Wednesday, 30 September 1998 **16:00-18:00**

PARALLEL SESSION

Epidemiology and prevention

93 INVITED

Chemoprevention of breast cancer – An update

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Because breast cancer is the commonest form of cancer in women in the Western world, a large amount of effort has been put into trying to discover its causes and possible means of prevention. Mammographic screening offers one approach to preventing mortality by detecting cancers at an earlier more treatable stage, but it will not prevent the development of cancers. At the other extreme there is interest in trying to reduce the incidence of breast cancer by restricting dietary fat intake or increasing the amount of exercise taken. However, in the short to medium term chemoprevention with hormonally active agents is likely to be the most effective approach. Four trials of tamoxifen prophylaxis have been undertaken and their current status will be reviewed. A range of new agents could also be considered including tamoxifen analogues such as raloxifene, pure anti-oestrogens, aromatase inhibitors, and phyto-oestrogens.

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Geographic distribution within the Netherlands of families with specific mutations in BRCA1 and BRCA2

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Purpose: To determine the origin within the Netherlands of families with a number of specific mutations in the breast cancer susceptibility genes, BRCA1 and BRCA2.

Methods: Families were identified through the family cancer clinic of the Daniel den Hoed Cancer Center and the department of clinical genetis, Erasmus University, Rotterdam. The origin of families with various specific Dutch founder mutations was mapped out. The place of birth was determined for the ancestors, most likely to have transmitted a mutation in each of the families.

Results: Presence of a BRCA1 or BRCA2 germline mutation was detected in 70 and 14 families, respectively. 6 BRCA1 and 1 BRCA2 mutation that were previously described as specific Dutch founder mutations were detected ≥ 5 times. 4 of these mutations appear to be originated from distinct regions in the south-west Netherlands. One of these mutations, a large 3.8 kb genomic deletion encompassing exon 13 of the BRCA1 gene is the most frequently encountered BRCA1 mutation within the Rotterdam famillies (n = 15, 21% of 70 BRCA1 families). All of the families with this mutation originated from one small region with approximately 150.000 inhabitants. Breast cancer incidence among these families was heterogeneous and no specific breast or ovarian cancer phenotype could be assigned to any of these founder mutations.

Conclusion: For some of the specific Dutch founder mutations in BRCA1 and BRCA2, the origin within the Netherlands can be traced back to distinct regions.

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Mutations in the BRCA1 and BRCA2 genes: Uptake of presymptomatic DNA test, preventive choices and breast cancer risk after prophylactic mastectomy

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Purpose: Mutations in the BRCA1/2 genes in females cause a 60%–85% and a 20–60% risk for breast-and ovarian cancer respectively. Mutations in these two genes attribute to approximately 5% of the total of breast cancers. We wanted to determine the uptake of presymptomatic. BRCA1/2 DNA testing (PST) in families in which a mutation was known. In addition we analysed the chosen preventive interventions and the incidence of breast cancer after prophylactic mastectomy.

Methods: After a mutation was detected in breast cancer prone families, the initial counsellee informed their family members about the possibility of PST. This was accompanied with written information on the pros and cons of DNA testing. The uptake of PST was determined after at least 6 months. We analysed the preventive choices made by female mutation carriers. We determined the incidence of breast cancer after prophylactic mastectomy (n = 93). This group consisted of 48 BRCA1/2 mutation carriers (18 breast cancer patients and 30 healthy women) and 45 women from high-risk breast cancer prone families (32 breast cancer patients and 13 healthy women).

Results: 196 healthy at risk persons applied for PST (5.8 persons per family). 113 out of 188 healthy female 50%-risk carriers (60.1%) and 44 out of 150 male 50%-risk carriers (29.3%) were tested. In 57 healthy women a mutation was found. Of these 32 underwent prophylactic mastectomy (56%). 22 out of 32 women who were older than 35 years underwent prophylactic oophorectomy (69%). Especially women in their thirties and forties decided for both PST and prophylactic mastectomy. In the prophylactic mastectomy group we expected 5 breast cancer patients during the period of follow up. Until now (mean 2.5 years) no cases of breast cancer occurred.

Conclusion: The majority of Dutch women from high-risk families wants a presymptomatic BRCA1/2 DNA test and take prophylactic surgical measures in case they carry a mutation. Our data suggest that prophylactic mastectomy reduces the risk for breast cancer in high-risk women.

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Ethnicity, diet, and mammographic density patterns

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Purpose: Mammographic density patterns refer to the distribution of fat, connective, and epithelial tissue in the healthy female breast and are strong predictors of breast cancer risk. This project investigated the hypothesis that ethnicity and diet are related to mammographic densities.

Methods: In a cross-sectional design, more than 400 White, Hawaiian, Chinese, and Japanese women with normal mammograms completed a reproductive history and a food frequency questionnaire. After digitizing the cranio-caudal mammographic films, the area with densities and the total area of the breast were measured using a computerized method.

Results: The mean dense area in the mammograms was approximately 15% smaller in Asian than in White and Hawaiian women. However, because of their relatively smaller breast size, the percent of the breast occupied by dense tissue in Asian women was equal to or higher than in White women. In a multiple linear regression model, daily intake of fruits, vegetables, soy products, as well as age, body mass index, age at menarche, and parity were inversely related to mammographic densities, while age at first live birth showed a positive association with densities.

Conclusion: Women from ethnic groups with low breast cancer risk have smaller areas of mammographic densities than women from high risk groups. A diet rich in fruits, vegetables, and soy foods may be related to mammographic density patterns that protect against breast cancer.

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The risk of breast cancer in women with affective or neurotic disorders

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Purpose: To test the hypothesis that women admitted into psychiatric departments with affective or neurotic disorders have an increased incidence of breast cancer compared to the general population of women adjusted for age and calendar period.

Methods: The base population comprised all 66,648 women registered during the period 1970–1993 in the nation-wide Danish Psychiatric Case Registry with a psychiatric admission including a diagnosis of affective or neurotic disorder.

Results: In all 1,270 affective or neurotic women developed breast cancer compared to 1,242 expected. SIR = 1.02; 95% CI: 0.97–1.08.