

A better test than the Pap smear?

Results from the largest human papillomavirus (HPV) screening trial conducted to date indicate that the technique is superior to the Pap smear in sensitivity and should be considered as a routine screening tool for women at high risk of cervical cancer (*JAMA* 2000; 283:87-93). "We have discovered a set of viruses that cause cervical cancer. We have also discovered the amount of the virus you need to detect to have a clinically useful tool. We found the trade-off between specificity and sensitivity that's optimal for a clinical test," says lead investigator Dr. Mark Schiffman, a member of the Division of Cancer Epidemiology and Genetics at the National Cancer Institute in Maryland.

HPV is a very common sexually transmitted infection, with more than 30 genital types; however, only 10 to 15 types cause cancer. Current infection is measured most sensitively by DNA detection.

"Human papillomavirus is causal for cervical cancer," Schiffman said. "Some physicians don't yet accept that. It's backward thinking. It's been demonstrated in 30 countries."

Schiffman and his colleagues randomly selected more than 8500 women in Guanacaste, Costa Rica, a region with a high incidence of cervical cancer, to take part in the study. HPV testing detected nearly 90% of high-grade lesions, whereas traditional Pap smears detected only 73%. In addition, the referral rate for colposcopy was 12% with the HPV test and 7% with the Pap smear. Overall, the sensitivity of the HPV test was 88.4%, and the specificity was 89.0%. For the Pap smear groups, these numbers were 77.7% and 94.2%, respectively.

"Undoubtedly testing for the virus is more sensitive than Pap smears," Schiffman says. "However, the trade-off is that it pulls more women in who will have nothing [wrong with them]." The researchers concluded that the HPV test "will perform best in settings in which sensitive detection of high-grade lesions

and cancer is paramount. [But] because HPV prevalence varies by population, HPV testing's positive predictive value for detection of high-grade lesions and cancer will vary accordingly, with implications for utility relative to other cervical cancer screening methods."

In the future, says Schiffman, "I foresee that we will have double testing. Those who are negative on both tests will be able to extend the interval of their screening. We will have increased accuracy of testing." — *Donalee Moulton, Halifax*

Briefly . . .

X marks the chromosome for lung cancer susceptibility

A gene on the X chromosome may explain why lung cancer develops in women earlier and more often than in men (*J Natl Cancer Inst* 2000;92:24-33). Researchers at the University of Pittsburgh analysed the expression of gastrin-releasing peptide receptor (GRPR) in men and women with various smoking histories. The *GRPR* gene, located on the X chromosome, produces the receptor, which in turn leads bronchial cells to proliferate in response to gastrin-releasing peptide. This is thought to be the mechanism by which smoking may cause lung cancer. Previous studies have shown that lung cancer develops in women after less smoking exposure than in men, and more often in women who do not smoke than in male nonsmokers. This study detected GRPR expression in airway cells and tissues of more female than male nonsmokers and short-term smokers. As well, female smokers had GRPR expression in airways after less exposure to smoking than male smokers. This may explain women's increased susceptibility to lung cancer.

Audio interview with Nobel winner now on eCMAJ



A half-hour audio interview with Dr. James Orbinski, the first Canadian president of Médecins Sans Frontières/Doctors Without Borders (MSF), is now available on eCMAJ (www.cma.ca/cmaj). In December, Orbinski delivered the acceptance speech when MSF received the Nobel Peace Prize in recognition of its pioneering humanitarian work on several continents (www.msf.org/events/1999/nobel/index.htm).

Originally founded by French physicians in 1971, MSF is now "on the ground" during almost all major conflicts. The organization now has 2000 volunteers working in 80 countries. Although MSF is best known for its work during high-intensity conflicts, Orbinski stresses that much of its work is done in stable areas that simply have little or no access to health care.

In the interview, eCMAJ Editor-in-Chief John Hoey questions Orbinski about the nature of his organization's work and other issues. "What distinguishes MSF from other organizations," says Orbinski, "is our refusal to remain silent."