HPV and oral contraceptives linked to cervical cancer risk

Women who test positive for human papillomavirus (HPV) could have a three-fold increased risk of developing cervical cancer if they have used oral contraceptives for more than 5 years, and up to a four-fold increased risk if they have used oral contraceptives for more than 10 years (Lancet 2002; 359: 1085–92).

“We think that long term use of oral contraceptives increases the probability of the progression of HPV infection into cervical dysplasia and cancer,” says Sylvia Franceschi, lead author of the study, “the relative risk is comparable to the relative risk for multiparity or smoking.”

Franceschi and colleagues analysed the results of case-control studies from Thailand, the Philippines, Morocco, Brazil, Peru, Paraguay, Columbia and Spain. Eight of the studies were of women with histologically confirmed invasive cervical carcinoma (ICC) and two of the studies were of women with carcinoma in situ (ISC).

The women answered a detailed questionnaire about life-long use of oral contraceptives, which included whether they had ever used contraception, their age when first used, the total duration of use, the time since first use, and the time since last use. The researchers tested for the presence of HPV using a PCR assay and it was found that 94% of the women with ICC, 72% of women with ISC, and 13% of women without cancer, tested positive for HPV.

The study concluded that there was no increased risk for women who had taken oral contraceptives for less than five years. There was also no connection between oral contraceptives and cervical cancer in women who tested negative for HPV.

“Any causal relationship between long-term oral contraception and cervical cancer would be most important in the developing world, where cervical cancer is common and few women have access to high-quality cytological screening,” says David Skegg (University of Otago, New Zealand). “A key question is the extent to which effects persist after women stop taking oral contraceptives.”

The World Health Organization (WHO) has commissioned further research in this area but states “for young non-smoking women, the health benefits of oral contraceptive use (including an reduced risk of endometrial and ovarian cancers) far exceed the health risks”.

Emma Wilkinson

Burkitt’s lymphoma suicide can be driven by serotonin

Serotonin analogues could be used to fight Burkitt’s lymphoma (BL) following the discovery of serotonin specific transporters on BL cells.

Cell-culture studies done in the UK have shown that the mood-regulating neurotransmitter serotonin enters BL cells via a specific transporter and efficiently triggers cell death by apoptosis (Blood 2002; 99: 2545–53).

Researchers from the Universities of Nottingham and Birmingham in the UK, and collaborators from Vanderbilt University Medical Center, TN, USA, used Western blotting to confirm that the serotonin transporter protein was expressed on BL cells. They subsequently used transporter assays to demonstrate active serotonin uptake. These findings support a long-presumed link between temperament and cancer risk; optimism and high serotonin concentrations promote cancer resistance, whereas depression and low serotonin concentrations can increase cancer risk.

“Since serotonin can enter cancer cells and tell them to commit suicide, this shows a dialogue between brain and immune system,” said John Gordon (University of Birmingham, UK) who was part of the study team. “Here we have the first hint that this neurotransmitter could influence the development and behaviour of a tumour arising from peripheral immune system cells.” He continued: “Although we are still unclear how such bidirectional communication might operate, knowing that it happens puts us in a position to develop drug analogues of serotonin that will do the same job but have better pharmacological properties.” The group also showed that serotonin-driven apoptosis could be blocked by drugs that inhibit the transporter protein—many of which are widely used as antidepressants. These drugs, collectively known as selective serotonin reuptake inhibitors (SSRIs), include well-known compounds such as fluoxetine (Prozac), paroxetine (Paxil), and citalopram (Celexa). They act to increase the extracellular concentration of serotonin in the brain by stopping serotonin-producing neurons from taking it back up for degradation.

In theory, their apoptosis-blocking ability might increase cancer risk, but this idea is not supported by the evidence. Gorden pointed out that there have been several studies looking at antidepressants in relation to cancer, and none suggested that they increase cancer risk. He commented: “Although we’ve seen that high doses of SSRIs stop serotonin acting on cancer cells in the test-tube, we can’t say what’s happening in the body”.

“Patients should definitely keep taking any antidepressant prescriptions,” he added.

Ironically, if patients who fear cancer stop taking SSRIs they are likely to relapse into low-serotonin depression, which may in itself increase cancer risk.

Janet Stephenson