

Treatment and follow up data are collected using a specialist data collection proforma from the original hospital case notes and information held on the West Midlands Cancer Intelligence Unit (WMCIU) database. A pathological slide review has been undertaken by a consultant pathologist to obtain consistent information on diagnostic characteristics throughout the study period. The slides included in the slide review have undergone an extensive double blinding exercise to ensure that confidentiality can be maintained while still being able to compare original and review pathology results.

Results: To date, 840 cases are included in the study which were recorded as screen detected DCIS without invasive disease between 1st March 1988 and 31st March 1999. Interim results demonstrate that low grade DCIS is infrequent forming only 11% of the cases undergoing histological review. Calcification is present in 81% of cases reviewed and 80% of cases underwent a localisation procedure. The mastectomy rate in those cases reviewed so far is 21%.

Conclusions: This study when complete will provide valuable data on the significant factors which affect the likely outcome for women diagnosed with DCIS through the breast screening programme and will help to ensure that the prognosis of these women is good with minimal risk of recurrence.

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Epidemiology and prevention

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POSTER

The prevention of breast cancer induction by plant extracts and the postradiation alterations of DNA structure

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The goal of the present study was to reveal relationship between relatively early alterations of DNA structure in blood leukocytes and frequency of breast cancer (BC) in rats induced by radiation in case of some nutrition addition administrations.

The 755 female rats with initial mass 140–160 g were used in the experiment. The animals were irradiated totally with 4 Gy single dose at the "IGUR-1" unit (^{137}Cs). In 11 days after irradiation rats received with drinking water cyclically (administration during 3 weeks, then interval during 1 week) difluoromethylornithine (DFMO) - as a standard anticarcinogen in dose 2 g/l, and extracts of medicinal plants (1–2% solutions): *Plantago major* (L), *Eleuterococcus senticosus* (Rupr. et Maxim), *Rhaponticum carthamoides* (Willd. Iljin), bioginseng (BGS) biotechnological drug from root biomass of *Panax Ginseng* (C.A.Mey). A hot herbal extract of *Filipendula* (EF) - *Filipendula ulmaria* (L) was administered to rats with drinking water without interruption. The alteration of DNA structure in blood leukocyte was determined by means of two-parameters fluorescent analysis including ethidium bromide and 4',6-diamidino-2-phenylindole, as described earlier [Ivanov SD et al., 1999].

Irradiation of rats resulted in significant life span shortening (LSS) and increase of tumor frequency (from 22% to 77%). The frequency of BC increased in the most degree - almost 16-fold, while for other tumors - approximately 3-fold. The administered preparations did not influence on the LSS dynamics. The administration of DFMO, BGS and EF reduced the amount rats with tumors (1.5–1.6 fold), and a number of BC per animal (1.6–2.0 fold). These preparations (in contrary to others) did not changed the amount of blood leukocytes, but it resulted in alterations of their DNA structure. The correlation ($R = -0.683$) was revealed between a number of BC per rat after administration of all preparations and an index of DNA structure alterations in blood leukocytes, measured in 30 days after irradiation.

So, the DFMO, BGS and EF reduced the frequency of BC on the given experimental model, and the DNA structure alterations may be used as an early prognostic index for the acceleration of the anticarcinogenic preparation screening.

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Persistent adrenal gland activity observed in postmenopausal women (PMW) with breast cancer(BC); Preliminary results

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Purpose: adrenal gland synthesis of various sex hormone precursors have been reported to decrease by 60% or more in PM. High plasma testosterone and estrogen levels have often been associated with an increased risk of BC in PMW. DHEA and testosterone are considered beneficial to PMW to alleviate major complications of the menopause. Conflicting reports regarding this matter have been published. Despite the fact that the mortality of BC has decreased significantly in the past years, it is still a major health problem associated with a high morbidity in many of the more developed countries. We have yet to find a reliable marker to predict breast cancer occurrence.

Methods: In a case-control study in Montreal, a total of 70 newly diagnosed PMW with BC and 70 population-based controls, matched for age (within 5 years age groups), selected by random digit dialing telephone directory method or hospital admission offices. We measured fasting blood levels of cortisol, C-peptide, insulin, free testosterone (FT), total testosterone (TT), DHEAS, androstenedione, SHBG, estrone, estradiol as well as IGF-1 and IGFBG-3 from both cases and controls.

Results: No difference was observed on key demographics variables between groups. Among cases, the mean blood levels of DHEAS, TT, androstenedione were twice of that observed in the controls. Receiver Operating Characteristic (ROC) curves were performed for all laboratory variables and significant ($p < 0.001$) discriminatory accuracy (expected to observed ratio) of 0.82 (95%CI 0.74-0.90) is noted for TT as well as for FT (0.77;0.69-0.84), androstenedione (0.74;0.66-0.82), estradiol (0.72;0.63-0.80), DHEAS (0.68;0.59-0.76) and estrone (0.66;0.58-0.75). Fasting insulin, C-peptide, cortisol, IGF-1, and IGFBP-3 curves revealed a weak association if present.

Conclusions: Our results so far suggest that PMW with BC have increased/persistent adrenal gland activity contrary to the controls. TT has a significant discriminatory index for identifying PMW with BC. The adrenal gland activity should be further explored in PMW. supported by the Jean H. Picard foundation.

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Pedigree analysis of women attending a breast family history clinic

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The Nottingham Breast Family History Clinic, set up 10 years ago, serves a population of 1 million. Over 600 asymptomatic women per year are referred for assessment of their family history; 50% of these are considered low risk and are not further followed. 1800 women are being followed up regularly. This represents approximately 40% of all women eligible for screening within our catchment area. 5% per year are lost to follow up.

Retrospective review of family pedigrees showed that 31% were classified as high risk and 69% as moderate risk by standard risk assessment. Only 11% of women presented with a history of cancer in their father's side of the family, this reflecting a public under-estimation of the importance of the paternal family history in hereditary breast cancer. Overall, 8% of women had ovarian cancer family history. A history of colon cancer was more common in the high risk group than in the moderate risk group (13.4% vs. 5.5%, $p < 0.05$).

The running of a Breast Family History Clinic has significant service implications. Important and useful information to service provision and resources organisation can be obtained by audit. Adequate funding for data collection and data analysis is essential. Additional funding of genetic services for mutation analysis of high risk women, and funding for ovarian screening research, is required.

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Analysis of results of breast cancer screening programme according to the round incident and round prevalence

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Objective: The Valencia Breast Cancer Screening Program (VBCSP) began in 1992 with the aim of decrease the mortality for this type of tumours by means mammography studies of the women's between 45 and 65 years. 297,825 women have been studied.

Method: The women are called to the units of VBCSP where a mammography is made in double projection in first study and simple in successive studies. The case findings are remitted for confirmation it diagnoses and treatment to hospitals. The indicators are analysed according if in the first study was made (prevalence round) or successive studies (incident round) and their comparison with the requirements of quality of the Europe against Cancer Working Group.

Results: On 394,132 women called in the first round, 297,825 attended (participation rate 75.56%). On 300,844 women called in rounds successive, 271,185 attended (adhesion rate 90.14%). In round first 1,414 cancer were detected (detection rate 0.47%) and in rounds successive 888 become cancer (detection rate 0.33%). The rate of derivations to the hospital was 6.01% and 2.08% respectively.

The tumours <1 cm. were 21% and 25% of those detected, and the detection rate of ductal carcinoma in situ (DCIS) was 17.5% and 14%, respectively. The 70% and 71% of the invasive tumours don't have ganglion affection, according to rounds.

Conclusions: The results reach the standards quality of the EU. Differences are observed between round incident and rounds prevalence in women derived to the hospital, detection rate and precocity of diagnostic. These results allow waiting a decrease of the mortality next years.

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Breast cancer mortality and survival rates in the county of Nis (Serbia, Yugoslavia)

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In the last 10 years Serbia was affected with great economic and political crisis, even war and bombing. Many facts indicated that crisis influenced lower grade of health protection, increasing mortality and other negative influences on health in generally.

The aim of this investigation is to determine the mortality trend of female breast cancer in the county of Nis, as well as the survival rates of breast cancer before the economic crisis reach its peak (1986–1993) and after that (1995–1999).

Material and Method: Population and hospital cancer register data from 1986 to 1999 were used for analysis, as well as death certificates for all women who lived and died in the county of Nis. Surviving was calculated by Kaplan Meier method. Rates were calculated per 100000 inhabitants (1991 census) and not standardized.

Results: From 1986 to 1999 a total number of 455 women were died from breast cancer in the county of Nis. Polynomial trend of mortality showed increasing (1986–1992) and decreasing (1993–1996) tendency ($y = 0.1862x^2 + 3.21x + 18.69$, $R^2 = 0.3003$), although in the first period an average mortality rate was lower (28.7) than in the second period (30.45). Surviving rates were calculated for the period 1986–1993 and for period 1995–1998. In the first period 12 months survival was 84.7% and for second one it was 92%, 24 months survival rate in the first period was 76.6% corresponding to 87.9% in the second period; 36 month survival was 67.7% in the first and 80.5 in the second period and four years survival rates from 1986 to 1993 was 64.1% and from 1995 to 1999 it was 78.1.

Conclusion: Socio-economic and political crisis showed some influence on the breast cancer patients: in generally the mortality rates increased, but the whole period we can divide into two: In the first period (from 1986 to 1992) mortality rates increased, and after that decreased. Although the second period was more difficult in Serbia and whole Yugoslavia (that was

reflected on the therapy of all diseases as well as breast cancer too) the diagnosis of breast cancer have been improved, audit was made in the earlier stage of diseases which cause the better survival rates than in the first period.

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Effect of tamoxifen on breast surface temperature in women on hormone replacement therapy

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Recent advances in breast cancer prevention have utilised hormonal manipulation, specifically the selective oestrogen receptor modulator, tamoxifen. However there are no methods for monitoring the effects of such interventional strategies on the "normal" breast and no investigative tools to compare alternative approaches. It is likely that the actions of tamoxifen impact on the local hormonally controlled pathways in the breast. Breast surface temperature has been found to reflect the menstrual cycle independently of body temperature, suggesting a role for temperature as a surrogate marker of the local actions of hormones. To investigate this role further, this study was designed to compare breast surface temperatures in women on hormone replacement therapy before and during a one month course of tamoxifen.

Methods: Healthy women established on HRT were recruited from a local Menopause clinic. None had a past history of breast disease. Breast surface temperature was measured using an array of thermistors with a resolution of 0.05°C connected to a small data logger. Clothing and environmental conditions were standardised. Subjects had temperature measurements taken from three defined sites on each breast and at a reference point on adjacent skin. Measurements were taken on three occasions prior to a one month course of tamoxifen (with loading dose) and then repeated on a further three visits during the course of tamoxifen.

Results: Subjects acted as their own controls. Twelve subjects (24 breasts) were studied. A significant change in temperature with tamoxifen occurred at one or more sites in 18 breasts. The majority (10) of these changes were temperature reductions but 8 breasts showed an increase in temperature. Of note, breasts of the same subject often showed independent changes in response to tamoxifen.

Conclusion: These data show that breast surface temperature demonstrates measurable changes during a short course of tamoxifen. Interpretation of these changes is speculative at this stage. It is known that tamoxifen can act as both an agonist and antagonist of oestrogen which may explain the variety of temperature responses seen. These results support a need for further investigation of temperature as a potential surrogate marker of hormonal interventions on the breast.

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Hormone receptor status in primary postmenopausal breast cancers. Is there an association with hormone replacement therapy?

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Objectives: Some postmenopausal women with a malignant breast lump present while taking hormone replacement therapy (HRT). Data regarding the effect of HRT on oestrogen (ER) and progesterone receptor (PR) expression are inconclusive. We compared ER and PR expression in breast cancer tissue from HRT-users with those who never used it.

Methods: All consecutive postmenopausal women with an operable primary breast cancer (n = 67) admitted in the St.-Jan's Hospital, Brussels in the year 2000, were included in a retrospective way. 26 women reported HRT use at the time of diagnosis whereas 41 breast cancer patients never used HRT. For each patient, we recorded age and body mass index (BMI) at the time of first treatment. Formalin-fixed tumour tissue from the primary breast cancer was immunohistochemically (IHC) examined using the monoclonal antibodies NCL-ER-6F11 for ER and NCL-PGR-312 for PR. The interpretation of the IHC-staining intensity is semiquantitative and subjective. We opted for the immunoreactive scoring system (IRS) of Remmele and Stegner.

Results: Both ER and PR were negative ($IRS \leq 2$) in 34.6% of the HRT users whereas this was the case in 24.4% of the women never having used HRT. In those who expressed ER ($IRS > 2$), the mean intensity of receptor staining was 7.8 in the HRT users and 8.0 in the never users. In those who expressed PR ($IRS > 2$), the mean intensity of receptor staining was 6.3 in the HRT group and 6.5 in the never users. Descriptive statistics are presented in the table. All the distributions were Normal (K-S test; $p > 0.05$). HRT users and non users differed significantly for age (t-test; $p < 0.001$), but not for BMI, mean ER and mean PR. In multivariate analysis, HRT use (yes/no), age, and BMI appeared to be poor predictors of either ER intensity in ER expressors (multiple regression; $r = 0.06$) or PR intensity in PR expressors ($r = 0.121$). We performed a logistic regression analysis to measure the effect of HRT use on ER or PR qualitative expression (≤ 2 or > 2), adjusted for age and BMI: HRT users were less likely to express ER (OR = 0.43; 95% CI: 0.12–1.54) or PR (OR = 0.77; 95% CI: 0.24–2.47).

Conclusion: Our results suggest that HRT-users are more likely to have ER/PR negative breast cancers compared with never-users, even considering that in our series HRT users were younger and that age may play an important role in hormone receptor status. The observed association is not statistically significant but this may be attributed to a lack of power (too few subjects). Nevertheless, this association should deserve further attention. Once the tumour expressed the hormone receptor ($IRS > 2$), comparing HRT users with never users, there was no difference in intensity of expression, neither for the ER nor for the PR.

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Detection rate, recalls and positive predictive value by age in the Norwegian Breast Cancer Screening Program

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The Norwegian Breast Cancer Screening Program is a part of the public health service. The program started as a four years pilot project in four counties in 1996. Women (50–69 years) are invited to screening every second year. Recall take place at breast diagnostic centers. The primary objective of the program is to reduce the mortality of breast cancer among the invited women with 30%. This is not measurable within about ten years. Early indicators have been stated in a quality assurance manual.

The aim of this study was to describe some of the early indicators in the prevalent and first subsequent screening in accordance to birth cohorts. The results are based on the women who are screened twice.

In the prevalence screening 159 714 women born 1927–46 were invited whereupon 79.5% attended. Of those 86.9% re-attended the next screening round. There was minor variation by birth cohorts.

The detection rate was 6.8 per 1000 screened in the prevalence and 4.9 per 1000 screened in the subsequent screening. In the prevalence screening women born 1927–31 had the highest detection rate (10.2 per 1000 screened). Women born 1942–46 had the lowest rate (4.7 per 1000 screened). Corresponding rates for the subsequent screening were 5.0 and 4.0 per 1000 screened.

Recall due to positive mammogram were 4.2% in the prevalence and 2.7% in the subsequent screening. In the prevalence screening the recall was 3.9% for women born 1927–31 and 4.7% for women 1942–46. In the subsequent screening the rates were 2.4% and 2.8%.

In the prevalence screening the positive predictive value (PPV) due to all kind of recall varied between 20.4% (1927–31) and 7.2% (1942–46). In the subsequent screening PPV varied between 15.5% and 10.1%. Invasive procedure (cytology and/or biopsy) was used in 38.4% of all recalls in the prevalence screening. In 31.0% of the invasive procedures cancer was diagnosed. Corresponding rates for the subsequent screening were 31.7% and 43.3%. Invasive procedures were more usual for women born 1942–47 compared to those who were born 1927–31. The results indicated that the specificity of the invasive procedure was highest in the subsequent screening.

The detection rates, recalls and PPV decreased in the subsequent screening compared to the prevalence screening. The detection rate varied in different birth cohort, partly due to background incidence pattern. The mammograms of the youngest women seemed to be more difficult to read than mammograms of older women.

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Knowledge, attitude and practice regarding breast cancer among health professionals

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Objectives: Knowledge, attitude and practice of female health workers affect the quality of health services regarding breast cancer. In this study we measured these scales and to find some factors that may change them.

Methods: In a cross-sectional study, 382 women aged 20 to 64 years were studied by a structured questionnaire consisting of some questions about knowledge, attitude, practice and related factors. This factors were age, educational level, marital status, job and work sites. Multivariate analysis was performed by using analysis of variance and regression.

Results: Results indicated that the majority of women had good knowledge and attitudes, but poor practice. Breast cancer knowledge varied by age ($P=0.002$), education and job ($P<0.0001$). Mean rank of women's attitude had a significant difference by educational level ($P<0.0001$), job ($P=0.005$), and work sites ($P=0.01$). Women's practice regarding breast cancer screening programs varied by education level ($P=0.02$), marital status ($P=0.002$), job and age ($P<0.0001$). The most frequent barrier to do breast self examination was forgetfulness (52%) and for going to physician's consultation was "no problem in breasts" (40%).

Conclusion: This findings showed the significant affect of educational level and job, and therefore we suggest the necessity of educational programs in health system workers.

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Breast carcinoma (BC) in women below 40 years of age

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Introduction: Worldwide, 6.5% of all BCs occurs in women <40 years of age (with worse prognosis than in older age groups as two recent large studies demonstrate).

This study assesses BC incidence (in the periods 1986/1990 and 1997/2001), histopathologic type and disease stage at diagnosis in women <40 in the town of Niš.

Material and Methods: We used the data from the BC Registry of the Clinic of Oncology in Niš, processed them with EXCEL 97 and standard statistical procedures (linear tendency, chi square test, percent), with statistically significant difference established at $p < 0.05$.

Results: In the period 1986/90 there were 684 new BC cases with a significant increase ($y = 24.7x + 80.7$; $R^2 = 0.67$). There were 58 cases <40 years of age ($y = 2.4x + 4.4$; $R^2 = 0.47$). From Niš territory there were 229 new cases ($y = 6.7x + 39.7$; $R^2 = 0.26$), out of which 23 < 40 years of age ($y = 4.6$; $R^2 = 0$). In the period 1997/2001 there were 1882 new cases ($y = 4.48x + 390.8$; $R^2 = 0.09$), out of which 147 < 40 ($y = x + 26.4$; $R^2 = 0.133$). In Niš, BC was detected in 502 women ($y = 5.05x + 75.15$; $R^2 = 0.86$), with 41 < 40 ($y = 0.6x + 5.2$; $R^2 = 0.50$).

Number of BC cases was 2.19 times larger in Niš in the period 1997/2001 than in the period 1986/1990. In those <40, BC was 1.78 times more frequent in the period 1997/2001, the tendency steeper, with statistically significant increase ($R = 0.71$).

In the latter period, the percent of early BC in women <40 increased (72% to 87.1%), with markedly reduced percent of locally advanced (18.9% to 8.8%; $p = 0.07$) and metastatic disease (8.6% to 4%). However, tumour aggressivity increased: percent of women with BC N+ increased from 51.7% to 55.7%; percent of those with well differentiated lesions fell by 3.5%, moderately differentiated by 4.6%, and the percent of poorly differentiated cancers increased by 8.1% in the latter period. Ductal histopathology prevails in both periods, but with rise of ductulolobular (3.4% to 7.5%) and lobular (3.4% to 6.1%) types in 1997/2001.

Conclusion: Breast cancer incidence in women <40 significantly increased in 1997/2001 compared to 1986/1990; it is diagnosed earlier, but histopathology indicated higher tumour aggressivity.

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Stressful life experiences and breast cancer development

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The etiology of breast cancer is complex and far from being completely understood, as the importance of life events in breast cancer development.

The aim of this study is to examine the relationship between stressful life experiences and the onset of breast cancer.

Material and Method: This case-control study comprised 120 female patients with histologically verified breast cancer and 120 hospital controls matched with respect to age (± 2 years). To investigate the strength of association between hypothesized breast cancer risk factors and the development of breast cancer a targeted and detailed questionnaire was used. In order to obtain information about stressful life experiences in the ten years before diagnosis, the original life events scale developed by Paykel

et al. (1971), with 61 event items, ranging from most to least upsetting, was used. Conditional logistic regression and t-test were applied in statistical analysis.

Results: We found differences between the groups for the cumulative number of life events (RR = 1.50 CI 95% = 1.32–1.70), severe life events (first 5 from the scale) (t = 2.35 p = 0.039), life events that were important moderate threats (6 to 25 from the scale) (RR = 3.72 CI 95% = 2.50–5.53), and for the experience of single life events including: death of close family member (RR = 8.36 CI 95% = 3.13–22.32), husband unfaithful (RR = 15 CI 95% = 2.21–15.81), serious financial difficulties (RR = 7.27 CI 95% = 3.23–16.34), fired (t = 2.92 p = 0.004), divorced (RR = 3.80 CI 95% = 1.35–10.65), serious illness of family member (RR = 3.44 CI 95% = 1.97–6.02), begin extramarital affair (RR = 8.47 CI 95% = 1.05–68.72), child marries without approval (RR = 4.74 CI 95% = 1.31–17.08) and increased arguments with husband (RR = 3.92 CI 95% = 1.88–8.18).

Conclusion: These findings suggest a positive association between stressful life events and breast cancer, but there is a need for further elucidation of the role of these factors.