

The changing landscape for cervical screening

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Cervical cancer screening needs to take into account a partially vaccinated population and new technologies

A national, well funded and organised program of screening using the conventional Pap smear has significantly reduced the incidence of and mortality from cervical cancer in Australia.¹ While the program has been in place, there has been a great increase in knowledge of the pathogenesis of cervical cancer, with certain oncogenic subtypes of human papillomavirus (HPV) shown to be a necessary cause for development of this disease.² In addition, a national program of vaccination against two of the 15 oncogenic viruses began in April 2007, and tests to detect HPV are now available. Furthermore, research showing that new technologies for screening cervical samples are superior to conventional cytology has also been published.^{3,4}

How is the cervical screening program responding to the presence of a partially vaccinated population and these newly available tests?

When the Pharmaceutical Benefits Advisory Committee assessed the value of funding HPV vaccination, it noted that the current cumulative lifetime risk of cervical cancer in Australia's screened population is 0.78% — a substantial reduction from the estimated 2.4% risk in an unscreened population, reflecting the success of the screening program. With continued screening, this risk was predicted to further decrease to 0.38% following vaccination of 12-year-old girls, 0.43% for 14-year-old girls and 0.59% for 26-year-old women.⁵ The Committee further commented that there would be cost savings if vaccination were to completely replace cervical screening, but the cervical cancer lifetime risk would increase to 1.173%.⁵ The recommendation therefore is that screening must continue after vaccination. The screening interval and screening test for vaccinated women should be different to those for unvaccinated women and should be determined by population-based research over the next 5–10 years, as the vaccinated cohort reaches maturity. A national HPV vaccination register is being established, which will be critical for determining the appropriate screening regimen.

HPV testing is already recommended and funded as a “test of cure” for follow-up of high-grade cervical disease after treatment. The Digene HPV test is used in Australia and detects any one of 13 high-risk HPV subtypes but does not identify the specific subtypes. Although some individual HPV subtyping assays are available, these are expensive and not widely used, and no serological tests for HPV are available in routine practice. Use of the HPV test is therefore limited but, given its importance, should its use be expanded for screening and management of cervical disease?

There has been much discussion overseas about replacing cervical cytology tests with HPV testing for primary screening.⁶ Currently, there is no justification for this as HPV testing is highly sensitive but not specific. It has a limited role in women under the age of 30 years, as large studies have shown that about 25% of women in this age group test positive for the oncogenic viruses.⁷ The great majority of these women clear the virus naturally, usually via a cell-mediated immune response or, less often, through an antibody response. Such infected women may not show any sign of disease. It is when the virus persists that women are at greater risk of both high-grade cervical intraepithelial disease and invasive

cancer. HPV testing is also not recommended before vaccination⁸ in women who request it but are already sexually active as the decision to proceed with vaccination will not be altered by the results of the test.

HPV testing may have a greater role in the management of indeterminate abnormalities detected by cervical cytology tests. Data from large United States studies are fairly compelling in assigning a true risk of significant disease based on cervical cytology and HPV testing. The latter is more accurate than colposcopy in determining the significance of low-grade squamous intraepithelial lesions detected by cervical cytology. So-called “reflex” HPV testing in women with these findings is recommended in the US.⁹

Another major question for cervical cancer screening in the short term is whether image-guided liquid-based cytology samples should be used as the preferred screening test. The use of liquid-based cytology in this country has long been controversial.¹⁰ However, there is now good evidence that one of the techniques — the ThinPrep Imaging System (Hologic, Marlborough, Mass, USA) — is superior to conventional cytology.⁴ This technique decreases the number of unsatisfactory samples and detects more true abnormalities. There are also substantial laboratory efficiencies when using this technology, which could potentially overcome the chronic shortage of trained scientists. The increased sensitivity might allow the screening interval to be lengthened. This technique also provides a sample for HPV and other microbiological testing, and is ideal for a vaccinated population in which the number of screen-detected abnormalities will decrease.

Although Australia has an enviable record in the control of cervical cancer, new knowledge and associated technologies should be incorporated into screening and management of cervical disease, as they offer real benefits. Both HPV testing and ThinPrep imaging are more expensive than conventional cytology, but they could be cost-effective if used appropriately in conjunction with a comprehensive review of the cervical screening program.

Competing interests

I have received travel assistance to attend meetings from Cytoc, the manufacturer of the ThinPrep Imaging System.

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