biological marker is needed.

Factors associated with p53 overexpression in endometrial tumors Olson SH, Finstad CL, Harlap S, Kurian L, Saigo PA, Barakat RR

We studied the relationship between patient characteristics, including the use of tamoxifen, and overexpression of p53 in endometrial tumors in patients with a history of breast cancer. We obtained information on subject characteristics from medical records. We analyzed deparaffinized tumor tissue sections using an indirect immunoperoxidase method and a monoclonal antibody for the p53 protein.

Twenty-two percent of the 58 tumors showed strong positive staining for the p53 gene product. Tumors with more advanced stage or with serous/clear cell histology were more likely to overexpress p53 (odds ratio (OR)=4.7, 95% confidence interval (CI) 1.2-18.1 and OR=6.4, CI 1.4-29.2, for stage and histology respectively). After adjustment for stage and histology, we found an association between p53 overexpression and treatment with tamoxifen for breast cancer (OR=3.3, CI 0.77-13.7) and a slightly stronger association with treatment with both tamoxifen and chemotherapy (OR=4.2, CI 0.65-27.2). There was a strong relationship between having a first degree relative with breast cancer and overexpression of p53 (adjusted OR=28.0, CI 3.9-202.3).

These results suggest that use of tamoxifen may be associated with an increase in tumors that overexpress p53, particularly in conjunction with chemotherapy. Genetic predisposition to breast cancer is strongly associated with expression of p53 in endometrial tumors in this group of women.

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The Relation of Quantitative Fluorescence Image Analysis (QFIA) of Esophageal Cytology Smears to Subsequent Development of Esophageal Cancer. Nan H. Taylor PR, Liu SE, Hemstreet GP, Zou XN, Rao JY, Mark SD, Dawsey SM. National Cancer Institute, Bethesda, MD, USA; Cancer Institute, Chinese Academy of Medical Sciences, Beijing, China; U Oklahoma, Oklahoma City, OK, USA.

Purpose: This study evaluated the ability of quantitative fluorescence image analysis (QFIA) of esophageal cytology smears to predict which individuals in a high-risk Chinese population would develop esophageal cancer (EC) during a 3.5 year follow-up period. **Methods:** The cohort included 1331 subjects who had esophageal balloon cytology examinations, including 62 who later developed EC. A total of six QFIA variables (maximum and mean values for nuclear area, DNA content, and DNA intensity) were correlated with EC risk factors, and proportional hazard models were used to evaluate the relation of these QFIA variables to subsequent risk of EC. **Results:** The QFIA variables increased with age and were consistently higher in females, non-smokers, and non-drinkers. Values for five QFIA variables were significantly higher in EC cases than in non-cases. In regression models, there was a trend for increased EC risk with increasing values in five of the QFIA variables. There was also a significant trend for increasing EC risk with increasing cytology severity of traditional Chinese cytologic diagnoses in this cohort. A comparison of overall model chi-squares indicated that QFIA added important additional predictive value to the Chinese cytologic diagnoses. **Conclusion:** This study suggests that the QFIA values are independent predictors of EC and, in combination with traditional cytology, result in improved prediction of EC risk.

Smoking and Cervical Dysplasia among Black Women

Kanetsky PA, Gammon MD, Mandelblatt J, Zhang Z, Ramsey E, Wright TC Jr., Thomas L, Matseoane S, Lazaro N, Felton HT, Sachdev R, Richart RM, Curtin JP.

Purpose: To assess the relationship between smoking and cervical dysplasia among HIV-negative, non-hispanic, black women.

Methods: In a case-control study at an urban, public, New York City hospital, women were interviewed about smoking habits and other risk factors for cervical cancer. Human papillomavirus (HPV) infection was measured by hybrid capture.

Results: Thirty-two women with histologically confirmed incident dysplasia and 113 control women with normal Papanicolaou smears were enrolled. After adjustment for confounding factors, including HPV infection, cervical dysplasia was associated with current smoking [OR=1.8, 95% CI (0.54, 6.1)]. Smoking appeared protective of low-grade dysplasia [OR=0.64, 95% CI (0.08, 5.2)]. However, compared to control women, women with high-grade lesions were roughly four times more likely to be current smokers [OR=4.3, 95% CI (0.83, 21.9)], and dose-response trends approached statistical significance for total number of years ($p=0.07$) and pack-years of smoking ($p=0.08$) among these women.

Conclusions: This is first study of smoking and cervical dysplasia among black women since 1983. Results suggest that smoking may be independently associated with dysplasia, and that this association may be stronger among women with high-grade lesions than among those with low-grade dysplasia suggesting that smoking may be a promoter of cervical carcinogenesis. This study is limited by lack of power. These findings should be confirmed by larger studies among black women.

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Micronutrients and Cervical Dysplasia among Black Women

Kanetsky PA, Gammon MD, Mandelblatt J, Zhang Z, Ramsey E, Dnistrian A, Norkus E, Wright TC Jr., Thomas L, Matseoane S, Lazaro N, Felton HT, Sachdev R, Richart RM.

Purpose: To determine whether reported dietary intake of folate, carotenoids, and vitamin E is associated with cervical dysplasia among HIV-negative, non-hispanic, black women.

Setting: Three clinics in an urban, public, New York hospital.

Methods: The 60-food item HHHQ was administered to women in this case-control study. Information on other risk factors for cervical cancer was collected by questionnaire or molecular assay.

Results: Thirty-two women with histologically confirmed incident dysplasia and 113 control women with normal Papanicolaou smears were enrolled. Median levels of folate, vitamin E, and most carotenoids were lower among cases than among controls. For all micronutrients, a crude protective effect was noted for the upper tertile of intake. After adjustment for confounding factors, including HPV infection, a three to five-fold decrease in the odds of dysplasia was noted for women in the upper tertile of lycopene [OR=0.34, 95% CI (0.12, 0.97)] and vitamin A [OR=0.18, 95% CI (0.03, 1.1)]; borderline protective dose-response trends were apparent. A non-significant increased odds of dysplasia was apparent for the upper tertile of β -carotene and cryptoxanthin intake.

Conclusions: In this first study of micronutrients and cervical dysplasia among black women, results suggest that dietary lycopene and vitamin A may be protective against cervical dysplasia. Findings, however, are limited due to small numbers. Larger studies among black women, including validation studies of the reduced HHHQ, should be planned to confirm these findings.

Hoque A, Strom SS, Annegers JF, Spitz MR, Cooper SP, Ford C, Andreeff M.

The University Of Texas MD Anderson Cancer Center (MDACC) and School of Public Health, The University of Texas Health Science Center, Houston, TX 77030

Secondary acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) has been recognized as one of the most feared long-term complications of cancer therapy. The aim of this case-control study was to determine the prevalence of chromosomal abnormalities and family history of cancer (FHC) among secondary AML/MDS cases and de novo AML/MDS controls. Study population were 332 MDACC patients (pts) who were registered between 1986 and 1994. Cases were pts who had a prior invasive cancer before diagnoses of AML/MDS and controls were de novo AML/MDS. Cases (166) and controls (166) were frequency matched on age \pm 5 years, sex and year of diagnosis of leukemia. Cytogenetic data were obtained from the leukemia database of MDACC and data on FHC and other risk factors were abstracted from the patients' medical record. The distribution of AML and MDS among cases was 58% and 42% respectively and among controls 67% and 33% respectively. Prevalence of chromosomal abnormalities were observed more frequently among cases than controls. Reporting of FHC were similar among both groups. Univariate analysis revealed an odds ratio (OR) of 2.8 (95% CI 1.5-5.4) for deletion of chromosome 7, 2.3 (95% CI 0.9-3.8) for deletion of chromosome 5, 2.3 (95% CI 0.8-6.2) for deletion of 5q, 2.0 (95% CI 1.0-4.2) for trisomy 8, 1.3 (95% CI 0.8-2.1) for chromosomal abnormalities other than chromosome 5 or 7 and 1.31 (95% CI 0.82-2.05) for family history of cancer in a first degree relative (FHC-FDR). The OR remained significant for deletion of chromosome 7 (2.3, 95% CI 1.1-4.8) after adjustment for age, alcohol, smoking, occupation related to chemical exposure and FHC-FDR. Secondary AML/MDS among pts who received chemotherapy and had a FHC-FDR occurred earlier (median 2.25 ± 0.9 years) than among pts without such FHC-FDR (Median 5.50 ± 0.18 years) ($p < .03$). The implication of exposure to chemotherapy among pts with a FHC-FDR needs to be further investigated.

Hereditary Nonpolyposis Colorectal Cancer in Egypt

Soliman A.S., Bondy M. L., Hamza M.R., Ismail K., Khaled H., Ismail S., McPherson R. S., Levin B.

The high incidence of colorectal cancer in Egyptian children and young adults and the prevalent consanguinity in Egypt led us to investigate familial aggregation of colorectal cancer and hereditary nonpolyposis colorectal cancer (HNPCC) as a causative factor for this phenomenon. We conducted a pilot study and interviewed 34 unselected Egyptian colorectal cancer patients about their family history of colorectal cancer and other cancers. Approximately 15% of patients had a family history of one or more first degree family members under the age of 40 with diagnosed colorectal cancer. One of those families had a typical history of HNPCC, with four family members having colorectal cancer in three generations; three of these relatives were younger than 45 years at diagnosis, and other family members had extracolonic tumors. Another 15% of the patients had a family history of other cancers such as urinary and bone cancers that could also be related to HNPCC. The high incidence of colorectal cancer in children and young adults in Egypt along with the family histories reported in this study and the demographic and cultural characteristics (e.g.; prevalent consanguinity) of Egyptians justify further study of a larger population of colorectal cancer patients in Egypt.

Reproductive Risk Factors for Colorectal Adenomas: A Combined Analysis of Data from Four Case-Control Studies

J.S. Jacobson, J.D. Potter, L. Fosdick, A.I. Neugut, R.M.

Bostick, L. Peipins, R.S. Sandler, M.E. Martinez, R.S.

McPherson, T.A. Louis, and the Adenoma Study Group

The increasingly widespread use of exogenous hormones justifies fresh consideration of reproductive and hormonal patterns as risk factors for colorectal cancer. Because most colorectal cancers appear to arise from colorectal adenomas, in the past decade a number of investigators have studied cancer risk factors in adenoma cases and polyp-free controls. However, the lack of power associated with stratifying on sex has limited the scope of analyses of reproductive risk factors.

In the current study, we have combined data from four case-control studies and analyzed reproductive risk factors for adenomas in colonoscopically examined females who had no history of adenomas, cancer, or inflammatory bowel disease (521 adenoma cases and 1204 polyp-free controls). Menarche at ages 12-13 was associated with lower risk than menarche at other ages (OR= 0.7, 95% CI 0.5-0.9). Although parity per se showed no clear association with risk, among parous women late age at first birth was associated with nonsignificantly elevated risk, which increased with age at interview. Cases and controls did not differ in oral contraceptive use, but users of hormone replacement therapy (HRT) had significantly lower risk than nonusers (OR=0.6, 95% CI 0.5-0.8).

These observations suggest a hormonal mechanism for colorectal cancer somewhat different from that for breast cancer. Given that, among older females the incidence of colorectal cancer is as high as that of breast cancer, confirmation that HRT reduces the risk of colorectal neoplasia would have important implications.

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Risk of Breast Cancer in Relation to Induced Abortion in a Cohort of Chinese Women

Ye, Z and Thomas DB, Fred Hutchinson Cancer Research Center

The possible influence of induced abortion on breast cancer risk was assessed in a cohort of 267,040 women enrolled in a randomized trial of breast self-examination in Shanghai. Based on answers to a baseline questionnaire, subsequent breast cancer risk was not significantly associated with ever having an induced abortion (RR=1.10, 95% CI: 0.95 - 1.28), number of abortions, or time since first or last abortion. Analysis of data from more detailed interviews of 711 of the 823 cases after diagnosis and 744 age matched controls yielded similar results. A possible increase in risk was observed in women whose first pregnancy was aborted (based on only 10 cases and 5 controls; RR=2.42; 95% CI: 0.79 - 7.46), but not in women with an abortion only after a livebirth (347 cases, 361 controls; RR=1.13; 95% CI: 0.90 - 1.42). In the latter group, relative risk estimates for induced abortion were increased in women with an early first birth and decreased with age at first birth, were greater than unity in women over age 50 at diagnosis and whose first abortion was before age 25, and increased with gestational length, but all of these observations could be due to the chance. Breast cancer risk is not appreciably altered by induced abortion after a livebirth.

Vegetable and fruit consumption in the prevention of cancer: an examination of inferential methods in the review literature. Hord NG and Weed DL. National Cancer Institute, Bethesda, MD 20892-7105.

Epidemiologic evidence of vegetable and fruit (VF) consumption and cancer risk has been used as the primary source for preventive inferences and public health recommendations regarding diet. Typically, these conclusions appear in review papers and are made by applying qualitative inferential methods. We examine the use of these methods in 4 recent review papers written on the topic of VF consumption and cancer risk and 5 general reviews of diet and cancer (DC) hypotheses. None of the reviews specified the criteria used to make inferences. Implied use of three of Hill's nine inferential criteria (consistency, strength, and biological plausibility) formed the primary basis for determining causal associations in the VF reviews. Other criteria were used less frequently: dose-response, specificity of association, coherence, experimentation, and analogy. Half of the DC reviews cite either of two of the VF reviews in support of recommendations to increase VF consumption. The lack of rigor in the use of inferential criteria and the heterogeneous application of concepts associated with these criteria suggests that the formulation of inferences and public health recommendations from reviews of the epidemiologic literature may benefit from methodologic standardization. Guidelines for using inferential methods in review papers are presented.

Total Energy Intake, Physical Activity, Body Size Characteristics, and Risk for Incident Prostate Cancer
Bostick R, Zaccaro D, Vitolins M, Fleming R, Swarts S, Sgambati M, Ennever F

Compared to that for other common cancers, there are few analytic observational epidemiologic data available on potential risk factors for developing prostate cancer. To investigate the relation of total energy intake, physical activity, and body size characteristics to prostate cancer incidence, data were analyzed from a community-based case-control study in the Piedmont region of North Carolina of men aged 50 years and older and without a prior history of cancer. Through February 1996, 106 incident cases of prostate cancer and 253 frequency-matched community controls completed the study. Cases, with any stage or grade of prostate cancer, were identified through area urology and radiation oncology practices within days of diagnosis and studied prior to treatment. Controls were randomly selected from the community. Multiple logistic regression was used to adjust for age, race, and other risk factors. Multivariate-adjusted findings included: 1) total energy intake: odds ratios (ORs) across the quartiles = 1.0, 1.21, 0.82, 1.89 (95% confidence interval [CI] for the latter quartile, 0.99-3.61); 2) physical activity (low, moderate, high): ORs = 1.0, 1.55, 1.75 (CIs all include 1.0); 3) height: ORs across the quartiles = 1.0, 1.14, 1.02, 0.76 (CIs all include 1.0); 4) body mass index (BMI): ORs across the quartiles = 1.0, 0.99, 1.20, 0.78 (CIs all include 1.0); 5) waist-to-hip ratio (WHR): ORs across the quartiles = 1.0, 0.59, 0.99, 0.93 (all CIs include 1.0). These data 1) suggest that higher total energy intake or some other factor(s) associated with it may increase the risk of prostate cancer, 2) raise questions regarding whether physical activity is associated with risk, and 3) provide no support for relationships of risk of prostate cancer with body size characteristics such as height or indicators of overall or central obesity.

69 TESTICULAR CANCER: WHO HAS A HIGHER VOLUME OF DISEASE AT DIAGNOSIS?

Sigurdson AJ, Amato RJ, Mastromarino CL, Strom SS.
University of Texas M. D. Anderson Cancer Center (MDACC)

Testicular cancer (TC) is highly curable, but the proportion of patients achieving remission decreases as disease volume (DV) at diagnosis (Dx) increases. We sought to identify characteristics of higher volume disease patients to possibly direct cancer prevention efforts. Information on DV, age, race, income, education, insurance status and cryptorchidism were abstracted from medical chart reviews of 120 TC patients registered at MDACC between 1990-96 and from a separate risk factor questionnaire. DV score was rank ordered as: testis only = 1 (n=38), low = 2 (n=39), intermediate = 3 (n=19) and high volume = 4 (n=24). Student's *t*-test and one-way ANOVA were used for analysis. No differences in DV score were observed with income, race or cryptorchidism. Lower education level, young age and being under-insured were significantly related to a higher DV score:

	Mean	p
High school graduate or less	2.7	0.008
More than high school	2.0	
Age 18-24	2.8	0.0008
Age 25-34	2.0	
Age 35-50	2.0	
Medicaid or no insurance	2.6	0.007
Insured	2.1	

We expected cryptorchidism, a known risk factor, to have been related to a lower DV score, since men and their physicians should have been more alert for the development of TC. However this was not the case. Men under age 25 with less education appear to have the highest DV score at Dx. These results can be considered when developing physicians' and public TC awareness programs.

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CANCER INCIDENCE AND MORTALITY IN SICKLE CELL PATIENTS. Dawkins FW, Kim KS, Squires RS, Chisholm R, Kark JA, Perlin E, and Castro O. Howard University College of Medicine, Washington, DC.

The cancer incidence in pts. with sickle cell disease (SCD) is unknown. The 10 year follow-up data on 696 adult SCD pts. (66% SS, 23% SC, and 11% other Hb types) at Howard University Hospital (HUH) was analyzed to determine cancer incidence and mortality rates. The age at first HUH visit for these pts. ranged from 18 to 79 y (mean 28.8 y):

	Age group (y)			
	18-40	41-60	>60	All pts
Patients ⁺	293/327	25/46	1/4	319/377
Median f/u	3/3 [#]	2/3	3/4.5	3/3
Pt. years	1255/1324	94/179	3/18	1352/1521
Pts. with Ca.	2/1	0/2	0/0	2/3
Ca. incidence	1.6/1.75*	-/11.2	-/-	1.48/1.94

+ = male/female, # = y, * = per 1000 patient years

Five pts. developed cancer for an incidence rate 5/2864 or 1.74/1000 pt. yrs. The 95% confidence interval for this rate was 0.64 to 4.32/1000 pt. yrs. The Cancer diagnoses were lymphoma, testicular, breast, stomach, and unknown primary. The highest rate was in women age 41-60 y. There were 67 deaths, 3 of them from cancer (Ca. mortality rate 3/2873 or 1.04/1000 pt. yrs.). The proportion of SS patients among the 67 pts. who died (80.6%) was significantly higher than that of other genotypes (p = 0.022). These incidence rates may be useful as baseline in the cancer surveillance of SCD pts. exposed to potentially carcinogenic treatments such as hydroxyurea or bone marrow transplantation.

The Influence of Latitude on Malignant Melanoma Rates in California. *P. Reynolds, J. Von Behren*

Worldwide variations in melanoma rates among whites have shown that rates increase with increasing proximity to the equator. The relationship between latitude and malignant melanoma rates was explored in California, a large state covering almost 10 degrees of latitude. A total of 14,653 newly diagnosed cases of invasive melanoma was reported for white, non-Hispanic residents during the first five years of population-based statewide cancer reporting in California (1988-92). Latitude, climate zone, and urban/rural status were assigned to cases based on census tract of residence at diagnosis. Rate ratios were estimated using multivariate Poisson regression modeling, controlling for age and sex. For each degree of latitude the rate ratio was 0.98 (95% confidence interval: 0.97, 0.99), indicating decreasing rates with increasing latitude (greater distance from the equator). The melanoma rate in the most southern latitude of the state was 70% higher than in the northern most area. However the relationship between latitude and melanoma rates was not linear and was explained largely by urban and rural differences. The state's major urban areas, located in the south and middle of the state, had the highest rates. Striking climate zone variations that exist within the state appeared to explain rate differences better than did latitude and independent of urbanization. Once taking into account variations in urbanization and microclimates, latitude did not appear to be strongly associated with melanoma rate differences.

Cancer Incidence among California Teachers, 1988-1992 *P. Reynolds, M. Layefsky, E. Elkin, G. Lee*

A few studies have suggested that school teachers, while having a substantially lower standardized mortality ratio (SMR) for all causes of death, have a significantly elevated SMR for cancer of the female breast. We undertook a study to systematically examine the cancer incidence experience for this profession. Members of the California statewide active workforce of elementary and secondary school teachers during 1988-1992 (an annual workforce of approximately 160,000 women and 80,000 men) were matched to the California Cancer Registry statewide surveillance system for the same time period. A total of 4024 cases of newly diagnosed cancer of all types was observed, compared to 4341 cases expected based on state rates from the general population for the same time period (standardized incidence ratio(SIR)=0.9). Male teachers had lower SIRs than female teachers (0.81 vs. 0.99). The low incidence of cancer among male teachers was largely a function of very low rates for lung cancer (SIR=0.30, 95% confidence interval (CI)=0.24-0.37), although rates for male genital cancers were somewhat elevated (prostate SIR=1.16, testis SIR=1.24). Female teachers experienced more breast cancer than would be expected (1370 cases, SIR=1.21, 95% CI=1.15-1.28), as well as higher incidence of *in situ* tumors of the breast (308 cases, SIR=1.58, 95% CI=1.41-1.77). Consistent with what might be expected for a more highly educated population, female teachers also had a slightly higher incidence of cancer of the uterine corpus (SIR=1.17) but lower incidence of cancer of the uterine cervix (SIR=0.49, 95% CI=0.37-0.63).

Association between p53, cyclin D1 and erbB-2 protein and breast cancer

Shao, Q., Tang, D., Rundle, A., Zhou, J. and Perera, P.
Columbia University, School of Public Health, Division of
Environmental Health Sciences. N.Y., N.Y. 10032

This study was explored whether the markers of p53, cyclin D1 and erbB-2 (Her-2,neu) protein were co-expressed or independently expressed in breast tissue. Levels of markers were examined by immunohistochemical techniques in breast tissue from 15 cases and 16 benign breast disease (BBD) controls enrolled in a case-control study of breast cancer. All subjects were female from the Columbia-Presbyterian Medical Center and 35-75 years of age. Both p53 and cyclin D1 protein levels were measured quantitatively using the Cell Analysis System which measures the Optical Density (OD) of stained tissue sections. The intensity of membrane staining for erbB-2 was semi-quantitatively scored. For p53 protein, the mean OD of the BBD controls was 0.093 (n=15), while the mean OD of the cases was 0.157 (n=16, p=.001). For cyclin D1 protein, the mean OD of the controls was 0.181 (n=15) and was 0.280 for cases (n=15, p=0.004). Finally, for erbB-2 8/15 (53%) of the cases had intense staining while 0/16 (0%) controls exhibited intense staining. Among cases OD levels for p53 and cyclin D1 were not correlated ($r=.13$, $p=.67$). Among cases no association was found between erbB-2 and p53 expression nor between erbB-2 and cyclin D1 expression. This study indicates that breast tissue of breast cancer patients has significantly higher level of p53, cyclin D1 and erbB-2 protein than tissue from women with nonmalignant breast disease and that the three markers are independently expressed in breast tissue.