

# **PROGRAM AND ABSTRACTS**

**18th Annual Meeting**

## **AMERICAN SOCIETY of PREVENTIVE ONCOLOGY**

**March 6 - 9, 1994**

**Hyatt Regency Hotel  
Bethesda, MD**

**Program Chair: Margaret R. Spitz, MD, MPH  
The University of Texas  
M. D. Anderson Cancer Center**

**Sponsored by:**

**American Society of Preventive Oncology, The University of Texas M. D. Anderson Cancer Center, and a conference grant from the National Institutes of Health/National Cancer Institute. The Joseph W. Cullen Memorial Lectureship is sponsored by Marion Merrill-Dow, Inc. Tobacco-related sessions are sponsored in part by Lederle Laboratories and Ciba-Geigy Pharmaceutical Division.**



# ASPO

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 18th Annual Meeting of the American Society of Preventive Oncology participants should be able to:

- develop and communicate information on the causes of human cancer, including environmental exposures, lifestyle and host susceptibility states;
- develop and evaluate new methods and programs for the prevention and early detection of cancer;
- review and monitor programs designed to reduce cancer incidence, mortality and morbidity;
- design and present professional and public education related to cancer education; and
- train health professionals concerned with preventive oncology.

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.

## **ACCREDITATION:**

The University of Texas M. D. Anderson Cancer Center is accredited by the Accreditation Council of Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians.

The University of Texas M. D. Anderson Cancer Center designates this continuing medical education activity for 17 credit hours in Category I of the Physician's Recognition Award of the American Medical Association.

The evaluation form at the back of this program must be completed in order to receive CME credits. Please turn it in at the Registration Table before leaving.

American Society of Preventive Oncology speakers are in compliance with Disclosure of Interest Policies as outlined by the Accreditation Council of CME. Declaration documentation is available in the registration area throughout the duration of this conference.

# ASPO

The Executive Committee members listed below are interested in hearing from prospective and current members.

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## **Chemoprevention Study Group Co-chair**

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# ASPO

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Frederica Perera, Dr.PH  
Columbia University

William Blot, PhD  
National Institutes of Health/  
National Cancer Institute

# **ANNOUNCEMENTS**

## **MESSAGES**

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

## **CATERED MEALS**

We have attempted to include a variety of items at each meal function so those of you preferring vegetarian fare may be easily accommodated. For this reason we have chosen the buffet method of serving whenever possible.

## **SPECIAL ACKNOWLEDGEMENTS**

The ASPO Executive Committee offers special thanks to Program Chair, Dr. Margaret Spitz, for her extraordinary commitment and efficiency in arranging the program for this meeting.

The ASPO Executive Committee wishes to thank all the co-sponsors of this 18th Annual Meeting. The corporate sponsors have given the Program Committee complete latitude in choosing the speakers and program which are underwritten by their contributions.

# NOTES

# Sunday, March 6, 1994

8:30 am - 12:30 pm  
Cartier-Tiffany

**New Investigator Workshop** (Open only for those with accepted proposals)

Organizer: Alfred Neugut, MD, PhD, Columbia University School of Public Health

9:00 am - 12:00 pm  
Haverford-Baccarat

**Joint Meeting of NCI Cancer Prevention Fellows and Preventive Oncology Awardees**

1:00 - 5:00 pm  
Ballroom Foyer

**REGISTRATION**

1:00 - 5:00 pm  
Waterford-Lalique

**Special Genetics Workshop:**

*"Introduction to Molecular Genetics: From the Laboratory to Prevention"*

Co-Chairs: Caryn Lerman, PhD and Bruce Trock, PhD, Lombardi Cancer Prevention Center, Georgetown University

5:00 - 7:00 pm  
Diplomat-Ambassador

**ASPO Executive Committee and 1995 Program Committee Meeting**

# Monday, March 7, 1994

7:00 am - 5:00 pm  
Ballroom Foyer

**REGISTRATION**

7:30 - 9:00 am  
Waterford-Lalique

**Study Group Breakfast Meeting**

*Chemoprevention:*

Organizers: Mary Daly, MD, Fox Chase Cancer Center, and Gary Goodman, MD, Swedish Hospital Tumor Institute & Fred Hutchinson Cancer Research Center

9:15 - 9:30 am  
Haverford-Baccarat

**WELCOME:**

Ellen R. Gritz, PhD, President

# NOTES

# March 7, 1994, Continued

9:30 - 11:15 am

**Symposium:** *Retinoids in Chemoprevention Trials—An Update*

Chair: Frank Meyskens, Jr., MD, University of California, Irvine

*Retinoids - Mechanisms of Action*

Reuben Lotan, PhD, UT M. D. Anderson Cancer Center

*Retinoids in the Prevention of Upper Aerodigestive Tract and Lung Cancers*

Scott Lippman, MD, UT M. D. Anderson Cancer Center

*Retinoids in Skin Cancer Prevention*

John DiGiovanna, MD, National Institutes of Health/  
Dermatology Branch

*Retinoids in Cervical Intraepithelial Neoplasia and Chronic Myelogenous Leukemia*

Frank Meyskens, Jr., MD

**Panel Discussion:** *New Directions*

Moderator: Frank Meyskens, Jr., MD

11:30 am - 1:00 pm  
Waterford-Lalique

**Luncheon/Cullen Awardee Address**

C. Tracy Orleans, PhD, Fox Chase Cancer Center,  
Joseph Cullen Memorial Awardee

# NOTES

# March 7, 1994, Continued

1:00 - 2:45 pm  
Haverford-Baccarat

**Symposium:** *Behavioral Science Interventions in Cancer Prevention and Screening Trials*

Chair: Ellen Gritz, PhD, UT M. D. Anderson Cancer Center

*Dietary Interventions in Cancer Prevention and Screening Trials*

Susan Curry, PhD, Group Health Cooperative, Seattle, WA

*Multiple Risk Factor Interventions for Cancer Prevention in the Worksite*

David Abrams, PhD, Brown University

*Smoking Cessation Interventions for Urban Underserved Populations*

Mario Orlandi, PhD, MPH, American Health Foundation

*Risk Notification Intervention for Women at High Risk for Breast Cancer*

Roshan Bastani, PhD, University of California, Los Angeles

**Panel Discussion:** *New Directions for Behavioral Science in Translational Research and Public Health Approaches to Cancer Control*

Moderator: Ellen Gritz, PhD

# NOTES

# March 7, 1994, Continued

3:00 - 4:40 pm

**Presented Papers** (2 concurrent sessions)  
See printed abstracts in section to follow.

**Old Georgetown**

Session A: Miscellaneous

Chair: Marcy List, PhD, University of Chicago Cancer  
Research Center

3:00 - 3:20 pm

*Estrogen Replacement Therapy and Risk of Fatal Colon  
Cancer in a Prospective Cohort of Postmenopausal Women*

Eugenia Calle, PhD, American Cancer Society

3:20 - 3:40 pm

*Assessment of Mammography Technologists' Training to  
Perform Mammograms*

Manette Fine, DO, Fox Chase Cancer Center

3:40 - 4:00 pm

*Is Elevated Heart Rate a Risk Factor for Prostate Cancer  
Death?*

Peter Gann, MD, MS, Preventive Medicine Department,  
Northwestern University

4:00 - 4:20 pm

*Recruiting High Risk Women into a Breast Cancer Health  
Promotion Trial*

Caryn Lerman, PhD, Lombardi Cancer Research Center

4:20 - 4:40 pm

*Folic Acid Intake and Risk of High-Grade Cervical Dysplasia  
among Southwestern Hispanic and Non-Hispanic Women*

R. Sue McPherson, PhD, UT School of Public Health

# NOTES

# March 7, 1994, Continued

## Haverford-Baccarat

Session B: Breast Cancer

See printed abstracts in section to follow.

Chair: Melissa Bondy, PhD, UT M. D. Anderson Cancer Center

3:00 - 3:20 pm

*Serum Vitamin D and Breast Cancer: A Pre-Diagnostic Case-Control Study with Stored Serum*

Robert Hiatt, MD, PhD, Division of Research, Kaiser Permanente

3:20 - 3:40 pm

*Measurement of Estrogen Metabolites in Premenopausal Women*

Araxi Pasagian-Macaulay, PhD, University of Pittsburgh, Department of Epidemiology

3:40 - 4:00 pm

*Carotenoids and Estrogen Receptor Status in Breast Cancer*

Cheryl Rock, Dept. of Family Practice, University of Michigan

4:00 - 4:20 pm

*Adherence to Screening Behaviors and Psychological Distress in Women at Genetic Risk for Breast Cancer*

Kathryn Kash, PhD, Strang Cancer Prevention Center

4:20 - 4:40 pm

*Cigarette Smoking and Risk of Fatal Breast Cancer*

Eugenia Calle, PhD, American Cancer Society

5:00 - 7:00 pm

Waterford-Lalique

Poster Session and Reception

7:00 pm

Best Poster Award Presentation

Dinner on your own

# NOTES

# Tuesday, March 8, 1994

7:00 am - 5:00 pm  
Ballroom Foyer

## REGISTRATION

7:00 - 8:30 am  
Waterford-Lalique

## Study Group Breakfast Meetings

### *Women's Cancers*

Organizer: Kathy Helzlsouer, MD, MHS, Johns Hopkins University

### *Diet*

Organizers: Larry Kushi, MD, University of Minnesota and Gladys Block, PhD, University of Calif., Berkeley

8:30 - 10:15 am  
Haverford-Baccarat

## Symposium: *Biological Specimen Banking—An Investment for our Future?*

Chair: Barbara Hulka, MD, MPH, University of North Carolina at Chapel Hill

### *Practical Issues in Specimen Collection and Bank Operation*

Elaine Gunter, BS, Chief, NHANES Laboratory

### *Specimen Banking: Right From the Beginning*

Robert Murphy, MSPH, National Center for Health Statistics, CDC

### *Ethical and Legal Issues in Specimen Banking*

Diane Wagener, PhD, National Center for Health Statistics

## Panel Discussion: *The "Credits and Debits" of Sample Banking*

Moderator: Barbara Hulka, MD, MPH

# NOTES

# March 8, 1994, Continued

10:15 - 10:30 am

**Break**

10:30 - 11:15 am

**Business Meeting**

11:15 am - 12:00

**Distinguished Achievement Awardee Address**

*Screening for Cancer: Is it time for a paradigm shift?*

Anthony B. Miller, MB, FRCP, University of Toronto,  
Department of Preventive Medicine

**Lunch on your Own**

1:30 - 3:15 pm

**Symposium:** *Biomarkers of Exposure, Response, and Susceptibility*

Chair: Frederica Perera, Dr.PH, Columbia University

*Biomarkers of Cancer Susceptibility*

Peter Shields, MD, National Cancer Institute

*Biomarkers of Exposure—Aflatoxin Adducts and p53 Mutations in Hepatocellular Cancer*

John Groopman, PhD, Johns Hopkins University

*Gene-Environmental Interactions*

George Lucier, PhD, Chief, Laboratory of Biochemical Risk Analysis, National Institute of Environmental Health Sciences

**Panel Discussion:** *Environmental Carcinogenesis and Risk Assessment*

Moderator: Frederica Perera, Dr.PH

3:15 - 3:30 pm

**Break**

# NOTES

# March 8, 1994, Continued

3:30 - 5:10 pm

**Presented Papers** (2 concurrent sessions)  
See printed abstracts in section to follow.

**Old Georgetown**

Session C: Molecular Epidemiology

Chair: Bruce Trock, PhD, Lombardi Cancer Research Center

3:30 - 3:50 pm

*Molecular Epidemiology of Hepatocellular Carcinoma (HCC)*

W. Thomas London, MD, Fox Chase Cancer Center

3:50 - 4:10 pm

*Gender Difference in Mortality among Hepatitis B Carriers*

Alison Evans, ScD, Fox Chase Cancer Center

4:10 - 4:30 pm

*Genetic Susceptibility to Primary Liver Cancer*

Katherine McGlynn, PhD, Fox Chase Cancer Center

4:30 - 4:50 pm

*Genetic Susceptibilities for Lung Cancer among Ethnic Populations*

Loic LeMarchand, MD, Cancer Research Center of Hawaii

4:50 - 5:10 pm

*p53-Knockout Transgenic Mice: An in vivo Model of Spontaneous Tumorigenesis for Cancer Prevention Studies*

Stephen Hursting, PhD, MPH, Laboratory of Nutritional and Molecular Regulation

# NOTES

# March 8, 1994, Continued

**Haverford-Baccarat**

Session D: Breast Cancer  
See printed abstracts in section to follow.

Chair: Caryn Lerman, PhD, Fox Chase Cancer Center

3:30 - 3:50 pm

*Risk Factors for Carcinoma in Situ of the Breast*

Polly Newcomb, PhD, UW Comprehensive Cancer Center

3:50 - 4:10 pm

*Cohort-Specific Risks of Developing Breast Cancer to Age 85 in Connecticut*

Miriam Campbell, PhD, MPH, National Cancer Institute

4:10 - 4:30 pm

*Generational Shifting in Mean Age at Diagnosis of Breast Cancer*

Ruby Senie, PhD, Memorial Sloan-Kettering

4:30 - 4:50 pm

*Age-Specific Risk Factors for Breast Cancer among Young Black Women*

Marilie Gammon, PhD, Columbia University School of Public Health

4:50 - 5:10 pm

*Validation of a Breast Cancer Risk Assessment Model in Women with a Positive Family History*

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

6:30 pm

**Waterford-Lalique**

**Banquet**

Invited Speaker: M. Joycelyn Elders, MD  
U.S. Surgeon General

# NOTES

# Wednesday, March 9, 1994

8:00 - 9:30 am  
Waterford-Lalique

## Study Group Breakfast Meetings

### *Tobacco*

Organizer: Michael Fiore, MD, MPH, University of Wisconsin, Center for Tobacco Research and Intervention

### *Cancer Risk Algorithm*

Organizer: To Be Announced

9:30 - 11:15 am  
Haverford-Baccarat

## Symposium: *Esophageal Adenocarcinoma—An Emerging Cancer Problem*

Chair: William Blot, PhD, National Cancer Institute

### *Rising Incidence of Esophageal Adenocarcinoma in the United States and Abroad*

Susan Devesa, PhD, National Cancer Institute

### *Antecedent Barrett's Esophagus*

Stuart Spechler, MD, Beth Israel Hospital and Harvard University

### *Environmental and Host Risk Factors*

Thomas Vaughan, MD, Fred Hutchinson Cancer Research Center and University of Washington

## Panel Discussion

Moderator: William Blot, PhD

11:15 - 11:30 am

## Break

# NOTES

# March 9, 1994, Continued

11:30 am - 1:10 pm  
Haverford-Baccarat

## Presented Papers

See printed abstracts in section to follow.

Session E: Biomarkers

Chair: Katherine McGlynn, PhD, Fox Chase Cancer Center

11:30 - 11:50 am

*Biomarkers of Dietary Fat Intake*

Mark Kestin, PhD, MPH, Fred Hutchinson Cancer Research Center

11:50 am - 12:10 pm

*Serum Gonadotropic and Steroid Hormones in Relation to the Risk of Developing Ovarian Cancer*

Kathy Helzlsouer, MD, MHS, John Hopkins University School of Hygiene and Public Health

12:10 - 12:30 pm

*Fatty Acid Composition of Erythrocytes, A Biomarker of Squamous Carcinoma of the Skin: The Arizona Study*

Azadeh Stark, PhD, Arizona Cancer Center, University of Arizona in Tucson

12:30 - 12:50 pm

*Glutathione S-Transferase Activity: Potential Biomarker of Susceptibility for Colorectal Cancer*

Christine Szarka, MD, Fox Chase Cancer Center

12:50 - 1:10 pm

*DNA Repair: A Potential Marker for Cancer Susceptibility*

Qingyi Wei, PhD, UT M. D. Anderson Cancer Center

**Conclusion**

# NOTES

## Invited Speakers

DAVID ABRAMS, PhD  
Miriam Hospital, Brown University  
Dept. of Psych. & Human Behavior  
164 Summit Avenue  
Providence, RI 02906

ROSHAN BASTANI, PhD  
UCLA Jonsson Comprehensive  
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WILLIAM BLOT, PhD  
National Cancer Institute  
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SUSAN CURRY, PhD  
G H C, Center for Health Studies  
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Seattle, WA 98101

SUSAN DEVESA, PhD  
National Cancer Institute  
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JOHN J. DiGIOVANNA, MD  
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REUBEN LOTAN, PhD  
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GEORGE W. LUCIER, PhD  
Nat'l Inst. of Environ. Health Sci.  
Lab of Biochemical Risk Analysis  
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Research Triangle Park, NC

FRANK L. MEYSKENS, Jr., MD  
University of California at  
Irvine Cancer Center  
101 The City Dr., Bldg. 44, Rt. 81  
Orange, CA 92668

## Invited Speakers

ROBERT S. MURPHY, MSPH  
National Center for Health Statistics  
Centers for Disease Control  
6525 Belcrest Road, Room 900  
Hyattsville, MD 20782

MARIO ORLANDI, PhD  
American Health Foundation  
One Dana Road  
New York, NY 10595

FREDERICA PERERA, Dr.PH  
Columbia Univ. School of Public Health  
60 Haven Ave., Rm B-109  
New York, NY 10032

PETER SHIELDS, MD  
National Cancer Institute  
Lab. of Human Carcinogenesis  
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STUART SPECHLER, MD  
Beth Israel Hospital  
Harvard University  
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THOMAS VAUGHAN, MD  
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Seattle, WA 98104

DIANE K. WAGENER, PhD  
National Center for Health Statistics  
6525 Belcrest Road  
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# ABSTRACTS

## ORAL PRESENTERS

SESSION A Monday, March 7, 3-4:40 PM

ESTROGEN REPLACEMENT THERAPY AND RISK OF FATAL COLON CANCER IN A PROSPECTIVE COHORT OF POSTMENOPAUSAL WOMEN. EE Calle, HL Miracle, MJ Thun, CW Heath

Several recent studies suggest that the use of hormone replacement therapy may decrease the risk of colon cancer. We examined the association of fatal colon cancer and estrogen use in a large prospective study of U.S. adults. After seven years of follow-up, 1147 cases of fatal colon cancer were observed in a cohort of 482,004 postmenopausal women who were cancer-free at interview in 1982. Cox proportional hazards modelling found that ever use of estrogens was associated with a significantly decreased risk of fatal colon cancer (rate ratio (RR) = 0.66, 95% confidence interval (CI) 0.58-0.76). The reduction in risk was strongest among current users (RR = 0.50, 95% CI 0.37-0.68). Among former users who took estrogens within the last 10 years, the RR was 0.59 (95% CI 0.46-0.75); for those with former use more than 10 years ago, the RR was 0.80 (95% CI 0.66-0.98). Additionally, there was a significant ( $p < 0.0001$ ) trend of decreasing risk with increasing years of use; users of one year or less had an RR of 0.78 (95% CI 0.61-0.99) while users of more than 10 years had an RR of 0.50 (95% CI 0.36-0.69). These associations were not altered in multivariate analyses controlling for known colon cancer risk factors. In our data, estrogen therapy, particularly recent use and long-term use, is associated with a substantial decrease in risk of fatal colon cancer.

Assessment of Mammography Technologists' Training to Perform Mammograms. Manette Fine, Perry Watts, and Barbara Rimer. Fox Chase Cancer Center, Philadelphia, PA; Duke Comprehensive Cancer Center, Durham, NC

Accreditation of a breast imaging site by the American College of Radiology requires the technologists to be "certified" to perform mammograms. This study assessed the training received by practicing mammography technologists. Self administered training assessment questionnaires were completed by 748 practicing mammography technologists attending symposia sponsored by either the Dupont Corporation or by the American Society of Radiological Technologists (ASRT). 330 (44%) of the 748 technologists reported that they had no training in mammography at radiology school; another 105 (14%) of the technologists had less than 1 week of training; only 246 (33%) of the technologists had 1 to 6 weeks of mammography training. Of 641 technologists who responded to a question about on-the-job training, 358 (56%) had less than 1 week of training; of these, 50 had less than 1 day or no on-the-job training. 579 (77%) of the technologists reported that 0 to 10% of such training was provided by a radiologist. From examination of the ASRT list of registered technologists, 554/748 were certified radiological technologists, 167 of these had passed an optional mammography exam; 140 were not certified (the remaining 54 could not be identified because of discrepancies in the name or address). Thus, almost half of the technologists had received no mammography training in school and more than half had received less than 1 week of training on the job, yet 74% were "certified." To assure that technologists are properly trained in mammography, the optional mammography exam should be made mandatory. Radiology schools, to be accredited, should be required to provide a minimum mammography training program.

## RECRUITING HIGH RISK WOMEN INTO A BREAST CANCER HEALTH PROMOTION TRIAL

Caryn Lerman, Ph.D., Barbara Rimer, Dr.P.H., Mary Daly, M.D.,  
Ph.D., Ed Lustbader, Ph.D., Colleen Sands, Andrew Balshem, Agnes  
Masney, M.P.H., and Paul Engstrom, M.D.

**PURPOSE:** Women with a family history of breast cancer are being targeted for enrollment into a variety of breast cancer prevention and screening trials. However, recruitment to these trials often is suboptimal. This prospective study sought to identify factors which facilitate vs. hinder participation in a breast cancer health promotion trial among high risk women. **METHODS:** The subjects were 271 women ages 35 and older who had a positive family history of breast cancer in at least one first-degree relative. Structured telephone interviews evaluated sociodemographic characteristics, breast cancer risk factors, subjective risk perceptions, breast cancer worries and screening practices. Women who subsequently entered the trial were compared to those who declined to participate. **RESULTS:** In the full sample, participation was associated with being ages 40-49 (compared to ages 35-39 or 50+), being married, having education beyond high school, not having had a previous breast biopsy, and adhering to age-specific mammography guidelines. Also, rates of participation were higher among women who reported that their relative's diagnosis heightened their perceptions of personal risk, those who perceived their risk to be higher than women without a family history of breast cancer, and those who were more concerned and worried about breast cancer. However, education was a key moderator of the effect of these variables on participation. The results of logistic regression analyses which were stratified by education indicated that women with less formal education were most strongly influenced by subjective risk perceptions and emotional factors. By contrast, women with education beyond high school were influenced by objective risk factors and personal screening experiences. **CONCLUSION:** These findings suggest that women with less formal education may be more responsive to recruitment messages that highlight breast cancer risk factors and emphasize that participation is a positive strategy for coping with breast cancer worries.

## Is Elevated Heart Rate a Risk Factor for Prostate Cancer Death? Peter H. Gann, Martha Daviglus, Jeremiah Stamler. Northwestern University Medical School, Chicago, IL.

Laboratory data suggest that sympathetic nerve function is involved in regulating prostate cell growth. We used data from the Chicago Heart Association (CHA) cohort to measure the relation between indicators of sympathetic activity and prostate cancer mortality. The CHA cohort includes 22,320 men with baseline measurement of blood pressure (BP) and ECG heart rate (HR) between 1967-1973. Mean follow-up length was 19.2 years. We computed age-adjusted rates for prostate cancer death by variable of interest and fitted proportional hazards models to estimate relative risks adjusted for potential confounders. In a model controlling for age, body mass index, BP, serum cholesterol, smoking, race and education, the RR for a 10 beat/min. higher HR was 1.23 (95% CI: 1.03-1.48), while the RRs for BP were close to the null. Age-adjusted RRs across increasing quintiles of HR were 1.00, 1.14, 1.45, 1.69 and 2.27 (P trend=0.007). In Kaplan-Meier plots the elevated risk was not confined to the early years of follow-up. These results could be due to unmeasured confounders, but they are also consistent with the hypothesis that neurotrophic factors influence the progression of prostate cancer.

Folacin intake and risk of high-grade cervical dysplasia among southwestern Hispanic and non-Hispanic white women. RS McPherson, L Batey, TM Becker. University of Texas School of Public Health, Houston, TX & University of New Mexico, Albuquerque, NM.

Incidence of cervical dysplasia (CD) is high among both Hispanic and non-Hispanic white women in New Mexico. Although it is generally accepted that the major cause of cervical cancer is infection with the human papillomavirus (HPV), lower folate has been suggested to play a role early in cervical carcinogenesis by facilitating the incorporation of HPV genomes at a fragile chromosomal site. A clinic-based case comparison study was conducted to identify the risk factors for high-grade CD among Hispanic and non-Hispanic white women attending university affiliated gynecology clinics. Interviews and physical examinations of women provided data on dietary intake, sexual behavior, sexually transmitted diseases, smoking, cervical cytology and serum antibody assays. Multivariate adjusted odds ratios (OR) among women with histologically proven high-grade dysplasias for the risk of CD by quartile of intake of folacin were 2.25 (95% CI 0.81-3.39), 2.01 (95% CI 0.91-4.43) and 1.66 (95% CI 0.90-5.62) as compared to women in the highest tertile. The inverse association between dietary intake of folacin and risk of CD was statistically significant at the lower level before including HPV in the model. Lower dietary intake of folacin was associated with an increased risk of CD even after adjustment for HPV and other measures of sexual behavior.

SESSION B

Monday, March 7, 3-4:40 PM

Serum vitamin D and breast cancer: a pre-diagnostic case-control study with stored serum.

Robert A. Hiatt, Nancy J. Krieger, Bruce Lobaugh, Marc K. Drezner, Joe H. Vogelman, Norman Orentreich.

The higher incidence of breast cancer in Northern latitudes has led to the suggestion that sun exposure may protect a woman against this neoplasm through production of vitamin D. We studied the relationship of vitamin D in stored serum specimens among 98 white women who later developed breast cancer after menopause and 98 white controls matched on the age and date when the specimen was drawn and the length of follow-up to the case's diagnosis. These women were selected randomly from members of the Kaiser Permanente Medical Care Program in Northern California who took a multiphasic health checkup (MHC) from 1964 through 1972 and followed for the development of breast cancer until the end of 1990. 1,25 dihydroxyvitamin D was measured by calf thymus receptor assays. Breast cancer risk factor data was taken from the MHC questionnaire, supplemented by medical record data. We found that the known risk factors including weight, education, family history, and alcohol consumption were associated with breast cancer as expected. However, assays values for 1,25-dihydroxyvitamin D were not different between cases and controls. The odds ratio for the highest quartile compared to the lowest was 0.96 (95% CI 0.35-2.64) and there was no pattern or trend across the quartiles. Our preliminary conclusion in this California population is that there is no relationship of serum vitamin D to the subsequent development of breast cancer in postmenopausal women.

**Carotenoids and Estrogen Receptor Status In Breast Cancer**  
Rock Cheryl, Randall Dana, Ruffin Mack, August David. Depts of Community Health Programs, Family Practice, Surgery, University of Michigan Medical School, and School of Public Health. Ann Arbor, MI 48109.

**Purpose:** To determine the relationships between plasma levels of carotenoids and vitamin A and breast tissue estrogen receptor (ER) status in women with newly diagnosed breast cancer. **Methods:** Women with newly diagnosed breast cancer were recruited to complete a brief interview and to consent to the collection of plasma for carotenoid analysis. High performance liquid chromatography method of Bieri was used to separate and quantify plasma carotenoids and retinol. Plasma cholesterol and triglycerides were determined with a Kodak Ektachem Analyzer. **Results:** The interview and plasma nutrient analysis has been completed for 65 women. The mean plasma values (umol/L) were 0.532 lutein, 1.45 retinol, 0.215 beta-cryptoxanthin, 0.90 lycopene, 0.138 alpha-carotene, and 0.566 beta-carotene. Of this group, 47 were ER-positive and 18 were ER-negative. Significant univariant relationships to ER status were parity, plasma lutein, and family history of breast cancer. The plasma values were divided into tertiles to examine the relation to ER status further. The OR for only plasma lutein level was significant at 4.5 (95% CI 1.2-17.2) when contrasting the upper tertile with the lower tertile. Similar trends were seen in the other plasma levels, but were not significant. Preliminary logistic regression model with ER status as the dependent variable contains family history and plasma levels of lutein, beta-carotene, beta-cryptoxanthin, and triglycerides along with interactions between these variables. Further analysis using logistic regression awaits the completion of data collection. **Conclusions:** The evidence suggest that a carotenoid-rich diet may help improve the survival from breast cancer through the effect on ER status. For example, women with ER-positive status are 4.5 times more likely to be in the upper tertile of plasma lutein levels. This preliminary analysis appears to support observations made of breast cancer patients diet and ER status. (Support: Grant from the University of Michigan Breast Care Center)

**Measurement of Estrogen Metabolites in Premenopausal Women.** Araxi Pasagian-Macaulay, Elaine Meilahn, H. Leon Bradlow, Daniel Sepkovic, Alhaji M. Buhari, Rena Wing, Lewis H. Kuller.

Estrogen exposure has been linked to breast cancer risk. The influence of dietary fat intake on estrogen is also thought to be implicated in the etiology of this disease. Estrogen metabolite 2-hydroxyestrone (2-OHE1) shows little biologic activity, while 16a-hydroxyestrone (16a-OHE1) has shown strong estrogenic effects and is found elevated in breast cancer patients, in women at high risk of breast cancer and in mice strains susceptible to mammary tumors. Therefore, a higher 16a-OHE1 relative to 2-OHE1 is indicative of amplified estrogen activity. A new ELISA assay for the ratio of the two major urinary estrogen metabolites, 2-OHE1:16a-OHE1 was pilot tested. Morning baseline and six month follow-up urine samples were collected from 70 middle-aged healthy women enrolled in a randomized clinical trial of a low-fat diet intervention. The 2-OHE1:16a-OHE1 ratio was measured using blind duplicates at two time points to estimate the intra-assay reliability. Results showed good intra-assay reliability ( $r=0.94$ ,  $n=22$  at baseline and  $r=0.80$   $n=21$  at 6-month follow-up,  $p's<0.05$ ) from a subsample of the population. Samples were also assayed to assess the intra-person reliability at the two time points. Intra- individual correlation at baseline and six month follow-up showed  $r=0.81$  for the assessment group ( $n=30$ ) and  $r=0.64$  for the intervention group ( $n=40$ ) ( $p's<0.01$ ). There was little impact of age, race, weight, BMI, cholesterol, waist to hip ratio, socio-economic, and smoking status on the urine estrogen ratios. In conclusion, this ELISA assay can reliably measure urinary estrogen metabolites among premenopausal women. These measures will be used to examine the influence of a dietary intervention and of menopause in the clinical trial.

ADHERENCE TO SCREENING BEHAVIORS AND PSYCHOLOGICAL  
DISTRESS IN WOMEN AT GENETIC RISK FOR BREAST CANCER  
K.M. Kash, Ph.D., J.C. Holland, M.D., D.G. Miller, M.D., & M.P. Osborne,  
M.D., Memorial Sloan-Kettering Cancer Center & Strang Cancer  
Prevention Center, New York, NY 10021

Women with a family history of breast cancer are at increased risk for developing the disease. This study used the Health Belief Model and the Fear Arousing Communications Theory to investigate beliefs about breast cancer risk, surveillance behaviors, and psychological distress in women at high risk for breast cancer (one or more first degree relatives with breast cancer). Four hundred and sixty women, enrolled in a breast surveillance program, completed a questionnaire regarding health beliefs and behaviors, social support and psychological distress (BSI). Adherence to mammography (MA) and clinical breast examination (CBE) were obtained from the medical records. 50% came in for regularly scheduled mammographies and 52% came in for regular clinical breast examinations. Only 27% performed breast self-examination (BSE) monthly, 15% never performed BSE, and 58% did not perform BSE regularly. High BSE performance prior to coming to the program was the best predictor of current BSE and being more well educated and younger, along with greater cancer anxiety, predicted poor adherence to monthly BSE (Multiple R = .62). Greater psychological distress predicted less adherence to both MA ( $p < .006$ ) and CBE ( $p < .05$ ) in discriminant function analyses. For CBE greater cancer anxiety also predicted less adherence ( $p < .02$ ). The mean percentage of risk perception based on family history was 41-50% with a range from 11-100; although no woman's objective medical risk was greater than 50%. Over 30% of high risk women were defined as having a level of psychological distress consistent with the need for counseling. Women who reported more barriers to screening, fewer social supports, low social desirability, and higher perception of risk had more psychological distress (Multiple R=.64). Higher distress was directly related to poor surveillance behaviors. These data confirm previous reports of higher distress and less adherence to all three screening behaviors in high risk women. Targeted interventions to reduce anxiety and improve surveillance behaviors need to be developed if breast cancer is to be detected at the earliest stage.

CIGARETTE SMOKING AND RISK OF FATAL BREAST  
CANCER. EE Calle, HL Miracle, MJ Thun, CW  
Heath.

The authors examined the association of fatal breast cancer and cigarette smoking in a large, prospective mortality study of U.S. adults. After six years of follow-up, 880 cases of fatal breast cancer were observed in a cohort of 604,412 women who were cancer-free at interview in 1982. Cox proportional hazards modelling, adjusting for other risk factors, found that current smoking was significantly related to fatal breast cancer risk (rate ratio (RR) = 1.26, 95% confidence interval (CI) 1.05-1.50). A statistically borderline negative association was observed for former smokers (RR = 0.85, 95% CI 0.70-1.03). The association of current smoking with fatal breast cancer risk increased with increasing numbers of cigarettes per day, and with total number of years smoked. For smokers of 40 or more cigarettes per day, the RR was 1.74 (95% CI 1.15-2.62). The authors hypothesize that these results may be due to either a poorer prognosis among breast cancer cases who smoke, or to delayed diagnosis among current smokers who do not receive mammograms as often as never or former smokers. Smoking women should be targeted for breast cancer screening services.

Gender Difference in Mortality among Hepatitis B Carriers. Alison A. Evans, Tianlun Zhou, Gong-chao Chen, Fu-min Shen, W. Thomas London. Fox Chase Cancer Center, Philadelphia, PA; Haimen County Anti-Epidemic Station, Jiangsu Province, China; and Shanghai Medical University, Shanghai, China

The risk of hepatocellular carcinoma (HCC) is 3-4 times higher for men than women worldwide, even where hepatitis B virus (HBV) carrier prevalence is similar in both sexes. Death from HBV-associated chronic liver disease represents a non-independent competing risk among carriers. In 1986-87, a population of 34,232 adult residents of Haimen County, China, was screened for hepatitis B surface antigen (HBsAg). Mortality information is available for this population through 1991.

Using Poisson regression, we evaluated the effects of HBV carrier status and gender on age-adjusted all-cause, HCC, and chronic liver disease mortality. For all-cause mortality, male HBV carriers had a relative risk (RR) of 3.3 (95% CI 2.5-4.2) compared to male non-carriers. Among females, the RR for carriers was 2.2 (1.4-3.6). These RRs were significantly different ( $p = 0.04$ ). Excess mortality among carriers of both sexes was almost entirely attributable to HCC and chronic liver disease, but female carriers were at lower risk for both outcomes. For HCC, the RR associated with HBV carrier status was 8.2 (95% CI 5.6-11.9) and the RR for females vs. males was 0.31 (0.21-0.45). For chronic liver disease mortality, the RR for HBV carriers was 9.2 (3.8-22.0) and 0.25 (0.10-0.63) for females vs. males. There was no significant interaction between HBV status and gender for HCC or chronic liver disease mortality.

This analysis confirms significant gender differences in mortality among HBV carriers. Exogenous factors (e.g. alcohol, tobacco, diet) and/or endogenous factors (e.g. reproductive hormones, iron stores) could be responsible for the gender effect. The difference between male and female HCC mortality rates declined significantly with increasing age ( $p_{\text{trend}} = 0.03$ ). For chronic liver disease, however, the difference in mortality by gender did not change with age. These findings are suggestive of an effect of reproductive factors on HCC risk in women.

SESSION C      Tuesday, Mar. 8, 3:30-5:10

Molecular Epidemiology of Hepatocellular Carcinoma (HCC) in Haimen County, China—Initial Results. W. Thomas London, Alison Evans, Tianlun Zhou, Gong-Chao Chen, and Fu-min Shen. Fox Chase Cancer Center, Philadelphia, PA; Haimen County Anti-Epidemic Station, Jiangsu Province, China; and Shanghai Medical University, Shanghai, China

To test viral, environmental, and genetic hypotheses of the etiology of HCC, we are conducting a 5-year prospective, nested case-control study in Haimen County, China, one of the world's highest incidence areas for HCC. The cohort will consist of ~50,000 healthy men, ages 30 to 64, from the county's 35 townships. At entry, each subject completes a questionnaire, donates a 9.0 ml blood sample (for serum), 5 drops of blood on filter cards (for DNA), and toenail trimmings (for metal analysis). Each case of HCC that occurs is matched to 2 controls by age and township of residence. The first 25,964 men were enrolled in the study in the Spring, 1992. By July, 1993, 40 cases of HCC had been diagnosed. 28 HCCs occurred among 3007 chronic carriers of hepatitis B virus (HBV) (prevalence=931/100,00) and 12 cases among 22,954 non-carriers (52/100,000); odds ratio = 24.6 (95% c.i.=11.8-51.1). Case-control comparisons of questionnaire information yielded no associations of HCC with: cigarette smoking or alcohol intake; source of drinking water by decade (ditch, well or tap, a test of the contaminated water hypothesis); or corn (as a source of aflatoxin), wheat, and rice consumption by decade. Significant associations were found with occupation (peasants had higher prevalences of HCC than workers or functionaries), family history of HCC, and history of a medically diagnosed episode of hepatitis. The cases mean age at time of the hepatitis episode was 42 yrs, whereas HBV and hepatitis A infections are acquired in childhood. No serological evidence of hepatitis C or hepatitis D was detected in 100 to 200 serum samples from the cohort, suggesting that either a variant of a known hepatitis virus or a "new" hepatitis virus is circulating in this population and is associated with HCC.

### Genetic susceptibility to primary liver cancer.

K.A. McGlynn,<sup>1</sup> Y. Hu,<sup>1,2</sup> F.M. Shen,<sup>2</sup> G.C. Chen,<sup>3</sup> X.L. Xia,<sup>4</sup> A. Baffoe-Bonnie,<sup>1</sup> E.A. Rosvold,<sup>1</sup> T. Zhou,<sup>1</sup> & K.H. Buetow,<sup>1</sup> <sup>1</sup>Fox Chase Cancer Center, Philadelphia, PA; <sup>2</sup>Shanghai Medical University, Shanghai, China; <sup>3</sup>HCAS, Haimen Cty., China; <sup>4</sup>Indiana University School of Medicine, Indianapolis, IN.

Aflatoxin B<sub>1</sub> (AFB<sub>1</sub>) has been postulated to be a risk factor for primary hepatocellular carcinoma (HCC) in humans. Some, but not all, investigators have reported an association between AFB<sub>1</sub> exposure and mutations at codon 249 of the p53 gene. One explanation for this discrepancy may be that genetic variability in AFB<sub>1</sub> metabolism, via the epoxide hydrolase (EH) and glutathione-S-transferase (GST) loci, confers susceptibility to HCC.

To test whether there was genetic variability in AFB<sub>1</sub> detoxification, we conducted a study in Ghana which examined AFB<sub>1</sub>-albumin adducts, EH and GST $\mu$  genotypes in 54 individuals. EH genotype (1/2 or 2/2) and GST $\mu$  genotype (null) were each related to the presence of AFB-albumin adducts (EH:  $p=.03$ , GST $\mu$ :  $p=.02$ ).

To test whether the high-risk genotypes, as defined by the Ghana study, were related to HCC, we conducted a study in China. The EH and GST $\mu$  genotypes of 45 individuals with HCC and 147 control individuals were contrasted. Consistent with the Ghana results, the cases were significantly more likely to be GST $\mu$  null ( $p=.048$ ) and to have an EH 1/2 or 2/2 genotype than were the controls ( $p=.01$ ). Thirty-seven of the 45 Chinese tumors have been tested for p53 codon 249 mutations. Mutations were found in 8 of the 37 (22%). All 8 mutations occurred in persons who had an EH 2 allele. All but one of the mutations occurred in persons who were GST $\mu$  null. These results indicate that susceptibility to liver cancer may exist due to genetic variability in AFB<sub>1</sub> metabolism and constitutional differences may determine susceptibility to p53 mutations.

**GENETIC SUSCEPTIBILITIES FOR LUNG CANCER AMONG ETHNIC POPULATIONS.** Loïc Le Marchand, Lakshmi Sivaraman, Mary P. Leatham, Lynne R. Wilkens, Alan F. Lau. University of Hawaii Cancer Research Center, Honolulu, HI 96813.

We have shown that for a given diet and smoking history, the risk of lung cancer in Hawaii is more than two-fold greater in Hawaiians than in Japanese, and that the risk of Caucasians is intermediate (Cancer Epidemiol. Biomarkers Prev. 1992;1:103-7). In addition to further studying the role of diet in explaining these risk differences, we are also assessing several germ line polymorphisms (CYP2D6, CYP1A1, CYP2E1, GST1, HRAS1 and p53) in Japanese, Caucasian and Hawaiian lung cancer patients and ethnicity-matched population controls. To date, 160 samples have been analyzed. Although the frequencies of most of these polymorphisms are clearly different among the three ethnic groups, a case-control difference has emerged so far for CYP1A1 ( $p=0.003$ ) only. After adjustment for smoking, the MspI polymorphism in the 3'-flanking region of the CYP1A1 gene was associated with lung cancer with an odds ratio of 6.0 (95% CI: 0.7-50.2). Although the number of subjects in each ethnic group are still small, there was no indication that this association was limited to Japanese, as suggested by past studies. The adjusted odds ratio for rare HRAS1 alleles was also elevated: 2.8 (0.7-50.0). The accumulation of more data may confirm these associations and clarify their importance in determining lung cancer risk in these three ethnic groups.

**Risk Factors for Carcinoma in Situ of the Breast.** Polly A. Newcomb, Barry E. Storer, Pamela M. Marcus. Univ. of Wisconsin Comprehensive Cancer Center, Madison, WI 53706

In Wisconsin, carcinoma in situ (CIS) of the breast has increased 328% since 1982. While the increase is largely believed due to early detection, other possible explanations include the identification of early stage tumors of limited malignant potential. To evaluate risk factors for non-invasive breast cancers, we conducted a population based case-control study in Wisconsin during 1988-91. Cases of newly diagnosed carcinoma in situ (n=321) were identified from a state-wide tumor registry and interviewed by telephone to ascertain their reproductive experiences, beverage consumption, family and medical histories, and other characteristics. For comparison, controls (n=963) were randomly selected (from driver's license lists and Medicare beneficiary files) for interview. Age adjusted odds ratios (OR) and 95% confidence intervals (95% CI) were estimated from logistic regression models. The strongest associations were observed between CIS and a history of biopsied benign breast disease (OR 2.4, 95% CI 1.8-3.5) and family history of breast cancer (OR 2.6, 95% CI 1.9-3.7). Nulliparity, later age at first birth among parous women, and high levels of alcohol consumption were also associated with significantly increased risk. While risk factors for ductal CIS (n=221) and lobular CIS (n=66) were generally similar, biopsied benign breast disease was associated more strongly with lobular CIS (OR 4.5, 95% CI 2.6-7.8). This latter relationship may reflect lesion detection rather than a true risk factor. These results suggest that risk factors for CIS are overall concordant with determinants of invasive disease.

**p53-Knockout Transgenic Mice: An *In Vivo* Model of Spontaneous Tumorigenesis for Cancer Prevention Studies.** Stephen D. Hursting, Susan N. Perkins and James M. Phang. Laboratory of Nutritional and Molecular Regulation, Division of Cancer Prevention and Control, National Cancer Institute, Frederick, MD 21702.

Transgenic mice with both alleles of the p53 tumor suppressor gene knocked out by gene targeting provide a potentially useful model for cancer prevention research because i) these mice rapidly develop spontaneous tumors; and ii) p53 mutations are common in human tumors. To determine if tumorigenesis in p53-knockout mice is sensitive to experimental manipulation, tumor development in response to calorie restriction (CR; a potent inhibitor of rodent tumors) was evaluated. Weanling male nullizygous p53-knockout mice and wild-type littermates were fed AIN-76A diet *ad libitum* (AL) or were restricted to 60% of AL calorie intake (30/group). Tumor development and morbidity were monitored for 48 weeks. By 28 weeks, mortality from spontaneous tumors in AL/p53-knockout mice was 100% (median survival=16 weeks); in contrast, mortality in CR/p53-knockout mice was 57% (median survival=24 weeks; p=0.0002). Also, 34% of AL/p53-knockout mice developed multiple primary tumors compared to 16% of CR/p53-knockout mice (p=0.04). No differences in tumor types were observed between AL-fed and calorie restricted p53-knockout mice; ~70% of tumors were malignant lymphomas and 20% were sarcomas. Mortality in wild-type littermates on either diet treatment was <10% through 48 weeks. These data demonstrate that tumorigenesis in p53-knockout mice genetically predisposed to spontaneous tumors can be suppressed by CR. We conclude that p53-knockout mice provide an attractive *in vivo* model for exploring the nutritional and pharmacological prevention of cancer because tumorigenesis in these mice is rapid; does not require carcinogen induction; is responsive to nutritional intervention; and is relevant to human cancer since p53 mutations are the most commonly observed genetic lesions in human tumors.

**COHORT-SPECIFIC RISKS OF DEVELOPING BREAST CANCER TO AGE 85 IN CONNECTICUT.** Miriam K. Campbell, PhD, MPH, Eric J. Feuer, PhD, and Lap-Ming Wun, PhD. National Cancer Institute, Bethesda, MD.

Previous estimates of the lifetime risk of developing breast cancer have used cross-sectional estimates of incidence. Cross-sectional rates, however, yield a biased picture of cohort risks when rates are unstable, as breast cancer trends have been. We developed cohort life tables for Connecticut women born from 1888-1892 to 1948-1952 to generate more specific estimates of breast cancer risk to age 85. Multiple decrement life tables were produced for each birth cohort. We included as cases only the first reports of breast cancer in women with no earlier malignancy. Our results indicate that widely circulated lifetime risks of one in nine may be inflated slightly owing to changing incidence. We estimate that of those women 40-44 years old in 1992, one woman in ten will develop breast cancer by age 85. For women born between 1928 and 1932, one in thirteen will be diagnosed with breast cancer by age 85. The results are insensitive to mortality trends in the past. Error in the estimates are more likely to arise from changes in incidence and mortality in the future.

**GENERATIONAL SHIFTING IN MEAN AGE AT DIAGNOSIS OF BREAST CANCER.** RT Senie, A Simkovich, K Brown, PI Borgen. Memorial Sloan-Kettering Cancer Center, New York, New York, 10021

Although relatives of women with breast cancer are known to be at high risk of developing the disease, debate exists concerning age recommendations for mammography screening. To address this question, we studied age at diagnosis of breast cancer among affected relatives of the 1027 women enrolled in our High Risk Surveillance Clinic. The 367 (36%) women with two or more affected relatives were selected to analyze age at diagnosis by generation among paired relatives. A statistically significant downward shift by generation to earlier age at diagnosis was observed ( $P < .01$ ). Among the 116 grandmother-mother pairs, the mean age of the grandmothers (57 yrs, SD 18) was significantly older than the mean age of the mothers (49 yrs, SD 11). A similar difference was noted when the ages at diagnosis of the 91 mother-sister pairs were assessed; the mean age at diagnosis of the mother (53, SD 11) was significantly older than the affected sister (42, SD 10). Analysis of age at diagnosis of mother-maternal aunt pairs (women of the same generation) revealed no significant difference. These findings encourage the initiation of breast cancer screening at an age ten years younger than the affected relatives. Due to the downward shift in age at diagnosis, women of the younger generation may develop the disease prior to their older relatives. Therefore, more vigilant screening of older women should be encouraged following diagnosis of breast cancer in younger family members.

**Validation of a Breast Cancer Risk Assessment Model in Women with a Positive Family History.** Melissa L. Bondy, Edward D. Lustbader, Susan Halabi, Eric Ross, Victor G. Vogel.

Gail et al. (JNCI 81:1879-1886, 1989) developed a statistical model for estimating the risk of developing breast cancer in white women screened annually with mammography. The model is used for both counseling and admission to clinical trials but has not been validated in a prospective study. *Purpose:* To evaluate the model in a prospective cohort of women with a family history of breast cancer. *Methods:* We followed a high-risk subgroup of women, those with a family history of breast cancer, who participated in the American Cancer Society 1987 Texas Breast Screening Project to determine who had developed breast cancer after initial screening. We evaluated the Gail model using composite background rates from both the Breast Cancer Detection and Demonstration Project (BCDDP) and Surveillance and Epidemiology and End Results (SEER). We also evaluated the statistical significance of the variables in the Gail model by conducting a case-control study. *Results:* The case-control study showed that the relative risk component of the model performed well. None of the coefficients from the logistic regression determined by Gail et al. were rejected. However, the observed to expected number of breast cancers using either the BCDDP or SEER background rates overestimated the risk of breast cancer in women younger than age 60, but underestimated risk for women older than age 60. *Conclusions:* The Gail model may not accurately estimate risk for women with a family history of breast cancer who select their own screening choices. The model should be used as it was intended, i.e. for women who receive annual mammograms.

**Age-Specific Risk Factors for Breast Cancer Among Young Black Women.** Gammon MD, Schwartz AV, Thompson WD. Columbia University School of Public Health, NY, NY.

Black women under age 50 have a higher incidence rate of breast cancer than do white women. The purpose of this study is to determine the age-specific risk factors among young black women, which have not been previously described, using data from the Cancer and Steroid Hormone Study. In this population-based case-control study, cases were women 20-54 years of age who were newly diagnosed with primary breast cancer in 1980-82 in eight geographic areas. Random-digit-dialing controls were frequency matched to cases by five-year age groups and geographic location. Among black women, 490 cases and 485 controls completed the in-person, 50-minute interview that assessed reproductive, contraceptive, and medical histories, body size, tobacco, alcohol, and family history of cancer. Using multivariate-adjusted logistic regression, four risk factors were found to significantly vary by age at diagnosis: ever use of oral contraceptives (OC) (versus the mean time since first use of OCs (i.e., the value assigned to never users), OR = 3.71 at age 25 years and 1.07 at age 54 years); time since first OC use (for every 24 months, OR = 1.32 at age 25 and 0.75 at age 54); surgical menopause with at least one intact ovary (versus premenopause, OR = 1.61 at age 35 and 0.28 at age 54); and adult Quetelet's index (for every 6.0 increase, OR = 1.79 at age 25 and 0.86 for age 54). Of the four factors that were found to be modified by age, the results regarding oral contraceptives are the least likely to be due to misclassification. Because contraceptive choice is potentially amenable to intervention, additional research is needed to replicate our findings, and to explore the reasons for the increase in breast cancer risk in relation to use of oral contraceptives among young African-American women.

**BIOMARKERS OF DIETARY FAT INTAKE.** Mark Kestin PhD, MPH, Irena King PhD, Maureen Henderson, MD. Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center, Seattle, USA.

At present, there is no valid and sensitive biochemical marker of total fat intake for use in epidemiologic studies. The concentrations of the majority of fatty acids in body fluids and cells do not directly reflect their dietary intake as most fatty acids found in the human diet can be synthesized in the body.

Non-fasting serum samples were collected at the Seattle Clinical Center of the Women's Health Trial, a multicenter, randomized, primary prevention trial to study the effects of a low-fat diet on the incidence of breast cancer in post-menopausal women. The serum was obtained in 1986-1988 and stored at  $-70^{\circ}\text{C}$ . A random subset of serum samples (46 intervention and 53 controls at baseline and end of study) were analyzed for phospholipid fatty acids by TLC followed by GC.

The dietary intervention was successful with the intervention group having a much lower mean fat intake than the controls at an average of 11 months post-intervention (37.7 vs. 22.9 % Kcal from fat), as determined from a food frequency questionnaire. The two groups had a similar baseline age and body mass index. In comparison with the control group, there was a statistically significant fall ( $p < 0.05$ ) in serum concentrations of C17:0 (7%), C18:2, n-6 (8%), and 9t-C18:1 (8%), and a significant increase in the concentrations of C16:1, n-7 (11%) and C18:1, n-9 (13%) in the intervention women. These compounds are therefore potential biomarkers of total fat intake but they require further validation.

Serum gonadotropic and steroid hormones in relation to the risk of developing ovarian cancer. K Helzlsouer, A Alberg, G. Gordon, T Bush, C Longcope, G Comstock. The Johns Hopkins School of Hygiene and Public Health

Fertility drug use is reported to be associated with ovarian cancer whereas oral contraceptive use is protective. A nested case-control study was conducted among participants of a specimen bank (CLUE I) to examine the possible hormonal effects underlying these associations. Sera were collected in 1974 and stored at  $-70^{\circ}\text{C}$  from 11,009 women residents of Washington County Maryland. 31 ovarian cancer cases occurred among women not taking oral contraceptives and were matched to 62 controls.

Mean follicle stimulating hormone (FSH) levels were lower among cases (43.3 MIU/ml) compared to controls (54.4 MIU/ml) ( $p = 0.04$ ), particularly among postmenopausal women. No meaningful difference was noted for luteinizing hormone (LH). Prediagnostic androstendione and dehydroepiandrosterone levels were significantly higher among cases (1.3 ng/ml and 15.8 pmol/ml) compared to controls (0.96 ng/ml and 9.7 pmol/ml) ( $P = 0.03$  and  $0.02$  respectively). The directions of associations were similar among pre- and postmenopausal women.

A high androgen/low gonadotropin hormonal profile is associated with an increased risk of developing ovarian cancer. These results do not support a role of gonadotropins in the etiology of ovarian cancer. Hormonal interventions for the prevention of ovarian cancer must consider the effect of the intervention on androgen levels.

Glutathione S-transferase activity: potential biomarker of susceptibility for colorectal cancer. Christine E. Szarka, Gordon R. Pfeiffer, Paul F. Engstrom, Margie L. Clapper. Fox Chase Cancer Center, Philadelphia, PA 19111

The glutathione S-transferases are a family of detoxification enzymes which catalyze the conjugation of electrophilic compounds with glutathione to produce derivatives which are more water soluble and less cytotoxic. Large interindividual variability in glutathione S-transferase (GST) expression has been observed, including the inability of approximately 50% of healthy individuals to express the  $\mu$  isozyme because of a gene deletion. The contribution of glutathione S-transferase  $\mu$  (GST $\mu$ ) phenotype to cancer susceptibility remains equivocal. To date, we have characterized the expression of GST activity in blood lymphocytes (WBCs) from 55 individuals at high risk for colorectal cancer and 63 healthy volunteers without active medical problems. The high risk category included individuals with a history of polyps, family history of colon cancer or a personal history of colon cancer ( $\geq 2$  years from definitive treatment). Total GST activity was determined in WBCs spectrophotometrically using 1-chloro-2,4-dinitrobenzene as a substrate. An enzyme-linked immunoadsorbent assay kit supplied by Biotrin International (Dublin, Ireland) was utilized to detect GST $\mu$  in whole blood. The total GST activity (mean  $\pm$  S.E.) of WBCs of high-risk individuals was  $62.43 \pm 3.1$  while that of healthy individuals was  $76.59 \pm 3.3$  (nmol/min/mg) ( $p \leq 0.0019$ ). Subsequent analysis indicated that differences in GST activity were unrelated to the subject's age, sex or GST $\mu$  phenotype. Thirty-three percent of high-risk individuals and 44% of healthy volunteers possessed the GST $\mu$  null phenotype. These results suggest that individuals at high risk for colorectal cancer are deficient in the cellular protection afforded by GST and support the further development of GST inducers as chemopreventive agents. We are currently conducting clinical chemopreventive trials to evaluate the response of Phase II detoxification enzymes to drug and dietary interventions. (Supported by the Hamilton Family Foundation.)

Fatty Acid Composition of erythrocytes , A Biomarker of Squamous Carcinoma of the Skin: The Arizona Study. Stark, A., Moon, T., McNamara, D., Rodney, S., and Cartmel, B., The University of Arizona in Tucson.

The association of erythrocytes membrane fatty acid composition as a biomarker for squamous carcinoma of the skin (SCC) was assessed among 100 patients with confirmed pathological diagnosis of SCC and 100 controls. Subjects who were anglo-Americans and between ages of 60 and 80 , were randomly selected from the greater Tucson area and the city of Green Valley. Subjects were free of any chronic illness and were screened for any oral or topical use of steroids and anti-inflammatory nonsteroid drugs. A 15 cc fasting blood sample was collected from each subject. Erythrocytes were separated and total fatty acid profile of their membranes were extracted and esterified. The relative percent concentrations of 20 fatty acids were assessed using gas-liquid chromatography. Analysis of data using non-parametric method revealed that cases had significantly ( $p=0.008$ ) lower relative concentration of linoleic acid (LA) and higher level of total fatty acids in the n-3 series ( $p=0.045$ ) than the controls. No other significant differences were observed for the remaining fatty acids. The odds ratios (OR) comparing the highest to the lowest quartile for trans linoleic acid was 2.54 (1.04-6.19); whereas, the OR of the highest quartile to the lowest for cis linoleic acid was 0.30 (0.14-2.46). The OR comparing the highest to lowest quartile for 22:4 n6 and 22:6 n3 were 1.17 (0.50-2.74) and 1.15 (0.49-2.69) respectively. The present data portrays an association between risk of squamous carcinoma of the skin and fatty acid composition of membrane of erythrocytes. .

**DNA Repair: A Potential Marker for Cancer Susceptibility** Qingyi Wei\*, Genevieve M. Matanoski, Evan R. Farmer, Mohammad A. Hedayati, and Lawrence Grossman

The etiological role of deficient DNA repair in skin cancer has been implicated in a rare genetic disease, xeroderma pigmentosum (XP). *Purpose:* To pursue DNA repair as a biomarker for cancer susceptibility. *Methods:* We used a new assay (host cell reactivation or CAT assay) to measure overall DNA repair capacity (DRC) in human lymphocytes. This assay was tested in a clinic-based case-control study of basal cell carcinoma (BCC) among 88 cases and 135 dermatological cancer-free controls. *Results:* We observed that in the presence of low repair (DNA levels below the median of controls) there was a four fold increased risk of BCC associated with sunlight exposure after adjustment for age. Furthermore, significantly increased adjusted odds ratio were observed in those with low repair, associated with six or more severe sunburns (OR=4.2, 95% CI, 1.6-0.7) and with moderate or severe actinic elastosis (OR=4.4, 95% CI 1.5-12.8). We also observed that a decrease in DRC was significantly correlated with an increase in the number of skin tumors ( $p < 0.05$ ). In addition, reduced DRC was associated with a family history of skin cancer ( $p = 0.05$ ) and early onset of skin cancer ( $p < 0.01$ ). *Conclusions:* These findings indicate that the paradigm of deficient DNA repair versus skin cancer seen in XP is also applicable to the general population, suggesting that DNA repair capacity may serve as a useful biomarker for cancer susceptibility. (This study was funded by NIH RO1-GM31110 to L.G. and NIEHG P30-ESO3819 to G.M.M.)

# ABSTRACT

Distinguished Achievement Awardee Address  
Tuesday, March 8, 1994, 11:15 am

**Anthony B. Miller, MB, FRCP**

Professor and Chairman, Department of Preventive Medicine  
and Biostatistics, University of Toronto, Canada

## ***SCREENING FOR CANCER: Is it time for a paradigm shift?***

The assumption that early detection through screening is always beneficial, and that the smaller the cancer is at the time of detection the better the outcome, was first challenged by lung cancer screening. This has been followed by evidence that mammography screening is not effective in women age 40-49 in reducing breast cancer mortality, at least in the first 8-10 years following initiation of screening, and some evidence that for cancer of the cervix, early detection of precursors may not be necessary to achieve a benefit. Now we are entering an era when there are legitimate concerns that screening for prostate cancer may result in a reduction in the overall quality of life of those screened.

Thus we need to carefully re-evaluate our assumptions from time to time. It is important to avoid transferring assumptions from one cancer site to another. In establishing policy, we must have good evidence on which to base our decisions. As was concluded many years ago, the only unbiased design is the randomized controlled trial, and the definitive outcome has to be mortality from the disease in question.

# ABSTRACTS

## POSTERS

1

### EFFICIENT USE OF BIOLOGICAL BANKS FOR BIOCHEMICAL EPIDEMIOLOGY: APPLICATION OF A SEQUENTIAL TEST.

Rudolf Kaaks<sup>1</sup>, Ingeborg van der Tweel<sup>2</sup>, Paul A.H. van Noord<sup>2</sup>, Elio Riboli<sup>1</sup>. <sup>1</sup>International Agency for Research on Cancer (IARC), France; <sup>2</sup>University of Utrecht, The Netherlands.

Biological banks of blood, urine or tissue specimens, collected in prospective cohort studies, make it possible to evaluate a multitude of etiological hypotheses, comparing biochemical parameters between cases of a given disease and disease-free control subjects. In practice, however, the amounts of biological material stored - in particular that of cases - will limit the number of possible studies. It is therefore useful to have a statistical method which, at the expense of as little biological material as possible, allows a distinction between promising hypotheses, which may be worth further investigation, and less promising ones.

In a sequential statistical design, laboratory analyses of biological specimens from cases and controls are conducted until sufficient evidence has accumulated to reject or not the null hypothesis of no association between a biochemical marker and disease risk. With normally distributed measurements, a sequential t-test can be used, performed as a sequential probability ratio test (SPRT). On average, less than half the number of biological specimens may be needed as compared to an equivalent, fixed-sample test procedure. If the null hypothesis of no association is rejected, additional biological specimens may be analyzed to improve the precision of relative risk estimates; if not, biological specimens can be spared for the evaluation of different hypotheses. Similarly, as in a SPRT on a dichotomous exposure variable (where the focus is on a difference between the proportions of cases and controls exposed or unexposed), the critical boundaries of the sequential t-test can be interpreted in terms of odds ratios.

2

### WEIGHT AND THE RISK OF LARGE BOWEL CANCER IN WOMEN. AT Dietz, PA Newcomb, PM Marcus. University of Wisconsin Comprehensive Cancer Center, Madison, WI 53706

Higher weight is considered to increase the risk of many diseases, including diabetes, heart disease and some cancers. To evaluate its effect on large bowel cancer, height and weight measurements were ascertained by telephone interview from 779 Wisconsin women with newly reported diagnoses of carcinoma of the colon and rectum. Population controls (n = 2315) interviewed for this case-control study were randomly selected from Wisconsin driver's license files and Health Care Financing Administration files. The effects of height, weight, and body mass index (kg/m<sup>2</sup>), as measured in quartiles, were examined in logistic regression models controlling for potential confounders. In this study, higher body mass index significantly increased the risk of large bowel cancer (odds ratio (OR) for  $\geq 27.37$  kg/m<sup>2</sup> vs.  $< 21.63$  kg/m<sup>2</sup>: 1.36, 95% confidence interval (CI): 1.05, 1.76, p-trend = 0.016), while height did not influence risk for either the colon or rectum separated or combined. Risk of colon cancer was significantly associated with weight (OR for  $\geq 72.57$  kg vs.  $< 58.06$  kg: 1.44, CI: 1.05, 1.96, p-trend = 0.03). Analyzed alone, risk of rectal cancer was not related to body measurements. These data suggest that a dose-response relationship exists between obesity and increasing risk of colon cancer, with heaviest women having about a 40% elevation in risk.

**Variation of Gut Epithelial Prostaglandins in Healthy Humans: Exploring Aspirin as a Chemopreventive Agent for Colorectal Cancer**  
 Ruffin MT, Krishnan K, Kraus E, Kelloff G, Boone C, Vaerten M, Bromberg J, Rock C, Boland CR, Brenner DE. Depts of Family Practice, Internal Medicine, Community Health Programs, Biostatistics, University of Michigan Medical School, School of Public Health and VA Medical Center, Ann Arbor, MI 48109 and CIDU, DCPC National Cancer Institute, Bethesda, MD 20892.

**Purpose:** To determine the variation in gut epithelial prostaglandins among healthy adults in order to initiate a study of aspirin as a chemopreventive agent for colorectal cancer. **Methods:** Healthy men and women over the age of 18 were recruited for rectal biopsies. The participants maintained the same diet for three days prior to starting the study and during the study time of two weeks with regards to calorie intake, distribution of calories during the day and macronutrients. Rectal biopsies were performed on two separate occasions 10-14 days apart between 1200-1400 hour and 1800-2000 hour. The biopsies were collected at 10 cm from rectal sphincter with no preparation of the rectum. Prostaglandins E<sub>2</sub> (PE<sub>2</sub>) and F<sub>2a</sub> (PF<sub>2a</sub>) from the rectal tissue were assayed using Cayman Chemical EIA system. **Results:** 15 subjects completed both biopsy procedures without any complications. The PE<sub>2</sub> levels were mean of 7.39 pg/ug protein in the specimen (range 2.51-12.86 pg/ug protein) for the afternoon specimens and mean 6.25 pg/ug protein (range 1.32-13.39 pg/ug protein) for the evening specimens. The two measurements were significantly different (p=.01). The PF<sub>2a</sub> levels were mean of 3.94 pg/ug protein in the specimen (range 0.81-7.264 pg/ug protein) for the afternoon specimens and mean 4.12 pg/ug protein (range 0.43-11.55 pg/ug protein) for the evening specimens. The two measurements were not significantly different (p=.15). **Conclusions:** There appears to be greater variation over time for rectal epithelial PE<sub>2</sub> than PF<sub>2a</sub> in healthy adults on similar diets. The mean values and variance of each will be critical in planning trials of aspirin as a chemopreventive agent for colorectal cancer with rectal epithelial prostaglandins levels as a drug effect intermediate biomarker.

(Support: NCI CN-15336 and PHS GCRC MO1RR00042)

**PARITY, AGE AT FIRST FULL TERM PREGNANCY AND COLORECTAL CANCER IN WISCONSIN WOMEN.** PM Marcus, PA Newcomb. University of Wisconsin Comprehensive Cancer Center. Madison, WI 53706.

In 1980, McMichael and Potter hypothesized that hormonal changes associated with pregnancy might decrease risk of colon cancer by decreasing production of bile acids. To investigate that theory, we interviewed 536 Wisconsin women with incident diagnoses of colon cancer, as well as 243 Wisconsin women with incident diagnoses of rectal cancer. Population controls (n=2315) for this case-control study were selected from both Wisconsin driver's license and Medicare beneficiary lists. Odds ratios (OR) and 95% confidence intervals (CI) were obtained with logistic regression models, and were adjusted for potential confounders. Increasing parity was not associated with decreased colon cancer risk; it was, however, significantly associated with rectal cancer risk (OR (CI) for each additional birth: colon: .98 (.94-1.02); rectum: .92 (.86-.99)). Age at first full term pregnancy was not significantly associated with colon or rectal cancer risk (OR (CI) for first pregnancy at age 30 or later vs. age 21: colon: 1.03 (.67-1.56); rectum: .77 (.41-1.45)). Neither parity nor age at first full term pregnancy confounded the other. The effect of each factor on colon subsite risk was evaluated; no significant associations were observed. These data suggest that changes in the hormonal milieu following pregnancy may not affect colon cancer risk. Observed changes in rectal cancer risk may be due to confounding, chance, hormonal changes or perhaps an unidentified biologic mechanism.

**Having Children and Risk for Colorectal Adenomas in Japanese Males.** Judith S. Jacobson, Suminori Kono, Isao Todoroki, Satoshi Honjo, Koishi Shinchii, Koji Imanishi, Hiroshi Nishikawa, Shinsaku Ogawa, Mitsuhiko Katsurada, Alfred I. Neugut. Columbia University School of Public Health, New York, and National Defense Medical College, Japan.

Parity has been found in some studies to reduce colorectal cancer risk. We investigated the association of having children with risk of colorectal adenomas in males aged 49-55 retiring from the Self-Defense Forces of Japan. The study participants received a preretirement health examination including flexible sigmoidoscopy at Self-Defense Forces hospitals from January 1991 to December 1992. The examinations identified 300 adenoma cases and 1480 controls (normal examinations up to 60 cm from the anus). Data on marital status, number of children, and covariates were obtained by self-administered questionnaire prior to physical examination. Multiple logistic regression was used to assess risk of adenomas in relation to these variables. In this relatively homogeneous group, more than 98% of study participants were currently married and close to 95% had children. The OR for the association of having children with risk of colorectal adenomas was 0.4 (95% CI 0.2-0.8), adjusted for body mass index, cigarette smoking, alcohol intake, and recreational physical activity. Marital status and work-related long-term absence from the family were not associated with adenoma risk. These findings suggest that colorectal adenomas and perhaps cancer risk may be associated with childlessness in men.

**PROPHYLACTIC OOPHORECTOMY: A SURVEY IN MARYLAND.**  
Florence Houn MD MPH and Kathy J. Helzlsouer MD MHS  
National Cancer Institute and Johns Hopkins School of Hygiene and Public Health

Ovarian cancer has the highest mortality rate of all gynecologic cancers. Prognosis is based upon the extent of disease at diagnosis. Unfortunately, no proven effective means of early detection is available. Prophylactic oophorectomy has been advocated for women at high risk of ovarian cancer. Its effectiveness is not certain; there are case reports of ovarian cancer post-oophorectomy. We surveyed all licensed Maryland general, plastic, and gynecologic surgeons about their attitudes and performance of prophylactic procedures, including oophorectomy.

803/1480 (54%) responded. 31% of gynecologists believed in the effectiveness of current ovarian cancer early detection means compared to 56% of general surgeons,  $p=0.0001$ . 68% of gynecologists agreed oophorectomy has a role in the management of women at high risk of ovarian cancer; this compares with 35% of general surgeons,  $p=0.0001$ . More gynecologists (69%) recommended this procedure than general surgeons (17%),  $p=0.001$ . In 1991, 1,255 bilateral prophylactic oophorectomies were recommended by the responding surgeons and 839 were performed.

Bilateral prophylactic oophorectomy is recommended and performed as a means of managing women at high risk of ovarian cancer. Studies should be conducted to determine the effectiveness, risks, and benefits of this procedure. The availability of effective screening and prevention strategies may have a significant impact on the amount of prophylactic surgery performed.

### Predictors of Participation in Cancer Screening Examinations

Robert M. Bostick, MD, MPH, J. Michael Sprafka, PhD, MPH, Beth A. Vimig, MPH, PhD, John D. Potter, MD, PhD  
*University of Minnesota, Minneapolis, MN*

To determine factors associated with participation in cancer screening examinations, random population samples of 25 - 74 year-old men and women in six various-sized communities in three upper-Midwestern states ( $n = 4,915$ ) were surveyed in 1987-1989. Multivariable adjusted means were calculated and compared using analysis of covariance. Statistically significant ( $p < 0.05$ ) strong predictors (other than age and sex) of ever having had each cancer screening test were as follows (the figures in parentheses following each listed association are the maximum differences in mean proportions among the levels of the predictors: 1) rectal examination: higher education (14%); 2) fecal occult blood testing: higher education (6%) and never smoker (5%); 3) sigmoidoscopy higher income (7%) and higher education (6%); 4) clinical breast examination: higher education (6%); and 5) mammography: higher income (25%), higher education (8%), and a positive family history of breast cancer (7%). There were no strong predictors (out of nine) of ever having had a Papanicolaou smear or a breast self-examination. Current challenges for cancer early detection are mammogram and sigmoidoscopy affordability and availability, population education, acceptance of breast cancer screening guidelines by physicians, and demonstration of efficacious, cost-effective, and reliable colorectal/prostate cancer screening tests.

**HYPOTHESIS: DOES TEA CONTAIN CHEMOPREVENTIVE SUBSTANCES FOR CANCER PREVENTION?** J.H. Weisburger, American Health Foundation, Valhalla, NY 10595

Epidemiological studies and laboratory experiments demonstrate that as a rule most types of cancer have a lower incidence through the regular consumption of vegetables and fruits. As part of a wholesome lifestyle, the type and amount of beverage consumed is usually not considered. Research in Japan and China has suggested that populations who drink 5 or more cups of green tea per day have lower risk of the prevailing cancers, especially stomach and esophagus cancer. The effect of the gastric carcinogen MNNG is decreased in groups of rats drinking tea. Research by groups at Rutgers University, the Cleveland VA Center and in our Institute has provided a battery of data in a number of animal models or through *in vitro* approaches that green tea, and also black tea used mostly in the Western world and India have chemopreventive attributes. Cancer of the skin and lung in mice, esophagus in rats, had a lower incidence in animals drinking green or black tea. Black tea and green tea, and the corresponding active polyphenol components epigallocatechin gallate and theaflavine gallate, decrease the mutagenicity of two heterocyclic amines, as found in fried foods. They also decreased the effect of these chemicals in the DNA repair test in liver cells. Thus, research on tea and active components in tea may provide an additional approach to the prevention of important types of human cancer.

**FEASIBILITY OF SCREENING FOR OVARIAN CANCER  
AMONG HIGH-RISK WOMEN:** Electra D. Paskett, Ph.D.,  
Kimberly C. Phillips, M.S.N., Judith O. Hopkins, M.D., Lewis  
H. Nelson, M.D.

Ovarian cancer is usually detected at later stages when survival is poor. Transvaginal ultrasound (TVUS) has emerged as a possible screening tool for ovarian cancer; however research into its ability to detect tumors is needed. The goal of this study is to assess the ability of TVUS with color doppler to identify ovarian tumors as well as the pelvic examination among women at high risk for the development of ovarian cancer. Eligible women include: 1) blood relatives of patients with a history of ovarian, breast, endometrial, or colon cancer; or 2) women with a history of breast or colon cancer. Women were recruited to participate from three cities in North Carolina. All women received a pelvic exam, TVUS exam and three laboratory markers (CA-125, UGP, and NB-70K). All exams were done independent and blinded from the results of the other exams. Any abnormalities detected are followed using a decision tree based on usual medical practice standards. A total of 606 women have been recruited to be screened annually for five years. To date, TVUS screening has detected 2 early stage ovarian cancers, 3 early stage endometrial cancers, 28 cysts and 23 benign pathologies in these women. Laparoscopic evaluation is recommended by the protocol and has been used when feasible. The results indicate that TVUS is a feasible screening modality for ovarian cancer. The efficacy of this modality in preventing death from ovarian cancer must now be tested in a randomized trial before widespread use is recommended.

**PARTICIPATION IN SCREENING AMONG EMPLOYEES  
NOTIFIED OF RISK FOR COLORECTAL CANCER.**

Ronald Myers, Ph.D., Sally Vernon, Ph.D., A. Carpenter, Ph.D., P. Lewis, M.D., A. Balshem, B.A., J. Hilbert, R.N., T. Wolf, M.A., E. Ross, Sc.M.

This study reports on factors related to employee participation in a worksite-sponsored cancer screening program. A chemical company in Philadelphia mailed a letter informing 5,547 employees of a possible occupational exposure and increased colorectal cancer risk. The letter also encouraged registration by mail for free screening. Only 13% of the employees registered for screening (responders); and 31% of responders were screened (adherers). Pensioned workers were more likely to be responders (25%) than active (13%) and separated (10%) workers. Pensioned workers also were more likely to be screening adherers (44%) than active (25%) and separated (24%) workers. Associations between independent variables (i.e., age, gender, race, education) and two outcomes (i.e., response to a mail-out risk notification and screening registration program, adherence to screening) were assessed separately for each employment status category using logistic regression analysis. Among pensioned workers, responders were more likely to be male and to have more years of formal education, and adherers tended to have more education. For active workers, responders had more formal education, and adherers were older. Among separated workers, responders were more likely to be male and White, and adherers had more education. Participation in worksite screening among workers considered to be at increased risk for colorectal cancer was low in response to a mail-out risk notification and screening registration program. More intensive approaches are needed to increase participation.

### Nutritional Intake and Cigarette Use among Bronchial Metaplasia Subjects.

Susan Halabi, Patricia Pillow, Margaret R. Spitz, John J. Fueger, Joanne Sider, Jin S. Lee, Steven Benner, Waun Ki Hong

Bronchial metaplasia has been proposed as a biomarker for lung cancer. *Purpose:* To compare subjects with high metaplasia index ( $\geq 15\%$ ) with subjects with low metaplasia index ( $< 15\%$ ) in terms of cigarette smoking and nutritional intake. *Methods:* Eighty one subjects who undergone bronchoscopy as a criterion for enrollment in a chemoprevention trial provided cigarette smoking and nutritional intake information. All subjects were chronic cigarette smokers ( $\geq 15$  pack years). Metaplasia index was computed as the percent of biopsy sections with metaplasia out of the total sections examined. Nutrient analysis was conducted using the Health Habits and History Questionnaire. *Results:* Subjects with high metaplasia index smoked more cigarettes per day (29 vs. 23,  $p < 0.05$ ), and smoked other tobacco products (29% vs. 11%,  $p = 0.006$ ) than subjects with low metaplasia index. Males with metaplasia  $\geq 15\%$  had lower intake of vitamin C, vitamin A per kilogram body weight and certain carotenoids thought to be protective. *Conclusions:* Metaplasia index, a potential biomarker for lung cancer, was found to be associated with intensity of smoking and low intake of carotenoids and antioxidants.

### RECEPTIVITY OF AFRICAN AMERICAN MEN TO PROSTATE CANCER CHEMOPREVENTION

Ronald E. Myers, Ph.D., D.S.W., Thomas A. Wolf, M.A., Andrew M. Balshem, Eric A. Ross, Sc.M., Gerald W. Chodak, M.D.

The study reported here assesses the receptivity of older (50 to 74 years of age) African American men to participating in a prostate cancer chemoprevention trial which includes daily pill-taking and annual surveillance examinations (i.e., digital rectal examination and prostate specific antigen testing). Data were collected through a telephone survey conducted in January and February 1993 among 86 men in Chicago on subject sociodemographic background and medical history and knowledge, attitudes, and beliefs about prostate cancer and prevention. Survey results indicate that a substantial proportion of African American men are receptive to participating in a prostate cancer chemoprevention trial. Logistic regression analyses show that receptivity to participation is strongly related to perceived risk for prostate cancer and financial concerns. Findings presented here suggest that the receptivity of African American men to a chemoprevention regimen may be facilitated by disseminating information about population risk and by taking steps to minimize costs associated with trial participation. These steps should be considered in the development of chemoprevention programs for this population group.

**CARET CERTIFICATION: A PROCESS TO ENSURE PROFICIENT STAFF AND CONSISTENT PERFORMANCE IN A LARGE, MULTI-SITE CHEMOPREVENTION STUDY**

Karen Anderson, Debra Guarnero, Corinne Powell, Peg Boyle, Gilbert Omenn. Fred Hutchinson Cancer Research Center, Seattle, WA.

Certification is a process that assesses uniformity of staff performance in the Carotene and Retinol Efficacy Trial (CARET), a multi-site, 18,000 participant lung cancer chemoprevention study. The process developed in CARET has three components: Written Exercise, Quality Assurance Checklists, and observation. The Written Exercise consists of 114 questions to evaluate staff knowledge of CARET Manuals. Twenty-two Quality Assurance Checklists evaluate ability to perform specific CARET tasks. Scheduled observation is done by the Supervisor, the study center Principal Investigator and the Coordinating Center during annual site visits. In addition, certification ensures that staff meet state and local regulatory requirements for specialized procedures such as blood drawing, blood processing, and spirometry. This process, designed by the Coordinating Center and approved by the Steering Committee, is implemented by the study centers. Since 1989, certification has evolved from a Coordinating Center-administered to a Study Center-administered process that has led to the certification of 360 staff. As a result, CARET has proficient staff who perform study procedures consistently across six sites. Certification is an effective tool to train staff, establish site-specific and study-wide consistency, and evaluate performance on an on-going basis. This process is essential for collecting data uniformly in multi-center trials.

**A novel CYP1A1 gene polymorphism as a marker of genetic susceptibility to tobacco in African-Americans.** Emanuela Taioli, Frances Crofts, Diane Currie, Greg Cosma, Paolo Toniolo and Seymour Garte. Nelson Institute of Environmental Medicine, New York University Medical Center, New York, NY 10016.

The CYP1A1 gene is of critical importance for metabolism of carcinogenic polycyclic aromatic hydrocarbons, such as those found in tobacco smoke. We have investigated the relationship of CYP1A1 genotypes to metabolic function and tobacco related cancer susceptibility as a function of race. The human gene has exhibited polymorphism in 2 sites, one in Exon 7, and the other producing an MspI restriction fragment length polymorphism (RFLP) in the 3' non-coding region, which have been associated with increased risk of lung in Asians, but not in Caucasians. We have found a novel MspI RFLP in the CYP1A1 gene in African-Americans. The heterozygous RFLP has been detected in 16% of African-Americans, but was not detected in 191 Caucasians or 30 Asians. Haplotypes resulting from the three RFLPs found to date should not be considered as variant alleles, but as distinct genotypes whose prevalence varies according to race. The most frequent genotype among Caucasians for example (designated C/C), is present in less than half of Asians and African-Americans. Preliminary data using PCR amplified DNA isolated from African-American lung cancer tissue blocks showed a high prevalence (28%) of the AA RFLP. The odds ratio of lung cancer with the AA RFLP is 2.4 (95% CI = 0.8-6.7). No differences in AA genotype were observed with histologic type and gender. This new CYP1A1 RFLP is a possible marker of genetic susceptibility to the carcinogenic effects of tobacco smoke, which may contribute to the high risk of lung cancer in African-Americans. Sponsored by NIH grants CA34588, CA13343, ES00260, & ES04895.

**BLACK-WHITE DIFFERENCES IN FACTORS INFLUENCING MAMMOGRAPHY USE AMONG EMPLOYED WOMEN HMO MEMBERS.** Karen Glanz, Ph.D., M.P.H., Cancer Research Center of Hawaii; Nancy Resch, Ed.D., Fox Chase Cancer Center; Caryn Lerman, Ph.D., Lombardi Cancer Center; Alicia Blake, B.A., Fox Chase Cancer Center; and Barbara Rimer, Dr.P.H., Duke University Cancer Center.

Trends in breast cancer incidence and mortality in the US reveal disparities between Blacks and Whites. Early detection with mammography holds promise for reducing avoidable mortality from breast cancer. Social factors associated with mammography use include white race, younger age, and higher education and income. This study examined racial differences in knowledge, attitudes and practices related to breast cancer screening of Black and White women HMO members over age 40 who are employed at 75 worksites in Pennsylvania and New Jersey (n=1,677, 20% Black).

Data are from telephone interviews querying background factors and concepts from the Health Belief Model. Blacks were younger and less likely to be married or have a history of breast cancer. They were also more likely to underestimate their cancer risk and fear radiation, and less likely to have a doctor advise them to get a mammogram. Black and White women did not differ in terms of self-reported mammography use. The results of multivariable modeling suggest that different sets of knowledge and belief variables may explain mammography adherence among Black and White women. These findings have implications for clinical prevention and community health education in minority populations.

Support: NCI Grants CA 34856, CA 45834; work conducted at Fox Chase Cancer Center.

#### **WORKER HEALTH CONCERNS, RISK-RELATED BEHAVIORS, AND OCCUPATIONAL EXPOSURES**

G. Sorensen, A. Stoddard, K. Hammond, and J. Hebert for the WellWorks Study, Dana-Farber Cancer Institute and the University of Massachusetts

This paper examines the relationship between risk behaviors, occupational exposures to carcinogens, and interest in behavior change in workers employed in 24 primarily manufacturing worksites. Data collected by self-administered questionnaire from a random sample of workers (response rate = 63%; n=6094) were analyzed using analysis of variance, with the worksite as the unit of analysis. 61% reported that they are exposed to harmful chemicals, 54% to dust, and 57% to gases, fumes and vapors. More women than men in this sample reported being cigarette smokers (27.4% vs. 23.5%). 79% reported consuming more than 30% of calories from fat. 48% of the men and 37% of the women surveyed report both high personal risks and high job risks. 58% of workers exposed to occupational hazards were extremely or very concerned about their exposures to harmful chemicals. No differences were found by exposure status in stages of readiness to quit smoking or interest in dietary modifications. These analyses suggest that for workers exposed to occupational hazards, worksite cancer prevention programs need to address both protection from these exposures as well as health promotion.

"THE DOCTOR DIDN'T RECOMMEND IT":  
THE IMPORTANT ROLE OF SOCIAL INFLUENCES  
ON MAMMOGRAPHY SCREENING.  
S. Fontana & R. Love.

Multiple surveys have confirmed the association between reported mammography use in women ages 40 and older and physicians talking with them about having a mammogram. Yet, explanations of physicians as key motivators of women to use mammography may be overlooking essential features of social settings in which attitudes, beliefs, intention, and behavior are changed. We examined intention to obtain mammography in the next two years in the context of social influences in the community (family, friends, norms, roles), communication from a regular physician, past mammography behavior (habit), affect, consequences, and barriers from responses to a mailed questionnaire based on the Triandis Model of Choice. Using logistic regression, responses from 3364 women ages 52-64 were analyzed. Results showed that social influences was the strongest predictor of intention followed by habit, barriers, and communication from a physician. In the same model but with habit excluded, the strongest predictors of intention were social influences, communication from a physician, barriers, and consequences. We conclude that clinicians and researchers need to focus on practice issues and specific analyses that emphasize a broader social context of mammography behavior.

Potential use of a mass screening program in the recruitment strategy for a prevention trial. W-F Ko, K.J. Helzlsouer, S. Watkins, D. Ford, R. Hayward  
The Johns Hopkins School of Hygiene and Public Health  
and The Anne Arundel Medical Center

We conducted a survey of 964 men who attended a prostate cancer screening program during Prostate Cancer Awareness Week to determine their interest in participating in a prostate cancer prevention trial. Participants were asked about risk factors for prostate cancer, perceived cancer risk and interest in participating in a prostate cancer prevention trial. A brief description of the trial, including side-effects of the study drug, was provided.

Ten percent of participants had a father and/or brother affected by prostate cancer. 17% rated their risk of prostate cancer as higher than average and estimated their lifetime risk of developing prostate cancer to be 50% compared to an estimated lifetime risk of 22% among men who rated their risk lower than average. The perceived lifetime risk of cancer was highest (61%) among participants with a family history of prostate cancer. 852 (88%) responded to the question concerning trial participation; 56% expressed interest in participating. Family history of cancer was similar between those interested compared to those not interested in participating; perceived risk of cancer was slightly higher among those interested in the trial (37% vs 32%).

Mass screening programs provide a resource for recruitment of intervention trial participants and should be incorporated into recruitment strategies.

SPECIAL POPULATIONS IN THE ASSIST PROJECT

Elmer E. Huerta, M.D., M.P.H.; Marc W. Manley, M.D., M.P.H. NATIONAL CANCER INSTITUTE. Bethesda, Maryland

We describe the ethnic and racial groups to be reached by ASSIST (American Stop Smoking Intervention Study on Cancer Prevention), the world's largest tobacco control program. This 7 year long project, currently in its intervention phase, involves 17 states in tobacco control activities. The goal of ASSIST is to reduce the prevalence of smoking in these states to 17% by the year 1998. Through the formation of community based coalitions and using five channels of action (schools, work sites, health resources, community organizations and community environment), it is estimated 91 million people will be reached over the study period. Ethnic and racial groups will receive special attention because their rates of smoking are higher, their access to and use of smoking prevention and cessation services is limited, and they are the focus of intense advertising by the tobacco industry. Approximately 18.8 million people in the project will belong to a racial-ethnic group. This represents 20.7% of the ASSIST total population. Those who will be reached by ASSIST are 10.9 million African Americans, 5.3 million Hispanic Americans, 1.9 million Asian Americans, and 0.6 million American Indians. In this regard, ASSIST can be considered the largest effort ever made in the U.S to reach racial-ethnic groups with tobacco control and health promotion interventions.

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USE OF RADIO AS A TOOL FOR PUBLIC HEALTH IN THE LATINO COMMUNITY IN THE WASHINGTON, D.C., METROPOLITAN AREA

Elmer E. Huerta, M.D., M.P.H.  
National Cancer Institute. Bethesda, Maryland

The use of radio as a vehicle to deliver daily health promotion / disease prevention (HP/DP) messages to the Hispanic community in the Washington, D.C. metropolitan area will be described. This voluntary project began on December 4, 1989, and consists of the broadcasting of five-minute shows on one of two local Spanish language radio stations. The program is aired Monday through Friday at 7:45 a.m., 12:15 p.m., and 4:45 p.m. Each day, the medical literature is reviewed and one article is chosen for broadcasting based on its HP/DP content. The article is then summarized, translated and written in 6th grade level Spanish.

As of July 2, 1993, 615 different programs have been produced, 11% on cancer, 15% on AIDS, 20% on tobacco control issues, 31% on preventive medicine issues, and 23% on miscellaneous issues. Informal ratings estimate 75,000 to 100,000 daily listeners. Although no systematic effort has been made to measure the program's impact, a recent successful campaign encouraging low income Hispanic women to participate in a state sponsored free Pap smear and mammogram program indicate changes in knowledge, attitudes and behaviors in the targeted population. Radio should be considered as a primary tool to reach communities with HP/DP messages.

A CANCER CONTROL INITIATIVE AMONG HISPANICS  
IN WASHINGTON, D.C.

Elmer E. Huerta, M.D., M.P.H.; John J. Lynch, M.D., F.A.C.P.; Sharada Shankar, Ph.D., M.P.H. The Cancer Institute of the Washington Hospital Center, Washington, D.C.; and The National Cancer Institute, Bethesda, Maryland.

We describe the development of a new cancer control initiative among the Hispanic population of the Washington, D.C.-Metropolitan Area. The 1990 U.S. Census Bureau reveals that Hispanics in the Washington, DC-Maryland-Virginia Metropolitan Statistical Area have grown from 95,016 in 1980, to 224,786 in 1990 (an increase of 136.6%). Including undocumented individuals, the estimated actual number is 500,000. Approximately 40% of this population are people from Central America, mainly Salvadorans. Two thirds are between the ages of 18 and 44 years, and one third have less than a 9th grade education. One third of the households and almost half of the people older than 65 years old are linguistically isolated, speaking only Spanish. Due to the lack of studies regarding cancer in this population, an initial workshop with the main region's health providers was convoked to develop an initial need assessment evaluation of the cancer status in the area. Subsequently, an instrument was developed to perform the first study on knowledge, attitudes, and practices towards cancer among 2,000 Salvadorans. Using 15 trained interviewers, the study will start in October, 1993 and will be completed by February, 1994. Strong support from community leaders, health providers, community organizations, The American Cancer Society, and the local media has been secured for the project.

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Behavioral and Social Factors that Predict Participation in the Breast Cancer Prevention Trial. Anita C. Yeomans Sally W. Vernon, Diane Weber, Jo Ann Bitsura, Victor G. Vogel.

This survey assessed prospectively what factors predicted a woman's participation in the NSABP Breast Cancer Prevention Trial (BCPT). The survey assessed components of the Health Belief Model (HBM), health status and health behaviors, beliefs and attitudes along with other factors that have been associated with breast cancer screening. Overall, 337 women attended one of the meetings and 72% completed the survey. The analysis was limited to caucasian women (n=232), since minorities were poorly represented. Among the analytic cohort, 45% (n=105) enrolled on the trial and 55% (n=127) decided not to participate. All but one of the items assessing perceived barriers were significantly associated with participation in the trial including not being able to take estrogen ( $p < 0.001$ ), frequent clinic visits ( $p = 0.002$ ), the experimental nature of the trial ( $p = 0.007$ ), the possibility of receiving a placebo ( $p = 0.01$ ), side-effects of tamoxifen ( $p = 0.03$ ), and costs of the trial ( $p = 0.04$ ). Taking a pill daily ( $p = 0.19$ ) was not associated with participation. Participants also were more likely than nonparticipants to note support from their significant others and or physician for their participation ( $p < 0.001$ ), to report that participation would give them peace of mind ( $p < 0.001$ ). Nonparticipants were more likely than participants to be postmenopausal ( $p = 0.007$ ), to be currently or ever on hormone replacement therapy ( $p < 0.001$ ), and to have had hot flashes ( $p = 0.02$ ). Information on facilitators and obstacles to recruitment can help in developing recruitment strategies in future trials as well as developing interventions for maintaining participation in such trials.

### Use of Volunteers in Cancer Prevention Research

Deborah Bowen, Alan Kristal, Dan Nixon, Robert Sponzo, Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center, Seattle, WA, USA.

The purpose of this study is to determine the feasibility of using a cadre of motivated volunteers to conduct a dietary intervention study with breast cancer patients. The Breast Cancer Dietary Intervention Study is to be a randomized controlled trial to determine whether a low fat dietary intervention, implemented by volunteers in communities, could reduce recurrence of breast cancer. In the feasibility study, volunteers were recruited in nine communities from upstate New York using media and networking recruitment strategies. A total of 121 volunteers were successfully recruited and trained for specific roles within the trial. Five types of volunteers were recruited and trained for each community: clinic coordinators, who monitor and coordinate all activities for the trial; assessment volunteers, who collect and review 4-Day Food Records and other assessment instruments for each participant; individual intervention volunteers, who conduct six individual dietary intervention sessions with each intervention participant; group intervention volunteers, who conduct group dietary intervention sessions later in the intervention period; and control volunteers, who meet with control participants to provide information and support. The backgrounds of all volunteers were varied: approximately half were nutritionists and over one-third were involved in breast cancer care or research. Volunteers reported several motivations for participating, including altruism, professional development, and satisfying personal needs. The ability of researchers to recruit and maintain community volunteers in health promotion trials has relevance for further health behavior change research at both the individual and community level.

### Participation in a Project to Control Cessation-Induced Weight Gains

Deb Bowen, Diane Powers, Anne McTiernan, Elliot Rosenberg, Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center, Seattle, WA, USA.

The purpose of the Smoker's Intervention for Good Health is to test fenfluramine as an adjunct to self-help cessation materials for women. This abstract describes the early recruitment experiences for the trial. Eligibility requirements included being ages 30-65, female, healthy, and under 150% of ideal body weight. Women were recruited via a minimal mass media solicitation. The results of this recruitment effort were unexpected and overwhelming. Over 2,000 telephone contacts were recorded from the general public in 48 hours. National and international media reported the recruitment efforts by the third day, and more calls, mail, and telefaxes began arriving at this time.

Demographic characteristics of randomized and non-randomized women were compared to determine the composition of the volunteer population. Frequent reasons for ineligibility included health problems and obesity. The randomized women had varied educational levels (50% with high school education or less) and were unusually adherent to questionnaire completion (baseline completion rated over 99%). Women are very interested in quitting smoking, and many are willing to request pharmacologic assistance other than nicotine replacement products. Weight gain after cessation is a particular concern for women.

### Changes in Taste for Fat After Participating in Dietary Intervention

Deborah Bowen, Mark Kestin, Pamela Green, Elizabeth Fries, Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center, Seattle, WA, USA.

Changing dietary fat is the subject of much research. Reducing dietary fat intensively could result in cravings for fat or other negative reactions. The purpose of this abstract is to investigate any effects, either positive or negative, of changing dietary fat on fat preference or cravings for fat. A series of follow-up studies of women in the original Women's Health Trial were conducted to address these and other issues. The Women's Health Trial was to be a randomized controlled trial of a low fat dietary intervention. At one year after randomization, intervention and control women reported similar satisfaction with diets and similar low frequency of craving for fat. Four years after randomization, there was no difference in rated taste of fat, but intervention women reported decreased liking for high fat foods, compared to control women. Intervention women reported that eating high fat foods produced discomfort, sleepiness, and gastrointestinal problems. Taken together, these data indicate no support for fat cravings after decreasing dietary fat. Rather, there is some evidence for the development of fat distaste among women who were successful at reducing dietary fat.

### Determinants of Breast Cancer Detection in Wisconsin Women 1986-1990. Mathew J. Reeves, Polly A. Newcomb, Patrick L. Remington, Pam Marcus. Comprehensive Cancer Center, Univ. of Wisconsin, Madison, WI 53706

We evaluated detection practices in 3197 invasive breast cancer subjects who participated in a case-control study of breast cancer etiology. As part of the risk factor telephone survey, case subjects were asked how their cancer was first detected. Method of detection, which was classified as self, mammography or physician, was modelled using polychotomous logistic regression. After controlling education, race, year of diagnosis, and previous use of mammography, significant associations between age, cancer stage, family history and body mass index (BMI) and the method of detection were found. Compared to self detected cases, younger women were significantly less likely to have physicians detect their cancer compared to older subjects. The odds ratio (OR) for physician detection among 40-49 year olds was 0.3 (95%CI=0.2-0.5), compared to women older than 70 years of age. Similarly, younger women were significantly less likely to have their cancer detected by mammography compared to older subjects. Compared to localized tumors, tumors that had spread were significantly less likely to be detected by either physicians (OR= 0.6; 95%CI=0.4-0.7) or by mammography (OR= 0.3; 95%CI=0.2-0.4), compared to self detected. A positive family history of breast cancer was associated with an increased likelihood of either physician detection (OR= 1.5; 95%CI=1.0-2.3) or mammography detection (OR= 1.4; 95%CI=1.0-1.8). A positive trend was observed between BMI and the likelihood of mammography detection. Women in the highest BMI quintile (>28.3) were 2.2 times (95%CI (OR)=1.7-2.9) more likely to have their cancer diagnosed by mammography, compared to women in the lowest BMI quintile (<21.2).

Education and Motivation by Peer Health Workers to Promote Breast Cancer Screening Compliance. Chrvalla CA, Hau B, Simons M, Boyd L, Mondragon NJ.

The DO IT FOR LIFE Speakers Bureau Program is an interactive, small group intervention to improve women's knowledge about breast cancer (BC), foster positive attitudes and promote compliance with regular BC screening. Educational content focuses on breast anatomy, BC symptoms and risk factors, mammography (MM), clinical breast exams (CBE), breast self-exams (BSE) and effective communication with health care providers. Group process emphasizes interpersonal sharing, problem-solving and role-playing to reduce barriers and enhance motivation for regular BC screening. Trained peer health educators have facilitated more than 100 groups involving over 1000 participants who are representative of diverse race and socio-economic groups with 33% minority participation and 43% low income. Knowledge of BC symptoms and risk factors was minimal with 36% of participants able to identify only 1 or 0 correct symptoms and 55% unable to specify even 1 correct risk factor. The majority of women indicated compliance with regular CBE but less than 40% reported having a MM in the past year. Approximately 50% of the women failed to do monthly BSE. Only 38% of respondents believed that CBE were very effective in BC detection while 50% and 70% of women, respectively indicated that BSE and MM were very effective BC detection exams. General evaluation of the presentations was very favorable with presenters viewed as credible and informative. This presentation will focus on comparison of six month follow-up survey data with pre-intervention responses to assess improvements in BC knowledge, attitudes and screening behaviors.

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#### ORAL CONTRACEPTIVE USE AND MAMMOGRAPHIC DENSITY AMONG WOMEN AT INCREASED RISK FOR BREAST CANCER

Victor G. Vogel MD, MHS; Eric Higginbotham; Anita Yeomans RNC, The University of Texas M. D. Anderson Cancer Center (MDACC), Houston, Texas 77030

We reviewed screening mammograms among 109 women in our Special Risk Clinic to evaluate the relationship between risk factors for breast cancer and mammographic density patterns. We included all women seen in the clinic since 1987 who had at least one screening mammogram at MDACC. We obtained demographic profiles and breast cancer risk factors from the information recorded in the Special Risk Clinic data base at the time of the initial clinic visit. Reports were classified into three categories: severely dense (stroma potentially obstructing small lesions, Wolfe P2 or DY, or "dysplastic"); moderately dense (Wolfe P1 or moderately or intermediately dense or glandular); or normal. The films were not independently re-read or reviewed. Severely dense mammograms were found in 42 of 109 women (38.5%). In univariate analysis, being younger than 45 years was associated with a higher proportion with dense patterns (43% vs 27%  $p=0.03$ ), and more current or former users of oral contraceptives (OC) had dense patterns compared to non-users (43% vs 31%  $p=0.01$ ). Duration of OC use did not correlate with greater density, but among postmenopausal women who had ever used OCs, 40% continued to manifest dense patterns compared to only 9% of non-users ( $p=0.02$ ). Family history and gynecologic history did not affect density patterns in the univariate analysis. Logistic regression confirmed that both menopausal status and the use of OCs were significant predictors of dense mammographic patterns. These data implicate OCs in the etiology of mammographic densities among women with a family history of breast cancer.

Comparison of Screening Behaviors and Outcomes of Women at High vs. Average Risk for Breast Cancer. Chivala CA, Mondragon NJ, Klein SA, Weatherford HA.

This study compares the mammography (MM) screening practices and outcomes of a cohort (n=12,525) of women at High Risk (HR) for breast cancer (BC) to those of an equal size cohort of women at Average Risk (AR). The 2 cohorts were selected from a statewide BC screening surveillance system that is currently tracking more than 105,000 women with 13.5% of these considered HR due to a personal or first-degree family history of BC. The 2 cohorts were similar with respect to age and race although significantly fewer HR women were of Hispanic origin. Significantly higher rates of MM rescreening compliance were noted for the HR cohort. Among women who have returned for rescreening, the mean interval between screenings was 13.0 and 13.5 months for HR and AR cohorts, respectively. HR women were more likely to have MM findings that were suspicious for cancer. Clinical breast exams and ultrasounds were more often recommended as diagnostic follow-up procedures for AR women while HR women were more likely to receive a recommendation for surgical consult. Biopsies were completed for 18.4% of HR women and 14.5% of AR. BC has been detected in 538 women from the surveillance system, with 31.2% diagnosed in the HR cohort. This presentation will examine in greater detail the differential impact of BC risk status on screening behaviors and outcomes and discuss the implications of these findings for efforts to implement BC screening programs.

Why does cancer occur more often in the left breast? do local factors within the target organ play a role?

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Dept. of Epidemiology Utrecht University The Netherlands

Why breast cancer consistently tends to occur more often in the left breast remains an enigma, especially since both breasts of an individual are assumed to have been exposed to the same risk factors since conception, such as hormonal development, diet and pregnancies.

The records of the mammographic evaluation of over 55,000 participants of the DOM project in Utrecht NL between 1974-1992, allowed the following analysis.

As expected from the literature a left over right predominance of breast cancers was found  $Le/Ri = 1.11$  (CI95% 1.10-1.12) However this  $Le/Ri$  ratio was reversed in "benign" lesions (Benign defined as mammographically suspect for cancer but upon follow-up not confirmed as malignancies)  $Le/Ri = 0.984$  (CI95% 0.979 - 0.987).

The age of the women at detection with left or right sided breast ca showed no difference.

When mammographically visible vascular calcifications were studied as a proxy for age/aging related processes a  $Le/Ri$  ratio of 0.86 (CI95% 0.84-0.88) was found. Vascular calcifications on mammograms are a biomarker of arterial sclerosis.

The results are interpreted as pointing to a relative difference in biological age of the left and right breast in an individual of a given calendar age and may reflect metabolic differences between the left and the right breast or left and right body half.

It can be hypothesized that differences related to vascular calcifications contribute to modify a target organ into differentiation or apoptosis in either a benign or more malignant track.

# PSYCHOLOGICAL ISSUES OF WOMEN IN THE NATIONAL BREAST CANCER PREVENTION TRIAL: PERCEPTIONS UPON ENTERING THE STUDY

Halper MS, Kash KM, Webb L, Osborne MP, Reichman BS, Schwartz M, Gronart MK. Strang Cancer Prevention Center, 428 East 72 Street, New York, NY 10021 USA

The Strang Cancer Prevention Center is a designated clinical center of the Breast Cancer Prevention Trial. The purpose of this trial is to test the efficacy of Tamoxifen in preventing breast cancer. Women met minimum eligibility criteria using the Gail Model of predictive risk, were between 35 and 78 years of age, and had no personal history of invasive breast cancer. Forty one women completed a questionnaire at baseline, looking at perceptions of health beliefs and potential problems of study participation. Ninety-two percent were White and ages ranged from 41 to 76 with a mean of 54. Risks ranged from 4% for women over 65 with no family history to 54% for women with lobular carcinoma in-situ. Seventy-seven percent believed that tamoxifen would be very or highly effective in preventing breast cancer. When asked what they would prefer to receive, 72% preferred tamoxifen, 7% preferred placebo and 21% said that it did not matter. While 47% thought support from family and friends was very important for their participation in the trial, 39% thought support was unimportant. Two of the most interesting findings were that women who thought support to be important would rather be on Tamoxifen ( $p<.07$ ) and perceived more benefits (e.g., careful medical follow-up, getting information about breast cancer) from participating in the study ( $p<.03$ ). Women who found it difficult to participate in the trial reported there was a good chance they would change their minds about participation ( $p<.004$ ) and anticipated more unpleasant aspects (e.g., side effects of drug, number of blood samples, taking two pills a day) of study participation ( $p<.0001$ ). We hypothesize that women who have more outside support for participation and see their participation as less difficult will be more likely to successfully complete the trial.

## TRIAGE PROCEDURES FOR GENETIC CANCER RISK ASSESSMENT (Mary B. Daly, Generosa Grana, Josephine Wagner, Agnes Masny, Tracy Jones, Doris Gillespie) Fox Chase Cancer Center, Philadelphia, PA

Approximately 50% of multi-case families with early onset breast and/or ovarian cancer are linked to chromosome 17q12-21. It is estimated that one in 200 women in the U.S. may carry a mutation in a gene, termed BRCA1, located in this region. We report on triage procedures for genetic cancer risk assessment established in the Family Risk Assessment Program (FRAP) at the Fox Chase Cancer Center. FRAP provides education and screening for women with a family history of breast and/or ovarian cancer. The triage procedures have been designed to handle increasing requests for genetic cancer risk information and to identify eligible high risk families for genetic linkage analysis. Prior to the first visit, the pedigree is assessed by a medical oncologist and genetic counselor. Based on standard genetic cancer risk criteria (i.e. number of affected relatives, age at onset, pattern of inheritance, and other related cancers), the pedigree is triaged to a preliminary category of sporadic, familial, or hereditary cancer. The two latter groups receive a formal family pedigree assessment session by a medical genetic counselor to expand and confirm reported cancers. Expanded pedigrees are then reviewed by a Pedigree Review Committee. This multi-disciplinary team formulates follow-up recommendations for genetic investigation and counseling. To date, 249 women have been seen in FRAP. Of these, 136 (55%) have multiple affected relatives. Those with a family history of breast cancer, ( $n=148$ ), 42% had relatives diagnosed  $< 50$  years, while 43% of breast/ovarian families ( $n=101$ ) had early onset, and 12 families have been selected for linkage studies. These procedures can help in the development of appropriate and efficient guidelines for genetic cancer risk investigation and counseling in high risk populations and meet future demands for such information.

**QUALITY OF LIFE OF LONG-TERM BREAST CANCER SURVIVORS. GWEN WYATT, RN, PhD & MARGOT KURTZ, PhD**

The objective of this study was to assess the quality of life of long-term (five or more years) breast cancer survivors through focus group discussions. The women ranged in age from 40 to 79 years (mean=61) and their years of survival ranged from 5 to 14 years (mean=10). The Ferrell Quality of Life Framework was utilized, encompassing physical, psychological, social, and spiritual well-being.

Data analysis resulted in four themes: a) integration of disease process into life, b) change in relationships, c) restructuring of life perspective, and d) unresolved issues.

Nursing can learn from these women's successes in integrating physical changes into their daily life, and intervene to facilitate adjustment with all breast cancer survivors. Further, since women experienced many unanticipated relationship changes, nursing can help prepare women and assist them with coping strategies to deal with such changes. Each woman was eager to discuss her profound shift in spiritual perspective. This points to a need for greater nursing emphasis on spiritual dialogue and support for women with breast cancer. Finally, long-term survivors continue to seek help from nurses to deal with unresolved issues. These women want to be more active participants in their health plan, including information on state-of-the-art breast cancer care and treatment, less delays with test results and more thorough exams to detect any recurrence at an early stage. Reducing ambiguity and increasing information is the key to quality of life.

**QUALITY OF LIFE OF LONG-TERM FEMALE CANCER SURVIVORS. GWEN WYATT, RN, PhD & MARGOT KURTZ, PhD**

The objective of this study was to assess the quality of life (QOL) of 200 female, 5-year or longer survivors of major cancers. This study utilized the components of the Ferrell framework to capture the domains of QOL: physical, social, psychological and spiritual well-being. The questions were: 1) What is the QOL of long-term survivors when measured by an established instrument, and 2) What additional QOL variables exist when elicited by focus group discussions and translated into a quantitative questionnaire.

Data were collected using an established QOL instrument, the Cancer Rehabilitation Evaluation System (CARES), which examines five key areas of QOL: physical, psychosocial, medical, marital and sexual functioning. A companion questionnaire developed from focus group discussions conforms to the format of the CARES but covers areas not addressed such as spirituality, support system changes, desire to assist other cancer patients, and change in appreciation for life.

The reliability of each of the CARES 5 subscales will again be tested on the sample of 200. Exploratory factor analysis techniques will be applied to the companion instrument. This mixture of conceptual decisions and statistical techniques can aid in establishing the underlying conceptual dimensions of QOL.

These data will contribute a unique addition to the QOL literature which currently focuses primarily on the first two years since diagnosis. QOL factors that promote longevity and well-being as well as the needs of long-term survivors will help in nursing tailor interventions for this population.

**The Impact of Mobile Breast Screening Services Among Rural Alberta Women Aged 50-69**

Zeva Mah and Heather E. Bryant. *Screen Test: Alberta Program for the Early Detection of Breast Cancer, Alberta Cancer Board, Calgary, Alberta, Canada.*

Since 36% of Alberta's population live outside of major urban centres and reside in over 95% of the land area, delivery of screening mammography in these areas requires considerable attention. In our 1991 survey of Alberta women aged 40-75, we found that rural physicians were only 60% as likely to refer women for mammography than urban physicians; rural women also had more negative beliefs about breast cancer itself. In 1993 we re-surveyed two rural health unit areas - one which had received mobile screening services and community mobilization since the last survey (intervention area) and the other which had not (control area). The overall response rate for the random-digit-dial telephone survey was 73.3%; respondents were 679 Alberta women aged 40-75. Age and area stratified analyses showed that women 50-69 in the intervention area had different knowledge and attitudes than women in the control area. Specifically, intervention area women were 1.6 times more likely to disagree that symptoms were necessary for getting mammograms, were 4.7 times more likely to agree that most women 50 and over were getting screening mammograms, and were 2.0 times more likely to strongly agree that getting a mammogram would give them peace of mind than control area women ( $p < 0.02$ ). An analysis of differences in behaviours showed that intervention area women were 1.6 times more likely to have ever had a mammogram, were 5.0 times more likely to have initiated getting a mammogram appointment themselves, were 1.4 times more likely to intend to get another mammogram in two years, and were 1.4 times more certain to be able to discuss getting mammograms with their physician or encourage other women to get clinical breast exams and screening mammograms than control area women ( $p < 0.05$ ).

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Absolute risk of developing second primary breast cancer. Jonine Bernstein, W. Douglas Thompson, Theodore R. Holford, Neil Risch, and David Bruce.

The purpose of this study was to estimate age- and risk factor-specific probabilities for developing second primary breast cancer among women diagnosed with first primary breast cancer between 1980 and 1982. All subjects were interviewed as part of a multi-center, population-based, case-control study and followed through the end of 1989. Among the original 4,677 women, 331 developed a second primary breast cancer in the contralateral breast. The average age at diagnosis of the first primary was 44 years and the average length of follow-up was 73 months. Proportional hazards models were used to calculate individual probabilities among women with various combinations of risk factors. Further, the effect of the time interval since diagnosis of the first primary on the hazard ratio was considered in obtaining the probabilities. Specific risk factors evaluated were: age at diagnosis of the first primary, family history of cancer, menstrual and reproductive histories, tumor characteristics of the first primary, and demographic variables. The probability of developing contralateral breast cancer was increased among women reporting family history of breast cancer. Early age at onset in either a mother or a sister and bilateral breast cancer in a mother further increased the risk. Having a first primary classified as lobular and having a history of benign breast disease also increased the probability of developing a second primary breast cancer. These risk projections should help identify women who are likely to develop second primary breast cancer.

# The Use of Fear to Motivate Non-Responders in a Study of Mammography Use

Nicole Urban, Sc.D., Hendrika Meischke, Ph.D.

The purpose was to test the effectiveness of fear-oriented language in motivating persistently non-responding women aged 65-80 to return a postcard reporting use of mammography and evaluation of a brochure. The brochure represented a mail version of barrier-specific telephone counseling, which has been shown to increase mammography use among underutilizers.

A factorial, randomized design was employed using six versions of the brochure, such that versions #1-#3 were informational in language while versions #4-#6 were fear-oriented; versions #1 and #4 addressed barriers related to mammography, while versions #2 and #5 addressed barriers related to breast cancer, and versions #3 and #6 addressed both types of barriers. 3096 women were randomly assigned to receive one of the six brochures.

Logistic regression, controlling for language, suggested that addressing barriers related only to screening was less effective than including barriers related to both disease and screening ( $p < .02$ ). Rates of return were highest (15.4%) for women receiving version #6, and lowest (10.3%) for women receiving version #4. It was concluded that fear-oriented language is effective when barriers related to breast cancer as well as mammography are addressed.

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## BREAST CANCER KNOWLEDGE, ATTITUDES AND PRACTICE BEHAVIOR OF PUBLIC HEALTH NURSES IN NORTH CAROLINA. Irene Tessaro, James Shaw, Carla Herman, Elizabeth Geise, Monica Bynoe. University of North Carolina at Chapel Hill, NC.

Public Health Nurses (PHNs) have traditionally provided cancer prevention education and screening for medically underserved populations. To further our understanding of the cancer screening behavior of health care providers, a 12 page mail survey was sent to the 2,000 PHNs staffing the 87 health departments in North Carolina. The survey elicited self-reports of knowledge of breast cancer guidelines, risk factors, usual pattern of referrals and recommendations, training needs, as well as other items. Preliminary findings with 723 respondents are reported here.

87% of the nurses reported their self-assessed skills of performing clinical breast examination as excellent or very good. However, only 49% and 40% respectively rated their skills in educating clients about the need for mammography and their skills in counseling about cancer risk factors as excellent or very good. In addition, 37% of the respondents reported they did not have sufficient knowledge to counsel clients about cancer prevention.

ACS guidelines were the most commonly used among PHNs, followed by health department guidelines. When asked about which of the following increased a woman's chance of getting breast cancer, respondents reported:

	Risk Factor	Yes (%)	No (%)
(risk)	Increasing age	70	30
	Family history	98	2
	Delayed childbirth	44	56
	Obesity	36	64
	ETOH	24	76
(no risk)	Smoking	50	50

PHNs have greater interest and needs in acquiring knowledge about cancer prevention, risk assessment, and counseling than in acquiring clinical skills. To improve cancer screening among the medically underserved, the needs of PHNs should be addressed and interventions with PHNs should be initiated.

# FIELD TEST OF RECRUITMENT AND MANAGEMENT FOR A REPEATED MEASURES BREAST CA RISK FACTORS STUDY

Haines Carol S., Oster Frederick, Virag Felecia  
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Saskatchewan has a population of one million, requires that cancer registration precede physician reimbursement, and invites all women aged 50-69 biannually for mammography. In this enriched cancer research environment, we intend to recruit 80,000 women aged 20 to 72 to self-report annually on a variety of breast cancer risk factors.

A public awareness campaign involving 5% of the total population (1) promoted the study's objectives and (2) encouraged women to sign and return pledges distributed by school children, church and civic groups.

Promising management strategies for collecting risk factor data on the 5,000 who pledged to participate are being tested. These include (1) each woman self-reports directly onto a computer with a light pen - permitting the monitor to be used much like a paper and pencil form (2) hospitals, health centres and schools create a network of convenient reporting stations for completing each annual survey and (3) a volunteer-staffed telephone pyramid is used to schedule each survey.

Field trial methods will be extended province-wide in 1994. An international advisory panel, expected to be recruited early in 1995, will guide annual survey content. Concurrent collection of biologic specimens and/or anthropometrics should be quite feasible and economical, since over half the cohort will be reporting at health facilities.

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## USING 1944-1993 INCIDENCE DATA FOR BREAST AND PROSTATE CANCER CONTROL POLICY AND PLANNING

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Saskatchewan began free, comprehensive cancer care in 1932. Provincial insurance denies claims for cancer diagnostic or treatment services that lack cancer registry approval, granted only when the claimant submits satisfactory case confirmation. In the past 30 years, 98% of prostate & breast cases under age 70 (95% all ages) have pathologic confirmation. Earlier years are 80 - 85%. Registrations over the past 50 years have been analyzed to inform cancer control decision making and to determine surveillance needs for these diseases.

Age-specific prostatic cancer incidence has at least tripled in the last 25 years for every 5-year age group. Notwithstanding, only 14% of prostate cancers occur in men under age 65. Insurance claims data do not support incidental detection during evaluation of postatism as an explanation for these increases. Every succeeding birth cohort shows increased risk.

There is no evidence, over the last 50 years, of age or cohort specific increase in pre-menopausal breast cancer. Age-specific rates of breast cancer have at least doubled in 50 years for every 5-year age group 60 and older. Cohort analysis, however, suggests incidence may have peaked. Careful, timely surveillance of cohort effects is essential to avoid spurious attribution of declining disease rates to other causes (e.g. screening programs). Fully 45% of breast cancers occur before age 65.

# **HARDWARE AND SOFTWARE FOR DIRECT COMPUTER SELF-REPORT BY RESEARCH SUBJECTS**

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Costs of printing, distributing, coding, entering, and storing discourage investigators from collecting longitudinal - or even cross-sectional - data about quality of life or other psychosocial components of fully evaluated research trials. Direct computer entry by patients would eliminate some and drastically reduce other of the costs just mentioned.

However, many research subjects are not familiar with the two most common entry methods - keyboard and mouse. Cancer patients in particular are older, and consequently even more likely to be unfamiliar with these two computer entry methods. Touch-screen and stand-alone stylus systems are sufficiently expensive to be practical only when sizeable dedicated funds have been set aside specifically to procure such equipment.

We paired a commercially available light pen with software we developed. The pen can be installed on any existing computer (including otherwise obsolete 8088 equipment) - which remains fully available for other applications. The resulting system was preferred to paper and pencil reporting for Functional Living Index-Cancer by elderly cancer patients. Three programs in use - for quality of life measurement, for collecting new enrollees' breast cancer screening program baseline data, and for a cohort study of breast cancer risk factors - will be demonstrated.

## **DNA REPAIR IN HUMAN LYMPHOCYTES AND MONOCYTES J.J. Hu, B. Ma, D. Kurland, M. Berwick, and G. C. Roush, Cancer Prevention Research Institute.**

DNA damage/repair plays an important role in human carcinogenesis. Individuals with defective DNA repair may have higher risk for different types of cancer. Human peripheral mononuclear leukocytes (PMLs) have been routinely used for the measurement of DNA repair capacity in response to DNA damage. Our preliminary studies in PMLs have demonstrated wide intraindividual and interindividual variations of two DNA repair measurements, unscheduled DNA synthesis (UDS) and poly(ADP-ribose) polymerase (PADPRP) enzyme activities. UDS is measured after exposure to either *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine (MNNG) or UVC; the inducer of PADPRP is hydrogen peroxide. Different exogenous and endogenous factors may contribute to both types of variation. One very important source of variation may result from the heterogeneous cell population of the PMLs preparation. The objective of this study is to evaluate the DNA repair activities in two different fractions of PMLs: lymphocytes and monocytes. 10 healthy subjects were recruited for this study. Results suggest that UDS in response to both MNNG or UVC is higher in monocytes; however, PADPRP enzyme activity induction by hydrogen peroxide is higher in lymphocytes. Therefore, although these DNA repair measurements probably should be performed in defined cell populations in order to eliminate the possible sources of variation due to different cell populations, more study is required to substantiate the extent to which the variation due to type of cell population may contribute to overall assay variation. (Supported by NCI grant CA01634).

Serum oncoproteins and human cancer. Joel Weissfeld, Russell Larson, Henry Niman, Lewis Kuller. University of Pittsburgh.

This study asks whether oncogene-related serum proteins distinguish older men and women developing new cancers during a two year follow-up. In 1989, the Rural Health Promotion Project (RHPP) recruited 3884 ambulatory, non-institutionalized, 65-79 year-old Medicare beneficiaries. Study eligibility required no cancer diagnosis within five years, completion of 90 minute interview, and collection of a blood sample. During follow-up, 37 RHPP subjects died from cancer and 59 others developed breast, prostate, colon, or lung cancer. Blind, the laboratory measured 18 serum proteins detected in immunoblots by seven different monoclonal antibodies against ras, erb-B, FES, myb, and SIS oncoprotein polypeptide sequences. Controls included 58 RHPP subjects hospitalized between Jan 1988 and Dec 1991 with at least one discharge diagnosis coding to benign neoplasia (ICDA 200-239). A second control group included 94 randomly selected RHPP subjects without hospitalization with benign neoplasia or cancer on follow-up. At baseline, the groups were similar in age, body mass index, cigarette smoking, current alcohol use, chronic illness, and blood cholesterol. The group with benign neoplasia included more women and persons with recent medical disability. For five proteins with statistically different ( $p < 0.05$ ) median levels, the table compares baseline seroprevalence (in percent) among the 94 control subjects (CTL), 58 benign neoplasia subjects (BGN), 59 nonfatal incident cancer cases (NFT), and 37 fatal incident cancer cases (FTL).

Oncogene	Mol Wt	CTL	BGN	NFT	FTL
SIS	52,000	3.2	12.1	3.4	16.2
k-RAS	35,000	1.1	10.3	1.7	10.8
k-RAS	52,000	0.0	6.9	0.0	2.7
erb-B	28,000	10.7	8.6	1.7	16.2
myb	52,000	11.7	22.4	6.8	19.4

Over a brief follow-up, these serum markers were risk factors for fatal cancer, but not non-fatal cancer. Older persons hospitalized with benign neoplasia had higher levels of these proteins. Small numbers limited study serum markers and cancer at single sites.

#### THE ROLE OF PROPHYLACTIC OOPHORECTOMY IN AN OVARIAN CANCER RISK COUNSELING PROGRAM (Generosa. Grana, Mary B. Daly, Tracy. Jones, Agnes. Masny, Josephine Wagner, Doris Gillespie) Fox Chase Cancer Center, Philadelphia, Pennsylvania.

Prophylactic oophorectomy (PO) is currently the only form of primary prevention of ovarian cancer. Controversy exists as to the true effectiveness of the procedure, who are the appropriate candidates, and the optimal surgical approach. Currently there are no standards to guide high risk women and their physicians in choosing this option. We examined attitudes towards PO on the part of 196 women participating in ovarian cancer risk counseling program at baseline, and the subsequent decision to undergo the procedure 1 year later. Median age was 39 yr (range 21-72 yr) and all had at least 1 first degree relative with ovarian cancer. Most (114) of the women had heard of PO, and 29 (25%) had been advised by a physician to undergo the procedure. Physician recommendation (83%) and fear of getting ovarian cancer (73%) were most often cited as factors supporting a decision to consider surgery, while fear of surgery (31%) and reluctance to take hormone replacement (34%) were the major barriers noted. Although most women (76%) perceived their risk as "greater than the average woman," risk perception at baseline was not significantly correlated with interest in prophylactic surgery. Of 69 women completing a one-year follow up survey, 5 (7%) had chosen to have prophylactic surgery after receiving counseling. Baseline factors associated with this decision were age greater than 45, lack of confidence in both the effectiveness of screening tests and in the curability of early stage ovarian cancer, and frequent worry about ovarian cancer. Understanding the motivations for prophylactic surgery among women at risk for familial ovarian cancer will help us to design counseling interventions which address the key medical and psychological issues.

**Molecular Epidemiology of p53 Overexpression in Soft Tissue Sarcomas.** *S Hariap, ZF Zhang, D Pollack, M Drobniak, E Latres, M Karpeh, E Casper, J Woodruff, C Cordon-Cardo. Memorial Sloan-Kettering Cancer Center, New York, NY 10021.*

In a pilot study of risk factors and abnormal p53 we stained 108 incident adult soft tissue sarcomas with a monoclonal antibody, PAB-1801. Using a modified case-control design and multiple logistic regression, we adjusted odds ratios (ORs) and 95% confidence limits (CL), where appropriate, for age, sex and race. With a cut-off point at  $\geq 20\%$  positively stained cells, p53 protein was over-expressed in 27% of the total and in 12% of 42 liposarcomas, 40% of 25 leiomyosarcomas, 20% of 10 malignant fibrous histiocytomas and 39% of other types combined ( $p=0.02$ ). The p53 over-expression did not vary significantly with smoking or alcohol use. In liposarcomas, abnormal p53 was increased in patients having one or more relatives with a family history of breast cancer (crude OR=13.5, 95% CL=1.2-153) or any cancer (8.7, 0.87-86). Patient weight strongly predicted abnormal p53; adjusted ORs for abnormal p53 were 1 (reference group), 0.48(0.13-1.7), 0.13(0.02-0.67) and 0.05(0.01-0.51) in the four weight quartiles. This trend was not confounded by height, was seen both in liposarcomas and other tumors and was the reverse of the trend of abnormal p53 by weight observed by our group in colon cancer. These findings confirm the utility of a research strategy to explore the relationship of molecular abnormalities in tumors to conventional epidemiologic risk factors.

**P53 NUCLEAR OVEREXPRESSION IN COLORECTAL CANCER: A MOLECULAR EPIDEMIOLOGIC STUDY.**

Zhang, Z.F., Zeng, Z.S., Sarkis, A.S., Klimstra, D.S., Charytonowicz, E., Guillem, J.G., Cordon-Cardo, C., Cohen, A.M., Begg, C. Memorial Sloan-Kettering Cancer Center, New York, NY 10021.

To investigate the association between risk factors and p53 overexpression in colorectal cancer, we have analyzed a group of 107 consecutive patients with primary colorectal cancer seen at MSKCC from 1986 to 1990. We assessed p53 overexpression using a monoclonal antibody PAB 1801, and identified 42 (39.2%) patients displaying p53-positive phenotype defined as  $\geq 25\%$  of positive cells. The odds ratios (OR) of p53 overexpression were 1.3 (95%CI: 0.6-2.9) for patients with family history of cancer, and 1.3 (95%CI: 0.6-3.0) for those with first degree relatives with cancer. Patients with 2 or more first degree relatives with cancer had an odds ratio of 2.9 (95%CI: 1.0-8.3) for p53 overexpression, in comparison to those without family history of cancer. The odds ratios for p53 overexpression were 1.6 (95%CI: 0.5-4.8) and 5.4 (0.5-53.3) for positive family history of colon and stomach cancer in first degree relatives respectively. An association between body weight and p53 over-expression was observed. The ORs were 1.9 (0.5-6.8) for the second quartile, 1.9 (0.5-6.9) for the third quartile, and 3.4 (1.0-11.9) for the highest quartile in comparison with the lowest quartile (trend-test:  $P=0.056$ ). No association between smoking, drinking and p53 over-expression was observed. Results suggest that p53 may be an important molecular marker in assessing gene-environment interactions in colorectal cancer.

Anti-oxidized DNA base autoantibodies as a biomarker of cancer susceptibility  
 Emanuela Taioli, Jerzky Karkoszka, Todd Glassman, Paolo Toniolo, Krystyna Frenkel.  
 New York University Medical Center, New York, NY 10016

Oxidants produced during inflammation may cause genetic damage, reflected in formation of significant levels of oxidized bases in cellular DNA. This process may be enhanced in subjects predisposed to develop cancer. To test this hypothesis, we studied 3 groups of subjects: 1) normal controls (N; n=41); 2) subjects with a positive family history of cancer (F; n=23); and 3) healthy subjects at the time of blood donation, but who developed breast (BC; n=9), colon (CC; n=36) or rectal (RC; n=7) cancer 1 or more years later. All sera were tested for antibodies that recognize 5-hydroxymethyl-2'-deoxyuridine (HMdU) when it is coupled to bovine serum albumin (HMdU-BSA), as determined by the enzyme-linked immunosorbent assay (ELISA). Anti-HMdU titers were significantly higher among F ( $29.4 \pm 5.3$ ) than among N ( $16.5 \pm 2.3$ ;  $p=0.03$ ). Among subjects who developed cancer later, the anti-HMdU titers were:  $31.3 \pm 7.5$  in BC subjects ( $p<0.05$ ),  $23.0 \pm 2.1$  in CC subjects, and  $36.9 \pm 7.6$  in RC subjects ( $p<0.05$ ).

These results suggest that high titers of anti-oxidized DNA Ab may identify subgroups of subjects at high risk of developing cancer of various organs. (Support: CA37858; CA34588; NIEHS P42 ES04895; ES00260)

#### ARE SERUM TRIGLYCERIDES AND PLASMA GLUCOSE ASSOCIATED WITH COLORECTAL CANCER?

Gail McKeown-Eyssen, University of Toronto.

**Purpose:** This paper presents a new hypotheses for the molecular epidemiology of colorectal cancer; it suggests that the risk of colorectal neoplasia may be related to serum triglycerides (ST) and/or plasma glucose (PG).

**Methods:** A literature review (a) examined the relationship of ST and PG with lifestyle risk factors for colorectal cancer and with disease risk, and (b) identified possible biologic mechanisms.

**Results:** Western diets, obesity and alcohol are associated with increased risk of colorectal cancer; exercise, and diets high in vegetables, fruits or fish oil, are associated with reduced risk. The same risk factors exhibit parallel associations with ST and PG. These observations suggest the hypothesis that ST and PG may themselves be associated with colorectal cancer. Direct evidence of positive association between colorectal neoplasia and ST and PG was found in two studies of adenomatous polyps and three cohorts of diabetics. Further, three trials suggested that diets expected to increase ST and PG increased cellular indicators of colorectal cancer risk. Three biologic mechanisms might explain such associations. First, ST and PG may be indicators of increased insulin. This hormone is a growth factor and is also associated with other insulinlike growth factors which have been associated with colorectal cancer. Second, ST and PG may be sources of energy for neoplastic cells. Third, ST and PG are associated with fecal bile acids, acids positively associated with colorectal cancer risk.

**Conclusion:** Future research should examine associations between colorectal neoplasia and both ST and PG and explore possible biological mechanisms.

# **Development of a quantitative immunohistochemical method for the detection of 4-ABP-DNA adducts in single cells**

Al-Atrash, J. & Santella, R.M. Columbia School of Public Health, New York, New York, 10032

Urinary bladder cancer remains a significant health problem in the U.S. 4-Aminobiphenyl (4-ABP), an aromatic amine, represents a common link between cigarette smoking and urinary bladder cancer. To develop methods for monitoring exposure to 4-ABP by measurement of DNA adducts, a monoclonal antibody, 4C11-2, was generated from mice immunized with 4-ABP-DNA. In a competitive enzyme-linked immunosorbent assay (ELISA) 50% inhibition was at 20 fmol N-(deoxyguanosine-8-yl)-ABP. An immunohistochemical method for adduct detection was tested in a 4-ABP treated cell line expressing P450-1A2. To increase sensitivity and specificity, fixed cells were first treated with RNase to degrade any RNA present followed by proteinase K to remove histone and non-histone proteins from DNA and increase antibody accessibility. A fluorescein isothiocyanate (FITC)-labelled secondary antiserum was used to localize adducts in conjunction with 4',6-diamidino-2-phenylindole dihydrochloride (DAPI) staining for nuclei visualization. Fluorescence intensity of each nucleus was determined by densitometric scanning of photographic slides. A dose related increase in specific nuclear staining was observed in treated cells but not in controls. Female BALB/c mice were treated by ip injection with 3, 2, 1.75 and 0.5 mg/kg 4-ABP for 24 hrs. Both liver and bladder tissues demonstrated a dose-response relationship. Moreover, a homogenous distribution of FITC staining was generally observed except at the highest administered dosage (3 mg/kg) where a 20-30% variation was observed. The sensitivity of this approach may make it applicable to human monitoring especially since the levels detectable are comparable to those seen by others in human lung. Moreover, this technique can yield new information on cell specific localization of adducts.

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## **THE E.P.I.C. BIOLOGICAL BANK**

Elio Riboli, Rudolf Kaaks

International Agency for Research on Cancer (IARC), Lyon, France (on behalf of the EPIC Group)

The European Prospective Investigation into Cancer and Nutrition (EPIC) - coordinated by the Nutrition Programme of IARC-WHO - is a multi-centre prospective study aimed at investigating the links between diet, nutrition and cancer. The study is at the data collection phase in 17 centres located in 7 European countries, and will eventually include around 400,000 healthy adults who will be followed up for cancer incidence of the next 20 years.

A major feature of the project is the creation of very large banks of biological samples, to be used for future analyses on samples from cases and matched controls nested within the cohort. For storage of the samples, the following new and original procedures have been developed:

- a) For each study subject, 28 aliquots (0.5 ml) will be prepared in special plastic straws (8 serum, 12 plasma, 4 white blood cells, 4 erythrocytes).
- b) Straws are rapidly filled and sealed with an automatic machine, electronically operated.
- c) Straws are identified by a plastic jacket, the colour of which indicates the type of biological specimen and which has a preprinted ID number.
- d) The 28 aliquots from each individual are divided into 2 sets of 14. One set is stored at the local study centre, and the other sent to IARC. All aliquots are stored by immersion in liquid nitrogen at -196°C in 650-litre containers, 22 of which are operational at the moment.

Studies to test the possible effect of storage in plastic straws, at different temperatures and under different handling conditions, have revealed no changes which might be attributable to the type of storage material. The study was started in 1993, and already includes 110,000 subjects. This bank represents a major effort to integrate the most promising developments in biochemistry and molecular biology with a sound and powerful epidemiological approach.

**1994**  
**ATTENDEE QUESTIONNAIRE/EVALUATION**

We are anxious to get your feedback regarding this program, so that we may continue to make the Annual ASPO meeting suit your professional needs. Please take a moment to fill out this questionnaire and return it to the registration table before you leave, or drop it in the mail to the ASPO National Office, 1300 University Avenue, Suite 7-C, Madison, WI 53706.

What parts of the meeting were of greatest interest to you?

What were the weak point?

What subjects would you like to have covered in future meetings?

What should be covered in greater detail?

Do you have any suggestions for format changes?

Were you able to see and hear adequately?

Should ASPO continue providing concurrent sessions?

General suggestions (format, speakers, food, etc. . . .)

Thank you for your time!  
Ellen Gritz, President

