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A dietary study to investigate the effects of Soya milk ingestion on steroid hormone biosynthesis in women with a high risk of developing breast cancer compared to those at normal risk

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Epidemiological studies have been taken to suggest that women who have a diet rich in soy products have a lower incidence of breast cancer. Phytoestrogens, which are present in Soya milk, are thought to be the active constituent. They have been shown to increase SHBG levels, prolong the menstrual cycle and decrease the level of free oestrogens in some studies. This may result in a reduction of breast cancer risk. There is currently no conclusive evidence in the literature on the effect of dietary phytoestrogens on the metabolism and availability of endogenous oestrogens. This study examines the levels of the steroid metabolizing enzymes, steroid sulphatase and steroid sulphotransferases, before and after the daily ingestion of 500 ml of Soya milk for 7 days in women with a high risk or a normal risk of developing breast cancer. The effect of this dietary manipulation on circulating oestrone levels was also investigated. The results show that ingestion of phytoestrogens had no effect on steroid sulphatase activity but differentially inhibited the activity of the sulphotransferases. In the high risk population SULT1A1 activity was reduced by 37.9% ($p<0.01$) following the dietary intervention, whereas in the normal population there was a 3% decrease (non significant). E2 sulphation was decreased in the normal risk population by 56.8%, $p<0.01$, a 4% reduction was seen in the high risk group (ns). Such changes in enzyme activity may lead to increased levels of free oestrogens and thus increase the risk of developing breast cancer. However the analysis of oestrone levels revealed no such increase in free oestrone. Although the measured changes in enzyme activity did not lead to changes in circulating oestrone levels, they may influence intracellular steroid concentrations.

In conclusion our results demonstrate modification to sulphotransferase activity following the ingestion of Soya milk. The clinical significance of these changes and whether they translate into an effect on breast cancer risk is unclear. However our results suggest that we should observe caution in encouraging women at high risk of breast cancer from ingesting large doses of soy phytoestrogens.

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Pre screening breast history in women participating in the prevalent screening round in the Norwegian Breast Cancer Screening Program

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Previous breast biopsies and abnormalities in the breast are shown to increase the risk of breast cancer. The aim of this study was to investigate the pre screening breast history in women participating in the prevalent screening round in the Norwegian Breast Cancer Screening Program (NBCSP). The NBCSP invites all women aged 50–69 resident in Norway to a two-view mammography biennially. The women receive a questionnaire together with the invitation letter that states place and time for examination. The questionnaire is self-administered and handed over when attending the screening unit. It is filled in by approximately 97% of the women who participate. A bar code at the questionnaire makes it possible to identify all the women, including the breast cancer cases. The questionnaire maps among other factors, the women's breast history (self declared lump at screening time, previous biopsies, surgical treatment and previous mammograms) in addition to other known risk factors for clinical breast cancer. The results in this study are based on data from 182,100 women aged 50–69 years who answered the questionnaire before their prevalent screening examination in the NBCSP. The number of breast cancer cases was 1104 (0.61%). A total of 59.7% of the participating women reported to have a mammogram before their prevalent examination in the NBCSP. The OR for having a breast cancer was significant lower (OR=0.53, 95% CI; 0.47–0.60) among earlier examined. A self-declared lump had an OR for having a breast cancer of 3.36 (95% CI; 2.72–4.15), while a previous breast biopsy makes an OR of 1.4 (95% CI; 1.21–1.66) and a surgical treatment an OR of 1.33 (95% CI; 1.12–1.58). Previous mammography decreases the OR of being diagnosed with a breast cancer in the prevalent screening round in the NBCSP, while a previous biopsy and surgical treatment has the opposite effect. An increased OR of having a breast cancer among women who have a self-declared lump at screening point requires further diagnostic work up.

446 POSTER HIGHLIGHT

Prognosis of breast cancer in young women: a population-based study

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Background: The effect of age on breast cancer survival is still a matter of controversy. Breast cancer in young women is thought to be more aggressive and to have a worse prognosis but previous studies showed neither consistent nor definitive results. We assessed the impact of age at diagnosis on the pathologic features and the prognosis of breast cancer.

Material and Methods: We considered all patients diagnosed with breast cancer between 1990–2001 at the Geneva Cancer Registry. Clinical presentation, tumour characteristics, extent of disease, treatment and outcome were compared between three groups of patients, $\leqslant$35, 36–49 and 50–69 years old. Effect of age on prognosis was evaluated by Cox model after adjusting for other prognostic factors.

Results: The study included 82 women $\leqslant$35, 790 women 36–49 and 2125 women 50–69 years old at diagnosis. Patients younger than 50 years were more likely to be diagnosed with stage II or III cancers (52.4% in the group $\leqslant$35 years, 52.2% in the group 36–49 years and 44% in the group 50–69 years, p=0.001), and had more nodal involvement (39%, 41% and 35%, respectively, p=0.006). Young patients' cancers were more often poorly differentiated (37%, 29% and 22%, $p<0.001$), and oestrogen-receptor negative (23%, 15% and 10%, $p<0.001$). We found no differences by age in tumour size and morphology. There was no difference among the three groups in the provision of mastectomy and breast conserving surgery. Conversely, younger women were more likely to receive chemotherapy (68%, 61% and 38%, $p<0.001$) and less likely hormonotherapy (31%, 38% and 59%, $p<0.001$). Specific 5-year survival was not different in the three groups (91%, 95% CI=83–99 for the $\leqslant$35 years; 90%, 95% CI=88–92 for the 36–49 years and 89%, 95% CI=88–91 for the 50–69 years old). When adjusting for all the prognostic variables, age was not significantly related to mortality from breast cancer yielding Hazard Ratios (HR) of 0.8, 95% CI: 0.3–2.0, and 1.0, 95% CI: 0.7–1.3, for $\leqslant$35 and 36–49 years old patients respectively, as compared to women 50–69 years. Tumour size, stage, nodal involvement, oestrogen-receptor status and surgery were all independent determinants of mortality.

Conclusions: Younger women were diagnosed with a more advanced cancer, presenting more frequently poorly differentiated and oestrogen-negative tumours and received more often adjuvant chemotherapy. However, breast cancer survival among young women was comparable with that of older women. Age *per se* was not an independent prognostic factor when accounting for tumour characteristics and treatment.

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Breast cancer in the north of Iran (1999–2001)

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Background: The aims of cancer registry in Babol Research Station (BRS) are to improve the quality, comparability and availability of information from population-based cancer registry in the north of Iran (Mazandaran and Golestan provinces). This work attempts to describe the trend analyses by focusing on cancer registry among all age groups in the above two provinces during three years (1999–2001). In general, breast cancer increases with age and it is most common after the age of 50. All over the world about 794,000 women are diagnosed with breast cancer each year. BRS has been the first center of cancer registry in Iran.

Material and Methods: The BRS has established a plan of activities to promote standard practice in data collection and data analyses. A comprehensive search was carried out to survey and register all cancer cases during a period of 3 years (1999–2001) in the indigenous population of Mazandaran and Golestan provinces. Diagnosis of cancer was based on histopathology and reports of radio and chemotherapy. All the age groups in both provinces were included in the analysis. Breast cancer rates were computed for each province, year and age group (<20, 20–34, 35–49, 50–64, >=65).

Results: A total of 6444 cancer cases were found during the study in Mazandaran and Golestan provinces; 54% of these cases (3480) were male, and 46% of cases (2964) were female. During a period of 3 years (1999–2001), 687 cases of breast cancer were diagnosed in the north of Iran. Among them 97% were female and 3% were male. The age range was 21–95 years with the mean of 45.5 years. Moreover, the highest frequency of breast cancers was found in the age group of 35–49 years (54%).

Therefore, the 2000 raw incidence rate of breast cancer is approximately 10.6 per 100,000 women in the north of Iran.

Conclusions: Cases in this cancer account for 10.7% of total malignant neoplasms. Also, breast cancer constitutes nearly a quarter of all female cancers in Mazandaran and Golestan provinces during the last 3 years. The available epidemiological data suggest that breast cancer is a common disease in the north of Iran, and this point to the increasing need of establishing a cancer registration center in the north of Iran.

448 POSTER

Induction of apoptosis in mouse mammary epithelial cells RIII/MG by epigallocatechin gallate (EGCG)

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Green tea is a natural food ingested in daily life in Japan, and many studies regarding its preventive effect on carcinogenesis and anticancer effect have been performed. A major component of tea, epigallocatechin gallate (EGCG), has potent biological and pharmacological activity. EGCG has been reported to exert an antitumor effect on brain tumor, colon cancer, prostatic cancer, hepatoma, gastric cancer, lung cancer, Leukemia, oral cavity cancer, and a similar effect was shown for breast cancer. Although many studies of the antitumor effect of EGCG have been performed, there are few basic studies regarding how EGCG prevents carcinogenesis and the effect of EGCG on precancerous cells, and many points remain unclear. It is of interest to clarify how green tea ingested in daily life prevents cancers with few adverse effects. Thus, in this study, we investigated the effect of EGCG on precancerous mammary cells using the RIII/MG cell lines, which are mouse models of viral carcinogenesis in mammary epithelium, in vitro and in vivo to investigate whether green tea commonly ingested in Japan prevents carcinogenesis of precancerous cells. In the in vitro experiment, crude catechin (catechin) containing 50% or more EGCG significantly inhibited the growth of RIII/MG cells, which were precancerous cultured cells. Many cells died and a DNA ladder was observed. In the in vivo experiment, RIII/MG cells formed a tumor after 13 weeks in a group without catechin treatment and the tumor formation rate in the 20th week was 40%. In a group treated with 0.1% catechin, a tumor began to grow in the 13th week and the tumor formation rate in the 20th week was 20%. In a group treated with 1% catechin, no tumor was detected even in the 20th week. There was no significant difference in the change in body weight between the catechin treatment groups and the non-treatment group during the observation period. Tissue samples were stained by the nick end labeling method and apoptosis was observed in many cells. Based on the above findings, catechin inhibited growth in the mouse viral mammary epithelial carcinogenesis model, RIII/MG, and induced apoptosis, suggesting the usefulness of catechin as a chemopreventive substance.

449 POSTER

Familial risks of cancer as a guide to gene identification and mode of inheritance

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Background: Familial clustering of a disease is caused by shared genes or shared environment. If the effect of environment can be quantified, the remaining familial clustering can be assigned to heritable causes. Occurrence of cancer in parents and offspring may be due to dominant causes, whereas cancer affecting only siblings may indicate a recessive causation. Systematic comparisons of mode of inheritance have not been available for most types of cancer.

Methods: We use the nationwide Swedish Family-Cancer Database, which includes the Swedish population in families, totaling over 10.2 million individuals and cancers from the Swedish Cancer Registry up to year 2000. Standardized incidence ratios (SIR) and 95% confidence limits (CI) were calculated for offspring whose parents or siblings were diagnosed with the same cancer.

Results: The degree of environmental causation was assessed by spouse correlation and by comparing risks among siblings of different ages. We identified reliable familial risks for all common neoplasms, SIRs ranging from 1.6 to 4.3 when only a parent was affected and up to 8.5 when only a sibling was affected. Risks between siblings were particularly high for renal cancer. Spouse correlation was found only for lung and stomach cancer but the analysis of sibling risks by their age difference suggested that even for some other cancers environmental effects in childhood may contribute to familial aggregation.

Conclusions: The results from these analysis suggest that familial cluster of cancer at most sites is heritable, caused by dominant effects; for renal cancer recessive effects may be most important.

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Set-up of a population-based familial breast cancer registry in Geneva Switzerland: Validation of first results

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Background: This study evaluates the accuracy of family history (FH) of breast and ovarian cancer among first-degree relatives (FDRs) of breast cancer patients, retrospectively collected during the set-up of a population-based family breast cancer registry.

Methods: FHs of cancer of all women with breast cancer recorded at the Geneva cancer registry between 1990–1999 were retrospectively extracted from medical files. The accuracy of these FHs was validated among Swiss women born in Geneva: all 119 with a FH of breast cancer (n=110) or ovarian (n=9) cancer and a representative sample of 100 women with no FH of breast or ovarian cancer. We identified the FDRs of these women with information of the Cantonal Populational Office. All FDRs, resident in Geneva between 1970–1999, were linked to the cancer registry database for breast and ovarian cancer occurrence. Sensitivity, specificity, and level of overall agreement (kappa) were calculated.

Results: Among 310 FDRs identified, 61 had breast cancer and 6 had ovarian cancer recorded at the Geneva cancer registry. The sensitivity, specificity and kappa of the reported FHs of breast cancer were respectively 98%, 97% and 0.97. For ovarian cancer, the sensitivity, specificity and kappa were respectively 67%, 99%, and 0.66.

Conclusion: This study indicates that retrospectively obtained FHs are very accurate for breast cancer. For ovarian cancer, FHs are less precise and may need additional verification.

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Increased rates of chromosome breakage in BRCA1 carriers are reduced by oral selenium supplementation

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Women who are born with constitutional heterozygous mutations of the BRCA1 gene face greatly increased risks of both breast and ovarian cancer. The product of the BRCA1 gene is involved in the repair of double-stranded DNA breaks and it is believed that increased susceptibility to DNA breakage contributes to the cancer phenotype. We measured the frequency of chromosome breaks in BRCA1 carriers and in non-carrier relatives in cultured blood lymphocytes following in vitro exposure to bleomycin. Carriers of BRCA1 mutations demonstrated significantly greater mean frequencies of induced chromosome breaks per cell than the control relatives (0.58 versus 0.39; $p<10^{-4}$). We then supplemented 35 BRCA1 carriers with oral selenium for a period of one to three months. In all 35 carriers studied, the frequency of chromosome breaks was reduced, from a mean of 0.63 breaks per cell to 0.40 breaks per cell ($p<10^{-10}$) and the frequency was then similar to that of the non-carrier controls (0.39 breaks per cell). Oral selenium is a good candidate for chemoprevention in women who carry a mutation in the BRCA1 gene.

452 POSTER

Identification of women at high risk of hereditary breast cancer

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Objective: To identify women with moderate to high risk of hereditary breast cancer in order to offer them specific management strategies for cancer prevention and early detection.

Setting: Centro di Senologia della Delegazione Alto Lario della Lega Italiana per la Lotta contro i Tumori at Gravedona (Italy) and Centro di Senologia della Sezione Provinciale di Sondrio della Lega Italiana per la Lotta contro i Tumori at Sondrio (Italy).

Methods: 234 women with family histories of breast cancer completed, by themselves, simple questionnaires prior to undergoing a breast cancer