Decreasing cervical cancer risk by using intrauterine devices?

Epidemiological studies have consistently shown that the use of intrauterine devices (IUDs) reduces the risk of endometrial cancer, but the effect of IUD use on cervical cancer risk is not known. The current study by Castellsagué and colleagues (1) pooled analysis from 2 large studies consisting of 10 case-control studies done in 8 countries, and 16 studies of HPV prevalence from 16 countries. The goal of the analysis was to examine the risks for cervical cancer and HPV infection with IUD use. 2205 women with cervical cancer and 2214 matched control women without cervical cancer were included from the case—control studies, and 15 272 healthy women from the HPV surveys. Information on IUD use was obtained by personal interview. HPV DNA was tested by PCR-based assays. Odds ratios and 95% CIs were estimated using multivariate unconditional logistic regression for the associations between IUD use, cervical HPV DNA, and cervical cancer.

After adjusting the relevant covariates, including cervical HPV DNA and the number of previous Papanicolau smears, a strong inverse association was found between the use of IUDs and cervical cancer (odds ratio 0.55, 95% CI 0.42—0.70; p<0.0001). A protective association was noted for squamous-cell carcinoma (0.56, 0.43—0.72; p<0.0001), adenocarcinoma and adenosquamous carcinoma (0.46, 0.22—0.97; p=0.035), but not for HPV-positive women (0.68, 0.44—1.06; p=0.11). No association was found between the IUD use and the detection of cervical HPV DNA among women without cervical cancer. According to results, the authors concluded that IUD use did not protect women against HPV infection, but did protect against the development of cervical cancer.

The mechanism of action by which IUDs protects against cervical cancer is not known.

Authors of the study offered several theoretical explanations.

One of the mechanisms could be the induction of a reactive, chronic, low-grade, sterile inflammatory response in the endometrium, endocervical canal, and cervix that could modify, via changes in the local mucosal immune status, the course of HPV infections.

Also, the investigators found that there was no difference in the protective effect by years of IUD use. Both short-term users and those, who used it for as long as 9 years, were found to be protected, according to the odds ratio estimates. These findings could be associated with the local trauma to the cervical tissue associated with insertion or removal of the device, which induces local small foci of chronic inflammation and a long-lasting immune response similar to that noted in patients after colposcopically guided punch biopsies.

REFERENCE

1 Castellsagué X , Díaz M , Vaccarella S, de Sanjosé S , Muñoz N , Herrero R, et al. Intrauterine device use, cervical infection with human papillomavirus, and risk of cervical cancer: a pooled analysis of 26 epidemiological studies. *The Lancet Oncology.* 2011;12(11):1023–31.

Aljoša Mandić

Coffee consumption decreases risk of endometrial cancer?

Endometrial cancer is the most common gynecologic cancer in developed countries. One of the most important mechanisms in endometrial carcinogenesis is the prolonged exposure to excessive unopposed estrogens, resulting in stimulation of endometrium. Recent studies have demonstrated that at baseline, high circulating levels of estrogens, C-peptide, and fasting insulin were associated with an increased risk of endometrial cancer. Coffee has been reported to lower levels of estrogen and insulin.

In 1980, Youjin Je et al. (1) observed coffee consumption in relation to endometrial cancer risk in the Nurses' Health Study (NHS) with 67,470 female participants aged 34 to 59. Cumulative average coffee intake was calculated with all available questionnaires to assess long-term effects. Cox regression models were used to calculate incidence rate ratios (RR), controlling the other risk factors. The results of the study showed that women who consumed 4 or more cups of coffee had 25% lower risk of endometrial cancer than those who consumed less than 1 cup per day (multivariable RR = 0.75; 95% CI = 0.57–0.97; P_{trend} = 0.02). Similar association with caffeinated coffee consumption was found (RR for ≥4 vs. <1 cup/d = 0.70; 95% CI = 0.51–0.95). For decaffeinated coffee consumption, a suggestive inverse association was found among women who consumed 2 or more cups per day versus <1 cup/mo. Tea consumption was not associated with endometrial cancer risk. In conclusions authors suggested that these prospective data for consumption of four or more cups of coffee per day are associated with lower risk of endometrial cancer but that, on the other hand, we have to be aware that addition of substantial sugar and cream to coffee could offset any potential benefits.

REFERENCE

1 Youjin Je, Hankinson SE, Tworoger SS, DeVivo I, Giovannucci E. A Prospective Cohort Study of Coffee Consumption and Risk of Endometrial Cancer over a 26-Year Follow-Up. *Cancer Epidemiol Biomarkers Prev.* 2011;20(12):1–9.

Aljoša Mandić

Clinical significance specific alterations of the Wnt signaling in breast cancer

The aim of this study was to understand the importance of the Wnt/β-catenin pathway in the development of breast cancer (BC) and its association with different clinicopathological parameters. In the present study, alterations (deletion/methylation/expression) of some Wnt/β-catenin pathway antagonists like *APC*, *SFRP1/2*, *CDH1* and activator β-*catenin* (*CTNNB1*) were analyzed in primary BC.

Co-alterations of these genes were observed in 30% of samples with significantly high alterations in late-onset (37%) and estrogen receptor (ER) – progesterone receptor (PR) (37%).

Nuclear localization of β-catenin showed significant association with alterations in the antagonists and was also significantly high in the ER/PR−BC samples. Alterations of SFRP2 coupled with a late clinical stage and low nulliparity predicted the worst prognosis in BC patients. Therefore, the present study suggested that cumulative alterations in

more than one Wnt antagonist along with increased nuclear accumulation of β-catenin play an important role in the development of BC and have significant clinical as well as prognostic importance.

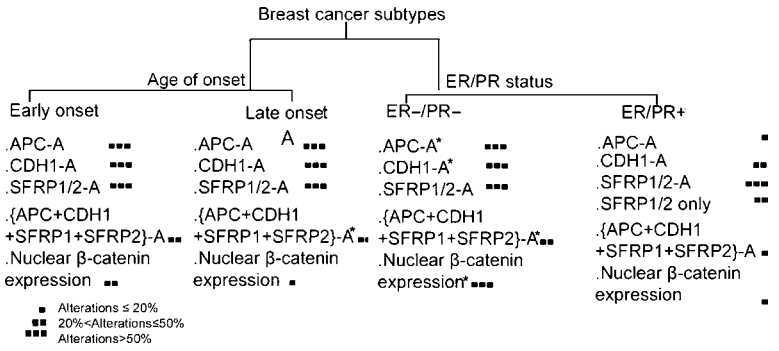


Figure 1. Summary of overall alterations in early/late-onset breast cacer (BC) and estrogen receptor/progesterone receptor (ER/PR) (+/-) BC patiens. *P<0.05 (statistically significant). A, alterations

REFERENCE

1 Mukherjee N, Bhattacharya N, Alam N, et al. Subtype-specific alterations of the Wnt signaling pathway in breast cancer: Clinical and prognostic significance. *Cancer Sci*. 2012;103:210-20.

The Nobel Prize in Physiology or Medicine 2011

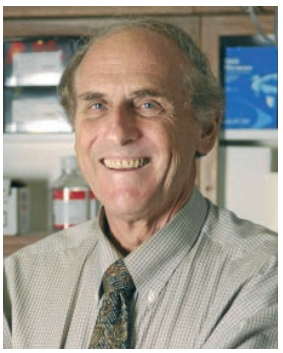
Last year's Nobel Laureates have revolutionized our understanding of the immune system by discovering key principles for its activation.

Scientists have long been searching for the gatekeepers of the immune response by which man and other animals defend themselves against attack by bacteria and other microorganisms. Bruce Beutler and Jules Hoffmann discovered receptor proteins that can recognize such microorganisms and activate innate immunity, the first step in the body's immune response. Ralph Steinman discovered the dendritic cells of the immune system and their unique capacity to activate and regulate adaptive immunity, the later stage of the immune response during which microorganisms are cleared from the body.

The discoveries of the three Nobel Laureates have revealed how the innate and adaptive phases of the immune response are activated and thereby provided novel insights into disease mechanisms. Their work has opened up new avenues for the development of prevention and therapy against infections, cancer, and inflammatory diseases.

Bruce A. Beutler was born in 1957 in Chicago, USA. He received his MD from the University of Chicago in 1981 and has worked as a scientist at Rockefeller University in New York, at UT Southwestern Medical Center in Dallas, where he discovered the LPS receptor, and the Scripps Research Institute in La Jolla, CA. Very recently, he rejoined the University of Texas Southwestern Medical Center in Dallas as professor in its Center for the Genetics of Host Defense.

Jules A. Hoffmann was born in Echternach, Luxembourg in 1941. He studied at the University of Strasbourg in France, where he obtained his PhD in 1969. After postdoctoral training at the University of Marburg, Germany, he returned to Strasbourg, where he headed a research laboratory from 1974 to 2009. He has also served as director of the Institute for Molecular Cell Biology in Strasbourg and during 2007-2008 as President of the French National Academy of Sciences.



Ralph M. Steinman was born in 1943 in Montreal, Canada, where he studied biology and chemistry at McGill University. After studying medicine at Harvard Medical School in Boston, MA, USA, he received his MD in 1968. He was affiliated with Rockefeller University in New York since 1970, where he was professor of immunology from 1988. Sadly, Ralph Steinman passed away before the news of his Nobel Prize reached him.

Taken from http://www.nobelprize.org/nobel_prizes/medicine/laureates/2011/press.html