



# QUICK QUERIES

Topical Questions, Sound Answers



## Cervical Cancer and Pap Smears



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### ► *What is the role of the Pap smear for cervical cancer prevention?*

Cervical cancer (CC) is the second most common cancer affecting women worldwide, caused by sexual transmission of the HPV. CC has decreased by 90% in developed countries where Pap smear screening is available down to an incidence of 1% from 10%.<sup>1</sup> The approval of the HPV vaccine and HPV testing have recently caused patients and physicians to review the state of CC prevention.

In Canada, CC affects one in 128 women and is the fourth most common cause of cancer in women aged < 45.<sup>2</sup> The majority of patients are the underscreened and never-screened. Fifty per cent of Canadian women with CC did not get an annual Pap test and 60% of CC occurs in women who have not been screened in the previous three years.<sup>3</sup>

The Pap smear is a simple, cost-effective method to detect pre-malignant changes in cervical cells. Despite the lack of any randomized controlled studies, it has been irrefutably concluded by epidemiologists and public health authorities that Pap smear screening saves lives and is responsible for the decrease in mortality from this devastating disease.<sup>4</sup> Ideally, Pap smear screening is delivered through an organized program with a registry and recall system.

The provinces are in various states of achieving this with most physicians offering Pap smears opportunistically (*i.e.*, during pregnancy related visits, contraceptive counselling, or for gynecologic problems) instead of an annual well-woman check. With ideal program-based Pap smear screening, the incidence of CC would decrease from 1% to 0.5%.<sup>5</sup>

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### ► *What are the problems with the Pap smear?*

The Pap smear is not diagnostic and has limitations, with one-third of errors due to sampling and two-thirds due to interpretation.<sup>6</sup> These deficiencies have created opportunities for the small proportion of women who get invasive CC despite having Pap smears. Liquid-based cytology, for instance, is now used to create a superior specimen devoid of debris and cell

clumping, facilitating review by the cytotechnician and pathologist. Diagnostic equipment such as the automated reader can pre-select abnormal appearing slides according to set parameters.<sup>7</sup>

The sensitivity and specificity of the Pap smear are only 51% and 98%, respectively. Given the long latency period of years for CC to develop, an annual Pap smear improves the sensitivity of the test to > 88% after three years annual screening.<sup>8</sup> Nonetheless, new technologies are being considered to improve upon this figure. HPV testing, for example, was proposed to be a better first screen to replace the Pap smear,<sup>9</sup> but is less specific and not useful in women < 30-years-of-age, many of whom would test positive for the virus, regardless of whether or not they will develop dysplasia. So while 90% of women will be exposed to HPV over their lifetime, it is persistent infection and inability to clear high-risk HPV which are associated with high grade dysplasia.<sup>3</sup>

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Presently, HPV testing is useful and cost-effective for women with ambiguous (atypical squamous cells of undetermined significance) Pap smears. Positive individuals are referred to colposcopy while negative ones can return to annual screening.<sup>10</sup> In some centers, women

> 30-years-of-age receive a Pap smear and an HPV test. Those who are negative on both are at low risk and can be screened at three year intervals.<sup>11</sup>

### ► *What does the HPV vaccine mean for Pap smear screening?*

In 2006, the quadrivalent HPV vaccine was approved in Canada against the two most common strains of HPV, 16 and 18, responsible for 70% of CC. The provinces are now challenged to coordinate the information regarding Pap smear screening and immunization status in their evolving registries.

In vaccinated females, the volume and frequency of abnormal Pap smears is expected to decrease. With a decline in HPV 16 and 18, a positive HPV test result will be less frequent among women in their 20s, improving the specificity of the test. In the non-vaccinated, precancerous lesions due to HPV 16 and 18 will still be present. Therefore, with time, vaccine and pre-vaccine cohorts will develop.<sup>12</sup>

We are at an exciting point in the prevention of CC. The FP is best poised to counsel and implement these new advances. In the short term, women should continue with the Pap smear as per their provincial guidelines.<sup>13</sup> As research continues, the Pap smear will incorporate new biomarkers to improve its sensitivity and HPV testing will be better defined as individual genotyping progresses.<sup>14</sup> In the final analysis, cost-effectiveness will be considered. However, the greatest improvement to decrease the incidence and mortality of CC in Canada today would be to access the underscreened and never-screened women.

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