Cigarette Smoking Linked to Increased Human Papillomavirus DNA Load

Higher baseline human papilloma virus (HPV) type 16 (HPV-16) and HPV-18 DNA load is linked to status as a current but not former smoker, according to a recent study by Xi et al in Cancer Epidemiology, Biomarkers & Prevention (2009;18:3490-3496). Women infected with HPV who currently smoke demonstrated an increased HPV DNA load compared with those who have never smoked.

Cigarette Smoking, HPV, and Cervical Cancer
Cigarette smoking has been found to increase the risk of cervical cancer in women infected with HPV. Similarly, smoking has been shown to increase the risk of an immediate precursor to cervical cancer, cervical intraepithelial neoplasia (CIN) grade 3.

Although HPV infection generally resolves without treatment and rarely leads to cervical cancer, the study by Xi et al adds more evidence to the association between smoking and CIN and cervical cancer. The Centers for Disease Control and Prevention (CDC) estimates that 11.8% of cervical cancer deaths are attributable to smoking (available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5745a3.htm; Accessed March 22, 2010).

“Based on previous publications, we know that increased HPV DNA load is associated with higher risk of cervical cancer,” says lead researcher Long Fu Xi, MD, PhD. “Based on our research, we know that higher viral load is associated with current but not former cigarette smoking. Therefore, quitting smoking may result in a reduced risk of cervical cancer.” Dr. Xi is research associate professor of pathology and adjunct research associate professor of epidemiology in the Department of Pathology at the University of Washington in Seattle.

Dr. Xi and his colleagues enrolled 1050 women in the study. Of those, 752 were infected with HPV-16, 258 with HPV-18, and 40 with both viral strains. Among the study subjects, 452 (43%) were current smokers and 101 (9.6%) were former smokers at the time of enrollment.

“The baseline viral load was statistically significantly greater for current compared with never smokers (P = .03 for HPV-16 and P = .02 for HPV-18), but not for former smokers,” the authors write. “Among current smokers, neither HPV-16 nor HPV-18 DNA load seemed to vary appreciably by age at smoking initiation, smoking intensity, or smoking duration.”

According to the study, the association between cigarette smoking and baseline viral load was not explained by race, parity, referral Papanicolaou test (atypical squamous cells of undetermined significance vs low-grade squamous intraepithelial lesion), current use of oral contraceptives, or coinfection with other HPV types.

Linear regression models were used to compare baseline viral load by a variety of measures of smoking intensity and smoking duration. Each measure of cigarette smoking was modeled independently of one another because of the strong correlation. Reducing smoking did not appear to result in a reduced HPV viral load or in a reduced risk of cancer. “Based on our results, it seems that there is no dose-response relationship between amount of smoking and HPV DNA load,” Dr. Xi explains.

One shortcoming of the study by Xi et al is that the researchers did not examine the effect of time since quitting smoking on HPV DNA load. In other words, the question of how long must a person quit smoking before their HPV viral load is reduced remains unanswered. “We have no data on date of quit smoking,” Dr. Xi notes.

Cervical Dysplasia and the Teachable Moment
The diagnosis of HPV infection or of cervical dysplasia clearly represents a “teachable moment” for the clinician, a time during which the patient is potentially receptive to medical advice and intervention. However, the teachable
moment related to HPV infection or even cervical dysplasia is in conflict with the powerful grip of smoking addiction.

The diagnosis of cervical dysplasia or a related condition offers an opportunity for the clinician to impress on the patient the need to quit smoking, says Carolyn D. Runowicz, MD, professor of obstetrics and gynecology in the division of gynecologic oncology and director of the University of Connecticut Oncology Center at the University of Connecticut Health Center in Farmington. Dr. Runowicz, who is also a former president of the American Cancer Society, reports having observed these teachable moments often in her career. “What this means is that when a person is in a health care encounter, that’s a particularly opportune time to intervene on their smoking,” says Richard D. Hurt, MD, professor of medicine at the Mayo Clinic in Rochester, Minnesota. “But, the intensity of the teachable moment has to do with the medical problem itself, how severe or how intense it is. The teachable moment is a real phenomenon, but HPV infection is on the low end of the required medical intensity for teaching.”

The finding of cervical dysplasia related to HPV infection might be a more intensely teachable moment than HPV infection. “Yes, that would move it up the ladder a little bit,” Dr. Hurt asserts.