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Hereditary factor in the onset of cancer of the gastrointestinal tract and female reproductive organs

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Having analyzed 138 questionnaires, we could isolate the following groups of risk according to the onset of oncopathology:

1. No oncopathology is noticed in 55% of family trees.
2. Cancer diseases of the endometrium, ovaries, mammary gland, stomach and intestine were marked in 20.3% in relatives of degrees I and II. The latter being marked in literature as lynch II syndrome.
3. The presence of endometrial carcinoma was revealed in 6.5% of female relatives, degrees I and II of relationship.
4. Neoplasms and endocrine-metabolic disturbances were registered among relatives in 7.3%.
5. Diseases of lung cancer of diverse localization are revealed in 10.9% among relationships of degrees I and II.

Thus, the results of our studies have shown three syndromes that are versions of the family cancer syndrome and are manifested by a systemic predisposition to the onset of ovarian carcinoma, breast cancer, endometrial or gastric and intestinal carcinoma, etc. These include: (1) the syndrome of familial cancer of the mammary gland/endometrium/ovaries/large intestine (the syndrome of lynch2); (2) the syndrome of familial cancer of the mammary gland/endometrium/the organs of the gastrointestinal tract/lung; (3) the syndrome of familial carcinoma of the endometrium/the organs of the gastrointestinal tract.

Results and Discussion: On the basis of the studies carried out by us tables of cancer accumulation on the uterine body as well as criteria of identifying cancer risk and genetic prediction have been investigated.

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Folate intake and risk of colon cancer in relation to p53 mutational status

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Considerable epidemiological evidence suggests that a low-folate diet is associated with an increased risk of colorectal cancer, although a recent randomized trial indicates that supraphysiologic folate supplementation may not reduce the risk of adenoma recurrence. Furthermore, the mechanism by which folate deficiency influences carcinogenesis remains unclear. We evaluated the effect of folate consumption on p53 mutation in colon tumors. We immunohistochemically assayed p53 expression in paraffin-fixed colon cancer specimens in a large prospective cohort, the Nurses' Health Study, to examine the relationship of folate intake and intake of other one-carbon nutrients to risks by p53 status. We used competing risks Cox regression to compare associations of folate intake with incident colon cancers classified by tumor p53 mutational status. During 1,861,916 person-years of follow-up among 88,691 women, 399 incident colorectal cancers accessible for p53 expression were documented. The effect of folate differed significantly according to p53 mutational status ($P_{heterogeneity} = 0.01$). Compared with women reporting less than 200 μg of folate per day, the multivariate relative risks (RRs) for p53 overexpressing (mutated) cancers were 0.54 (95% CI, 0.36 to 0.81) for women who consumed 200–299 μg per day, 0.42 (95% CI, 0.24 to 0.76) for those who consumed 300–399 μg per day, and 0.54 (95% CI, 0.35 to 0.83) for ⩾400 μg per day. In contrast, total folate intake had no influence on wild-type tumors (RR, 1.05; 95% CI, 0.73 to 1.51, comparing ⩾400 to <200 μg per day). Similarly, high vitamin B6 intake conferred a protective effect on p53-mutated cancers (RR, 0.57; 95% CI, 0.35 to 0.94; $P_{heterogeneity} = 0.01$) but had no effect on p53 wild-type tumors. Further, among women with a daily folate intake of less than 200 μg and vitamin B6 consumption in the lowest quintile, the relative risk of p53-positive colon cancer was 2.61 (95% CI, 1.73 to 3.95), compared to women with higher intakes in both nutrients; by contrast, the comparable risk for p53-negative colon tumors was 0.78 (95% CI, 0.48 to 1.25). We found that low folate and vitamin B6 intake was associated with an increased risk of p53 mutated (overexpressing) colon cancers but not wild-type tumors.

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Non-steroidal anti-inflammatory drug use, a common cyclooxygenase-2 polymorphism (T8473C), and risk for Barrett esophagus

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Purpose: To investigate whether the protective association between non-steroidal anti-inflammatory (NSAID) drugs and esophageal premalignancy is modified by a common polymorphism of cyclooxygenase-2 (COX-2 T8473C).

Methods: In this case-control study, a 102-point structured questionnaire was used to obtain detailed socio-demographic, lifestyle risk factor and NSAID medication use in patients with gastroesophageal reflux disease (GERD) (n = 126) or with the premalignant lesion, Barrett esophagus (BE) (n = 125), each defined according to strict clinico-pathologic criteria. Controls comprised 95 healthy asymptomatic individuals. Following extraction of genomic DNA from blood samples (obtained with informed consent), genotype analysis was performed using a polymerase chain reaction (PCR)-based primer introduced restriction analysis. The frequency of COX-2 T8473C genotypes among GERD and BE cases was compared with asymptomatic controls using the Chi-square test. Multivariate analysis was performed using logistic regression to calculate odds ratios (OR) and 95% confidence intervals (CI) adjusting for age, gender, smoking and alcohol consumption.

Results: Relative to asymptomatic controls, current use of NSAIDs was associated with a reduced risk for BE (OR 0.33; 95%CI 0.17–0.63). ORs for long-term (>5-yr) NSAID users (OR 0.41; 95%CI 0.20–0.88) and more frequent (>1/day) NSAID users (OR 0.52; 95%CI 0.27–1.0) were also reduced, but there was no evidence of a dose-response relationship. To improve the statistical power of the study, the analyses were also performed using a combined group (n = 221) of asymptomatic controls (n = 95) and GERD cases (n = 126), representing benign disease as a control group. A similar protective effect was again seen for current NSAID use (OR 0.46; 95%CI 0.26–0.81). COX-2 genotype frequencies were consistent with Hardy-Weinberg equilibrium (p = 0.84). However, when compared to asymptomatic controls, the polymorphic variant was not associated with risk for BE