ASPO

Twelfth Annual Meeting of the American Society of Preventive Oncology

March 14–15, 1988

Hyatt Regency Bethesda

Bethesda, Maryland

MASTER AGENDA

Monday, March 14

MORNING

Registration
7:30 am - 6:00 pm

Opening Welcome
8:50 am - 9:00 am

Poster Session Open
9:00 am - 6:00 pm

Symposium -
Biochemical Markers of Colorectal Cancer
9:00 am - 12:30 pm

AFTERNOON

Submitted Papers
1:30 pm - 2:30 pm

Symposium -
Recently Complete Etiologic Studies of Colorectal Neoplasms
2:30 pm - 5:00 pm

EVENING

Symposium
Issues and Recomme
in the Early Detecti
of Colorectal Cance
5:00 pm - 6:00 pm

Business Meeting
6:00 pm - 7:00 pm

Tuesday, March 15

MORNING

Registration
7:30 am - 5:00 pm

Welcoming Remarks and Presentation of Distinguished Achievement Award
8:15 - 8:40 am

Poster Session Open
8:15 am - 5:00 pm

Symposium
Strengths and Limitations of Methodologic Approaches to the Study of Diet and Cancer
8:40 - 12:00 pm

AFTERNOON

Submitted Papers
1:20 pm - 2:40 pm

Symposium -
Priorities/Barriers in Cancer Prevention and Control
2:40 pm - 5:00 pm

EVENING

Reception
6:30 pm - 7:30 pm

Banquet
"Cancer Prevention:
A Risky Business"
Dr. Vincent DeVita,
7:30 - 10:30 pm

Adjourn

PROGRAM AND SELECTED PAPERS

Welcome to Bethesda

Program Chairpersons: Joseph Cullen, Ph.D.
Susan Preston-Martin, Ph.D.
George Roush, M.D.

sponsored by:

American Society of Preventive Oncology

National Cancer Institute

ASPO

In its twelfth year ASPO is striving to:

- promote the exchange and dissemination of information and ideas relating to cancer prevention and control;
- identify and stimulate research areas in cancer prevention and control;
- foster the implementation of programs in cancer prevention and control.

A growing and active membership facilitates achievement of these goals. The Executive Committee and council members listed below are very interested in hearing from prospective or current members.

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The National Office for ASPO is at the University of Wisconsin, where the executive secretary, Carrie Fassil, may be contacted for any information or assistance: 1300 University Ave. - 7C, Madison, WI 53706, (608) 263-6919.

Messages

Please see Carrie Fassil at the registration desk if you expect or wish to leave a message.

Banquet

Please let Carrie Fassil know immediately of your plans to attend the banquet on Monday evening, if you have not already done so.

Special acknowledgement

The Executive Committee of ASPO wishes to offer special thanks to Drs. Joseph Cullen, Susan Preston-Martin, and George Roush, the program chairpersons for their tireless efforts in arranging this meeting.

PROGRAM AGENDA

Monday, March 14

7:30 am - 6:00 pm
BALLROOM FOYER

REGISTRATION

8:50 am - 9:00 am

OPENING WELCOME: David Schottenfeld, MD, President, ASPO

9:00 am - 6:00 pm
HAVERFORD /BACCARAT ROOM

POSTER SESSION OPEN

9:00 am - 12:30 pm

HAVERFORD /BACCARAT ROOM

SYMPOSIUM
Biochemical Markers of Colorectal Cancer

Moderator: Gail E. McKeown-Eyssen, PhD

Studies of Fecal Mutagenicity in Humans

Mark H. Schiffman, MD, MPH

Calcium and Measures of Cell Proliferation

Michael J. Wargovich, PhD

Ornithine Decarboxylase

Gordon D. Luk, MD, PhD

10:15 am - 10:30 am

REFRESHMENT BREAK

Adenosine Diphosphate Ribosyl Transferase as an Indicator of Oxidative Stress

Ronald W. Pero, PhD

Oncogenes and Markers of Signal Transduction

I. Bernard Weinstein, MD

Discussant

Alfred I. Neugut, MD, PhD

Panel Discussion

12:30 pm - 1:30 pm

LUNCH

1:30 pm - 2:30 pm

SUBMITTED PAPERS

Moderator: George C. Roush, MD

* 1 **Mammography Utilization Patterns In A Cohort of High Risk Women**

Lisa Begg, R.N., DrPH

* Number refers to the abstract printed in the selected paper section of this program.

* 2 **A Case-Control Study of Soft-Tissue Sarcoma: Farming and Pesticide Use**

Shelia Hoar Zahm, ScD

* 3 **Studies on Barrett's Esophagus: A Unique Metaplastic Premalignant Lesion for Adenocarcinoma**

H. S. Garewal, MD, PhD

2:30 pm - 5:00 pm

HAVERFORD /BACCARAT ROOM

SYMPOSIUM
Recently Complete Etiologic Studies of Colorectal Neoplasms

Moderator: John D. Potter, MBBS, PhD

Collaborative Case-Control Study of Colorectal Cancer in Chinese and Chinese Americans

Alice S. Whittemore, PhD

Case-Control Study of Colon Cancer in Los Angeles County

Ruth A. Peters, ScD

3:30 pm - 3:50 pm

REFRESHMENT BREAK

Inheritance of Colonic Adenomatous Polyps and Colorectal Cancer

Randall W. Burt, MD

Discussant

Walter Willett, MD

5:00 pm - 6:00 pm

SYMPOSIUM
Issues and Recommendations in the Early Detection of Colorectal Cancer

Discussants

Anthony B. Miller, MB, FRCP
Jack S. Mandel, PhD, MPH

6:00 pm - 7:00 pm

HAVERFORD /BACCARAT ROOM

BUSINESS MEETING

AGENDA (12th Annual Meeting)
David Schottenfeld, President presiding

Report of the President	Dr. Schottenfeld
Report of the Secretary/Treasurer	Dr. Love
Report of the Auditors (appended)	Dr. Love
Report of the Nominating Committee	Dr. Ernster
Secretary/Treasurer:	
Director(s):	

* Number refers to the abstract printed in the selected paper section of this program.

Tuesday, March 15

7:30 am - 5:00 pm BALLROOM FOYER	REGISTRATION
8:15 am - 5:00 pm HAVERFORD /BACCARAT ROOM	POSTER SESSION OPEN
8:15 am	WELCOMING REMARKS AND PRESENTATION OF DISTINGUISHED ACHIEVEMENT AWARD David Schottenfeld, MD President, ASPO
8:25 am - 8:40 am	AWARDEE ADDRESS
8:40 am - 12:00 pm HAVERFORD /BACCARAT ROOM	SYMPOSIUM **Strengths and Limitations of Methodologic Approaches to the Study of Diet and Cancer** Moderator: Peter Greenwald, MD, DrPH **Validity of International Migration and Time Trend Studies** Ross Prentice, PhD **Validity of Case-Control and Cohort Studies of Dietary Fat and Breast Cancer** Barbara S. Hulka, MD, MPH
9:40 am - 10:00 am	REFRESHMENT BREAK
	Clinical Metabolic Studies Philip Taylor, MD **Clinical Trials** David P. Byar, MD **Summary and Future Perspectives** Peter Greenwald, MD, DrPH **Panel Discussion**
12:00 pm - 1:20 pm	LUNCH
1:20 pm - 2:40 pm	SUBMITTED PAPERS Moderator: Susan Preston-Martin, PhD

	* 4	**Recruitment Strategies For Cancer Prevention Trials** Thomas E. Moon, PhD
	* 5	**Cancer Control Research in Defined Populations: Design and Methodologic Considerations** Bruce Trock, PhD
	* 6	**Analysis of Barriers and Incentives to Mammographic Screening in the American Cancer Society (ACS) 1987 Texas Breast Screening Project (TBSP)** Victor G. Vogel, MD, MHS
	* 7	**Using a Population-based Cancer Registry For Recruitment in a Cancer Control Study: The Wisconsin Tamoxifen Study** Polly A. Newcomb, PhD
2:40 pm - 5:00 pm **HAVERFORD /BACCARAT ROOM**		**SYMPOSIUM** **Priorities/Barriers in Cancer Prevention and Control** Moderator: Edward Sondik, PhD **Priorities** David M. Eddy, MD, PhD **Economic and Organizational Barriers** Edward H. Wagner, MD, MPH
3:30 pm - 3:45 pm		**REFRESHMENT BREAK** **Communications Barriers** Erwin Bettinghaus, PhD **Compliance Barriers** Kelly D. Brownell, PhD **Panel Discussion**
6:30 pm - 7:30 pm **BALLROOM FOYER**		**RECEPTION**
7:30 pm - 10:30 pm **WATERFORD /LALIQUE ROOM**		**BANQUET** **Cancer Prevention: A Risky Business** Vincent T. DeVita, Jr., M.D.
10:30 pm		**ADJOURNMENT**

* Number refers to the abstract printed in the selected paper section of this program.

INVITED SPEAKERS

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SELECTED PAPERS

These abstracts will be published in the journal
Preventive Medicine, Vol. 17, No. 2, 1988.

Mammography Utilization Patterns In A Cohort Of High Risk Women

Lisa Begg, R.N., Dr.P.H.

Jackie Dunbar, R.N., Ph.D.

Steve Belle,Ph.D.

Joyce Yasko, R.N., Ph.D.

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Mammography Utilization Patterns in A Cohort of High Risk Women

Breast cancer is known to aggregate in families. A family registry with the Pittsburgh area was established as a mechanism to ascertain breast cance detection practices in a group of healthy women at increased risk of breast cancer.(1) Data were obtained through a longitudinal registry of first-degr female relatives of 1,548 breast cancer patients treated at three area hospitals. All patients were confirmed to have histologically-proven breast cancer. Written informed consent was obtained from each patient and their relatives. Questionnaires were administered via phone to determine the baseline frequency of mammography, professional and self-breast examinations A follow-up phone interview, at one year, was obtained to determine changes baseline practices.

Seven-hundred-eighty-nine relatives, aged 35 and above, were interviewed baseline. Only relatives of this age were chosen because of the policy recommendation on screening mammograms put forth by such national groups as American Cancer Society, National Cancer Institute, and American Medical Association.(2) There were 487 sisters, 225 daughters and 77 mothers of brea cancer patients in this cohort. In terms of mammography utilization, 57% of relatives had had at least one mammogram with no difference (58% of sisters, 57% of mothers and 56% of daughters) by relative status.

Because the recommendations for repeat mammography vary with age, we evaluated the 470 relatives who were age 50 and older at baseline interview. The policy recommendations for this age group call for mammograms to be repeated on an annual basis.(2) Follow-up data was available for 91.50% of these relatives (n=430) and showed no differences in response rates by relati status or hospital. Of these 430 relatives, 294 (68%) women overall reported

having had at least one mammogram. The rates by relative status were not statistically different, ranging from 67% of the sisters to 72% of the mothers. Of those women who reported never having had a mammogram at baseline, 26% reported doing so in the one-year follow-up period. If the entire sample is evaluated for relatives aged 35 and older who have never had a mammogram, only 27% report obtaining a mammogram within the previous year. Thus, it appears that age, relative status and locations within an urban area do not influence these relatives to obtain screening mammography. While simple education and advice can improve mammography utilization rates by enrolling 27% of those women never screened, a substantial number of women at high risk of breast cancer do not avail themselves to this procedure.(3,4) Thus, more intensive efforts need to be directed toward those high risk women to promote increased utilization of this efficacious procedure.

REFERENCES

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2. American Cancer Society Ca-C Cancer Journal for Clinicians 1982;32 (4): 3-7.

3. Reeder S, et al. Breast Cancer Detection Behavior Among Urban Women. Public Health Rep 1980;95:276-281.

4. American Cancer Society, Women's attitudes regarding breast cancer, Gallup Poll, no. 0501, 1980.

2

A CASE-CONTROL STUDY OF SOFT-TISSUE SARCOMA: FARMING AND PESTICIDE USE

Shelia Hoar Zahm, Sc.D. (1), Aaron Blair, Ph.D. (1), Frederick F. Holmes, M.D. (2), Cathy D. Boysen, B.A. (2), Robert J. Robel, Ph.D. (3)

1- Epidemiology and Biostatistics Program, National Cancer Institute, Landow Building-4C16, Bethesda, MD 20892.

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Reports from Sweden, Denmark, Italy, and the United States have suggested that persons exposed to herbicides have up to a sixfold excess risk of soft-tissue sarcoma (STS) (1-8). A population-based case-control study was conducted in Kansas to examine the relationship between exposure to pesticides and the development of soft-tissue sarcoma (STS). Data from telephone interviews with 133 STS cases and 948 controls, or their next-of-kin, did not show any association between STS and agricultural use of herbicides (Odds ratio [OR] = 0.9; 95% CI= 0.5,1.6). STS was associated with insecticide use on animals (OR=1.6; 95% CI=0.9,2.5) but not on crops (OR=0.8; 95% CI=0.4,1.6). STS risk was higher among farmers who themselves mixed or applied insecticides to animals (OR=1.7; 95% CI=1.0,2.9) than among farmers who had someone else do these tasks (OR=1.1; 95% CI=0.4,2.6). Farmers who failed to use any protective equipment to reduce insecticide exposure were at significantly elevated risk of STS (OR=1.9; 95% CI=1.1,3.3). Risk rose with early calendar year of first use, even after adjustment for duration of insecticide use. The duration- and age-adjusted ORs for STS among farmers who first used insecticides after 1965, during 1956-1965, 1946-1955, and prior to 1946 were 1.0 (referent category), 0.3 (95% CI=0.01,4.7), 2.6 (95% CI=0.3,26.7), and 4.9 (95% CI=0.6,64.1), respectively. The excess risk appeared to be primarily among fibrous and myomatous sarcomas with no or little association seen for lipomatous or other STS neoplasms. Myomatous sarcomas increased significantly with time since first use of insecticides on animals. If the reported association between STS and insecticides is causal,

these data suggest that exposure to the agent(s) responsible may have been reduced in the mid 1950s, for example, by changing insecticides or by increasing mechanization of dairy farming, or have an average latent period for STS of at least 20 years.

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3

STUDIES ON BARRETT'S ESOPHAGUS: A UNIQUE METAPLASTIC PREMALIGNANT LESION FOR ADENOCARCINOMA

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Barrett's esophagus (BE) is a condition in which metaplastic columnar epithelium replaces the normal squamous lining of the esophagus. It is a premalignant lesion associated with an increased risk of esophageal adenocarcinoma (2). We have used BE as a model lesion for laboratory and clinical studies of adenocarcinoma premalignancy. Epithelial cell cultures were established from endoscopic biopsies of Barrett's mucosa. Six cultures have been karyotyped; 2 of the 6 showed clonal cytogenetic abnormalities. The effect of retinoids, carotenoids and ornithine decarboxylase (ODC) inhibitors on the growth of the cultured cells was studied. The drugs used were 13-cis retinoic acid (RA), 4-hydroxyphenylretinamide (4-HPR), beta carotene (BC), canthaxanthene (C) and α-difluoromethylornithine (DFMO). Methods used were quantitation of

cell number, the ATP drug sensitivity assay developed in our labora and colony formation. Continuous drug exposure was used with concentrations of 10^{-9} to 10^{-6} M for RA, 4-HPR, BC and C; 0.05 to 5 for DFMO. The retinoids and carotenoids did not have significant inhibitory effects on growth except at the highest concentrations t (10^{-6} and 10^{-7} M) which resulted in approximately 50% inhibition. is consistent with the results of our clinical study of RA in BE. trial was initiated because of the known activity of RA in other premalignant conditions (1). Thus far, 13 patients have been treat with RA with no responses. In contrast to the in vitro results wit retinoids and carotenoids, DFMO had an inhibitory effect on growth cultured cells even at the lowest concentration tested (60% growth 0.05 mM) with >50% inhibition at 0.5 and 5 mM. Consequently, inhib of ODC may have a role in the treatment of this disease. A clinica trial with DFMO is planned. This cell culture system should prove in studying the characteristics of premalignant cells and screening agents for activity against premalignant lesions.

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4

Recruitment Strategies For Cancer Prevention Trials

Thomas E. Moon, Ph.D., Madelyn L. Ferro, B.A.,
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Recruitment Strategies For Cancer Prevention Trials

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Recruitment for cancer prevention studies may be impacted by the strategy used to identify subjects. Between October 1985 through September 1987, strategies were evaluated to recruit subjects for 2 related trials evaluating vitamin A compounds in prevention of skin cancer. Strategies included physician refer and use of print, radio and TV media, and referral by spouse/friend. People willing to participate were screened usi common protocol and asked how they heard of the trials. Of 875 inquiries during the 24 months, 44% were screened with 23% enrolled. Extent of community physician involvement and amount regular medical care used by subjects effected recruitment strategies. Type of strategy did effect recruitment. Use of m (paid advertisements plus articles/interviews) was effective in recruiting 43% and 87% of subjects for the 2 trials, costing $3 and $47 per subject enrolled. Physician referral accounted for remaining 13% and 57% of recruitment, costing $78 per subject. Referral by spouse/friend was unsuccessful as a strategy. Fact related to media success include format, institutional affilia and use of non-technical language. These strategies can be ap to other prevention trials providing cost effective recruitmen

5

Cancer Control Research in Defined Populations: Design and Methodologic Considerations

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This paper critically assesses problems in conducting Phase IV or defined population studies of cancer control interventions. Defined population studies (DPS) are intended to quantify the impact of interventions of demonstrated efficacy in stable, well-characterized populations. The objectives of DPS are to evaluate the performance of interventions and generalize the results to a target population, and identificaiton of barriers to implementation (2,3). Current problems in the conduct of DPS are analyzed within the context of constraints on study design imposed by these objectives. In particular, the use of a randomized controlled trial design

for Phase IV studies is shown to involve problems in logistics, demonstration of a significant result, ability to generalize results, and ethical problems. Quasi-experimental studies using intermediate endpoints are proposed as a feasible alternative to randomized trials in Phase IV. Previously demonstrated intervention efficacy in a Phase III study helps to reduce the dangers of unmeasured sources of bias (1), and may also improve ability to detect a significant result.

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6

Analysis of Barriers and Incentives to Mammographic Screening in The American Cancer Society (ACS) 1987 Texas Breast Screening Project (TBSP).

Victor G. Vogel, MD, MHS, George N. Peters, MD, FACP, John J. Fueger, MA, Rodger J. Winn, M.D., and the Scientific Review Committee.

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Despite the ability of screening mammography to reduce breast cancer mortality, the procedure is not widely used by physicians due to the suspected radiation risk and its perceived low yield or ineffectiveness (1,3). Low levels of compliance by women with screening recommendations are due to cost (1,2), lack of public awareness, and other published barriers to wide acceptance of mammography (4,5). The ACS TBSP promoted low-cost ($50.00) mammographic screening at 300 participating screening centers following an intensive media campaign; 61,162 women presented for mammography. Each was given a 31-item questionnaire which

examined beliefs about breast cancer and screening-related risks and barriers. Data from 758 questionnaires are presented here. Although 60% had seen a physician in the preceding year, only 43% had ever had mammography. Of those women who had prior mammograms, 79% had only two or fewer exams. Low cost was identified as an important reason for having mammography in this project by 85% of the screenees. While 29% of screenees stated that their health insurer did not pay for screening mammograms, 58% did not know whether their insurance coverage included screening mammography. Only 49% said physicians' referrals influenced their decision to participate; 92% cited ACS publicity. These data indicate that public and physician education, coupled with a decrease in screening mammography cost, would substantially increase women's compliance with mammographic screening recommendations.

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7

USING A POPULATION-BASED CANCER REGISTRY FOR RECRUITMENT IN A CANCER CONTROL STUDY: THE WISCONSIN TAMOXIFEN STUDY

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Cancer control investigations in the United States have not yet used population-based registries as a resource for recruitment. We are conducting a placebo-controlled, double-blind, randomized toxicity trial of tamoxifen in postmenopausal women with node negative breast cancer. This study is potentially a pilot for a major breast cancer chemosuppressive trial using this antiestrogen. To achieve our accrual goal of 140 in this single institution study, we have used the Wisconsin Cancer Reporting System, a population-based cancer registry. Registry information from the last nine years was used to identify 3,335 women who met the study criteria with respect to age, stage, and previous therapy. The vital status of identified women was confirmed using the state death records. For physicians reporting cases, rosters were prepared and sent to the physician with a cover letter and study description. The physicians were asked to update the lists and, if appropriate, to sign letters to possibly eligible and interested women. Thirty-four percent of women receiving a letter and study information from their doctors contacted the study office about participation. One year from its initiation, 100 women are entered on study and we project complete accrual in five to six months. This successful use of a population-based cancer registry illustrates an efficient recruitment method which could be modified for other cancer control/chemoprevention trials.

SELECTED POSTERS

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WHAT IS SAFE SEX? James J. Goedert, M.D.

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Existing "safe (or safer) sex" guidelines either prohibit intercourse for all or advise measures that are not entirely safe, such as use of condoms. However, rational, scientific, and truly safe standards can be defined by the human immunodeficiency virus (HIV) status of the subject and his/her partner (1). A monogamous couple proven to be HIV negative-negative can engage in unprotected sexual contact of any kind, provided that outside risks (such as parenteral drug abuse) or partners have been eliminated for at least six months. A couple proven to be positive-positive must not have sex with HIV-negative or HIV-unknown partners but may themselves have intercourse if they use effective birth control to prevent HIV infection of babies. Safe sex standards must be stringent, not to exceed mutual masturbation, for HIV-discordant (positive-negative) and HIV-unknown couples. Fortunately, HIV-discordant couples are relatively uncommon, and most HIV-unknown couples can be tested and recategorized to the more lenient positive-positive or negative-negative standards. The HIV antibody test is an extremely sensitive and specific

tool that has been used with few adverse consequences in more than 10 million Americans (2). Now is the time to minimize the fear and eliminate the risk of transmitting HIV to loved ones by urging universal voluntary testing and by developing HIV-defined safe sex standards.

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The Forsyth County Cervical Cancer Prevention Project

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Black women suffer mortality from cervical cancer at a rate over four times higher than for white women in Forsyth County, NC.[2] This disparity provides the basic motivation for development of a five-year, NCI funded public health education project. The ultimate goal of the project is to reduce the death rates from cervical cancer in all women, and particularly to reduce the disparity in death rates between black and white women, by increasing rates of early detection of cervical cancer and its precursors by increasing Pap smears in the target population (black females age 18 and older residing in Forsyth County, NC).

The intervention will consist of two components, mass media education and a program of direct education through small groups. Development of the intervention will be guided by the Communication-Behavior Change (CBC) model.[1] Focus groups, applied to development as well as review of message prototypes, will be used to insure that content and image are appropriate for the target population. Messages

will be produced for print and electronic media.

Evaluation will include both qualitative and quantitative measures. Data will be collected from black and white women residing in Forsyth County, NC and a comparable control county. Qualitative evaluation data will be collected by interviews. Quantitative evaluation to develop an estimate of efficacy of the program as a whole, will be carried overall by pre and post random-digit-dialed telephone surveys.

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The Forsyth County Cervical Cancer Prevention Project

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PERSONAL, SOCIAL AND HEALTH CARE SYSTEM FACTORS AND STAGE OF DISEASE AT THE DIAGNOSIS OF COLORECTAL CANCER

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In an effort to identify factors contributing to a late diagnosis of colorectal cancer, patients in Southern Alberta were interviewed to determine if early stage and late stage cases differed on any of six dimensions of an illness behaviour model. Forty seven males and thirty three females diagnosed in 1985/1986 were interviewed in their homes. Information was collected on six areas from Cummings Illness Behaviour Model[1]: demographics, social network, attitudes toward health care, health care system variables such as doctor visits, knowledge about cancer and perceived health threat. Logistic regression was used to assess variables within each of the six areas and was then used to assess the full model including variables from all six areas. In a single area logistic regression, factors which significantly

contributed to predicting a late stage diagnosis (using remove and enter limits of .15 and .10 respectively) were attribution of symptoms to causes other than cancer, higher knowledge level about Pap tests, lower knowledge level about hemoccult tests, more visits to a general practitioner prior to diagnosis, more friends, neighbours and ministers in their support network and a lower perceived level of tangible aid. In the full model logistic regression, the only two factors remaining in the model after adjusting for effects of the others were the tendency of late stage patients to attribute the cause of symptoms to something other than cancer (perceived health threat) and their increased number of visits to the general practitioner before being diagnosed (health care system). A multiple causation model was an instructive approach to studying this problem as the results of the full model multiple logistic regression was somewhat different than the single area analysis.

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THE STEVE FONYO CANCER PREVENTION PROGRAM: A DEMONSTRATION PROJECT IN FOUR ALBERTA CITIES

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A Cancer Prevention Demonstration Program began in Alberta in early 1987. The program is taking place in four Alberta cities whose population totals 140,000. This program is being done collaboratively by the Cancer Authority in the province and the Boards of Health in the four cities. The objectives of the program are:

1. To demonstrate the feasibility of the Cancer Board's involvement in community prevention programs.

2. To determine the most effective approach to risk reduction and early detection in the community setting.

3. To evaluate compliance with such programs and their efficiency in relation to cost.

4. To compare the efficacy of risk related individual intervention (personal counselling and individualized mailed information) in reducing the prevalence of modifiable risk factors and increasing the prevalence of behaviour favouring early detection.

The two interventions being used are based on an individual intervention approach and a community organization approach. A factoral design is being used so that the independent and interactional effects of the two approaches can be assessed. In the two cities with the individual intervention program, program staff will go door-to-door, offering risk assessment questionnaires to all individuals in the target age range (35-64). Program offerings from that point will depend on the individuals risk appraisal. In the two cities with the community organization, community organization strategies are being be used, as well as social marketing approaches to plan and deliver a public education program aimed at prevention and early detection.

Breast Abnormality Detection: breast self-examiners versus nurse examiners

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Breast abnormality detection: breast self-examiners versus nurse-examiners

Cornelia J. Baines and Ted Krasowski

Proxy estimates of sensitivity, specificity and predictive value of breast self-examination (BSE) were developed and compared to levels of BSE competence in over 40,000 women.

Women attending their third screening visit in the National Breast Screening Study (2) were stratified according to their BSE competence score which was the unweighted sum of nine BSE components (1). Scores of 7-9 were good, 4-6 adequate and 0-3 poor. The women's reports of finding a breast lump were compared, side-specifically, to the findings of expert nurse-examiners on physical examination.

For good, adequate and poor BSE performers, Kappa ($p < .001$) expressing agreement between the examiners was 0.113, 0.107 and 0.076 (right) and 0.133, 0.105 and 0.079 (left) respectively. Proxy sensitivity was highest (right and left respectively) in good (0.088 and 0.110) and lowest (0.056 and 0.061) in poor performers. Mean specificity (0.99) and positive predictive value (0.45) were highest in poor performers.

Clearly good scorers show a higher (though still very poor) level of agreement with the clinical examiner and higher "sensitivity" than poor scorers.

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SMOKESCREEN: A STUDY DESIGN

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The National Lung Program experience demonstrates the potential of detecting early stage lung cancers through screening heavy cigarette smokers with chest x-rays(1). The aim of our project is to evaluate biochemical tests in the prediction and early detection of lung cancer. These tests measure an isozyme of glutathione transferase using trans-stilbene oxide (GT-tSBO) as substrate, adenosine diphoshateribosyl transferase (ADPRT) and other biochemical markers (2,3). GT-tSBO has been inversely associated with lung cancer risk among persons who smoke(3). The epidemiologic risk factors family history, diet, occupational exposure and smoking history are incorporated into the design because of their importance in identification of lung cancer risk and as potential correlates of the biochemical markers. Three thousand heavy smokers over the age of 55 will be screened

annually for a period of three to five years with a PA chest x-ray and biochemical markers. The study will have at least 90% power to detect the estimated contribution of the biochemical markers in the identification of lung cancer for this high risk cohort. The purpose of this abstract is to inform the ASPO members of the study design and goals.

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RELATIONSHIP OF MONONUCLEAR ORNITHINE DECARBOXYLASE TO ADENOSINE DIPHOSPHATE RIBOSYL TRANSFERASE: IMPLICATIONS FOR IMMUNE SUPPRESSION BY TUMOR BURDEN

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This study was designed to test the relationship between ornithine decarboxylase (ODC) and adenosine diphosphate ribosyl transferase (ADPRT) in human mononuclear leukocytes (HML), and their application to the study of immune response (2). We have correlated ODC levels (4) in unstimulated cells with their proliferative status ([^{3}H]-Thymidine incorporation; $r = 0.57$, $p = 0.02$, $n = 17$). In further samples ($n = 20$), multivariate analysis related unstimulated ODC to a function of constitutive ADPRT , H_2O_2-activated ADPRT (1,5), and their separate interactions with age and gender ($R^2 = 0.68$, $p = 0.004$). In HML stimulated with phytohemagglutinin (PHA) or pokeweed mitogen (PWM), ODC correlated significantly with both constitutive and H_2O_2-activated ADPRT in non-smokers (e.g. PWM-induced ODC/Constitutive ADPRT: $r = 0.71$, $p = 0.0015$, $n = 18$); in smokers the correlation was significant between PHA-induced ODC and constitutive ADPRT ($r = 0.56$, $p = 0.024$, $n = 18$). There is, therefore, a significant relationship between ODC and ADPRT measurements: this strongly suggests that ADPRT relates to the proliferative capacity of HML. Since that capacity, and other lymphocyte reactions, are affected by tumor factors (4), we are studying ODC and ADPRT assays in relation to immune responsiveness, with special reference to immune suppression, and the possibility of providing a screening test for the presence of tumor.

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FORMATION OF GLUTATHIONE DISULFIDE FOLLOWING TREATMENT OF HUMAN MONONUCLEAR LEUKOCYTES WITH HYDROGEN PEROXIDE REVEALS INTRAINDIVIDUAL DIFFERENCES IN RESPONSES TO OXIDATIVE STRESS

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The rate of glutathione disulfide (GSSG) formation following exposure of cells to an oxidative agent is believed to reflect the extent of free radical-induced oxidative stress within those cells (3). Using human mononuclear leukocytes (HML) from peripheral blood samples, this study was undertaken to determine whether individuals vary in their responses to oxidative stress. This was achieved through determining the rate of GSSG formation

following exposure to H_2O_2 (2). Treatment of HML with H_2O_2 resulted in the oxidation of intracellular reduced glutathione (GSH) to GSSG in a dose dependent manner. Following a one minute exposure of cells to H_2O_2 at 37°C in the presence of glucose, HML from individual to individual varied greatly as to the percent of GSH that was oxidized. Such variation was seen regardless of the concentration of H_2O_2 used. In the presence of 500 μM H_2O_2, anywhere from 8%-73% of the GSH was oxidized to GSSG. 100 μM H_2O_2 resulted in a 21%-60% oxidation. Furthermore, while the oxidation of GSH was dose dependent, concentrations of H_2O_2 required for maximal oxidation also varied from individual to individual (100 μM-500 μM). It therefore appears that individuals are not all equal in their responses to oxidative stress. Since oxidative stress is believed to be involved in carcinogenesis (1), intraindividual differences in glutathione oxidation by H_2O_2 could be a useful biochemical marker to study susceptibility to cancer. This is currently being pursued by our laboratory.

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ASSOCIATION BETWEEN DIESEL EXHAUST EXPOSURE AND MULTIPLE MYELOMA: AN EXAMPLE OF CONFOUNDING

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In 1982 the American Cancer Society volunteers enrolled over 1,200,000 American women and men in a six years mortality prospective study. The subjects filled out a questionnaire on cancer risk factors; every two years their vital status is ascertained and death certificates for dead subjects are traced. An analysis on diesel exhaust exposure and two years mortality for different causes among 461,981 males aged 40-79 has been carried out, and the results will be published elsewhere (2). Among the causes of death that were associated ($p<0.05$) with diesel exhaust exposure in a crude analysis, multiple myeloma (MM, ICD-9 203) had not been previously reported (3). The crude relative risk (RR) was 2.1, and the 95% confidence interval (CI) was 1.2-3.9, (9 exposed and 37 unexposed deaths): they were not modified after controlling for age and smoking. The RR was

reduced by controlling for asbestos exposure to 1.3 (95% CI 0.6-2.7), this fact showed a confounding effect of asbestos: the result was not modified by controlling for coal and stone dusts, tar, pitch, or gasoline exhaust exposures. The RR for MM of asbestos exposure was 2.0 (95% CI 1.0-4.3, after controlling for age, smoking, and other occupational exposures), but the result is still preliminary. The evidence of an association between asbestos and MM derived from the literature is inconclusive (1), and further analysis from our study will be undertaken.

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THE EFFECTS OF SINIGRIN AND INDOLE-3-CARBINOL ON DNA METHYLATION, O^6-METHYLGUANINE-DNA-TRANSMETHYLASE, AND ^3H-THYMIDINE INCORPORATION IN TARGET TISSUES OF NNK-INDUCED TUMORIGENESIS.

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Glucosinolates and their hydrolysis products, widely distributed in cruciferous vegetables, have been found to possess significant antitumorigenic activity in some animal models (1). In order to evaluate the potential activity of the glucosinolate sinigrin and indole-3-carbinol (a product of glucobrassicin hydrolysis) on tumorigenesis induced by the tobacco-specific nitrosamine NNK, the effects of these compounds on NNK-induced DNA methylation, O^6-methylguanine-DNA-transmethylase activity, and ^3H-thymidine incorporation were examined in the liver, lung, and nasal mucosa of Fischer 344 rats. In all studies, rats were pretreated with control diets or diets containing sinigrin (0.003 mmole/g diet) or indole-3-carbinol (0.03 mmole/g diet) for

periods of 7-14 days. In the DNA methylation studies, pretreated rats were administered $^{3}H\text{-}CH_3$-NNK s.c. (0.6 mg/kg, 0.12 Ci/mmole) for four consecutive days. Pretreatment with sinigrin decreased 7-methylguanine levels in hepatic DNA by 30% compared to control. However, no effects on 7-methylguanine levels were observed in lung or nasal mucosa following sinigrin pretreatment. Pretreatment with indole-3-carbinol increased hepatic 7-methylguanine levels by 33% while resulting in decreased 7-methylguanine levels in DNA of both lung and nasal mucosa. The effects on hepatic 7-methylguanine levels are consistent with previous results in which sinigrin pretreatment decreased demethylation of NNK while indole-3-carbinol increased demethylation of NNK in hepatic microsomal preparations (2). O^6-Methylguanine-DNA-transmethylase activity was not affected in the target tissues of rats pretreated with sinigrin or indole-3-carbinol. The effects of these compounds on cell proliferation was assessed by their effects on ^{3}H-thymidine incorporation. Sinigrin was found to decrease hepatic ^{3}H-thymidine incorporation by more than 30%.

These results suggest that sinigrin may act as an inhibitor of NNK-induced hepatic tumors, while indole-3-carbinol may enhance NNK tumorigenicity in liver and inhibit NNK tumorigenicity in lung and nasal mucosa.

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