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Papillomavirus, or HPV facts are not always clear. Fiona Hale answers the most commonly asked questions.

WHAT IS HUMAN PAPILOMAVIRUS?

Human Papillomavirus, or HPV, is an extremely common virus, which can cause genital warts, cervical cell changes and cervical cancer. There are over 100 types of HPV. Types 6 and 11 are associated with genital warts. Types 16 and 18 are regarded as the types, which most often lead to cervical cancer. Cervical cancer kills more women worldwide than childbirth. Approximately 80%

Cervical cancer is the most common cancer affecting women in developing countries, where 80% of all cervical cancer deaths occur. It is a leading cause of mortality in HIV positive women.

of all cases of cervical cancer worldwide occur in less-developed countries (WHO, 2007), because prevention programmes are either nonexistent or poorly executed (ACCP, 2004).

HOW DOES HPV RELATE TO HIV?

HIV positive women have a high prevalence of HPV infection. Studies have found that HIV positive women are five times more likely to have a high-risk HPV type, than women who are HIV negative (Moodley et al, 2006), and are infected with a broader range of HPV types than HIV negative women (Clifford et al, 2006). HIV positive women are also more likely to develop HPV-related cervical lesions and aggressive forms of cervical cancer (Danso, Lyons & Bradbeer, 2006).

Cervical cancer is recognised as an AIDS-defining illness (National Center for Infectious Diseases, 1992), and is a leading cause of mortality in HIV

positive women (PATH, 2007). Unlike some virus-association conditions, such as Kaposi's sarcoma or non-Hodgkins lymphoma, HAART (Highly Active Anti-Retroviral Therapy) does not appear to have led to a decline in the incidence of cervical cancer (Palefsky, Gillison & Strickler, 2006). Like HIV, HPV is often stigmatised as a sexually transmitted infection (Khan et al, 2007).

HOW IS CERVICAL CANCER DIAGNOSED AND TREATED?

Cervical cancer is one of the most preventable and treatable cancers (ACCP, 2004). Cervical abnormalities are detected with a cervical smear test, also known as a Pap smear or papanicolau smear. It is generally recommended that HIV positive women should receive an annual Pap smear. However, in many countries this does not happen. Pap smears need to be sent to a laboratory and the results then sent back to the doctor. Results may take some time, or get lost. For some women, it may be difficult to return to collect the results (PlusNews, 2007). In many places, the health system does not have the resources to make sure cervical screening happens effectively – even when there is a screening policy in place (Stevens & Bomela, 2008).

Successful trials of new techniques which would cut down the need for laboratory analysis of cell samples, have taken place. VIA – or visual inspection with

acetic acid – is simple, inexpensive and uses ordinary vinegar. Women get their results immediately, and follow-up and treatment can be arranged on the spot (PAHO, 2003; Sankaranarayanan et al, 2004). When abnormalities are detected early and confirmed through colposcopy (examination of the cervix to assess the extent of the abnormality), progression to invasive cervical cancer can often be avoided through outpatient treatments, such as cyrotherapy and loop excision, which remove the affected cells in the neck of the womb.

WHAT IS THE HPV VACCINE?

Since 2006, two new HPV vaccines have become available. They are licensed for use in a number of countries, and national vaccination programmes are now in place in the United Kingdom and the United States – though the cost of approximately US\$375 places it out of reach for many countries. One vaccine (Cervarix) protects against HPV types 16 and 18, and the other (Gardasil) protects against types 16, 18, 6 and 11 (which cause genital warts). The World Health Organisation (WHO) recommends that the primary target for vaccination should be adolescent girls of 9 to 13 years of age, aiming to reach them before sexual debut and, thus, before any exposure to HPV. WHO also recommends consideration of 'catch-up vaccination' for a secondary target group of young women aged 14-26 (WHO, 2006).

IS HPV VACCINATION SAFE FOR HIV POSITIVE WOMEN?

In some contexts, significant numbers of girls and women in both 'primary' and 'secondary' target age ranges for vaccination, may be HIV positive. Information on the safety and efficacy of HPV vaccines in HIV positive people is not yet available (WHO & UNFPA, 2006). Safety trials in HIV positive women are currently being conducted and due to be completed by 2010. If mass vaccination is to be promoted in countries with high HIV prevalence, it will be important to take into consideration the outcome of safety trials. Many researchers think that safety will not be a major issue. The vaccines are not live (eliminating concern that they may cause infection), and experiences with other vaccines in immune-compromised people is reassuring. However, it will be important to evaluate possible toxicity and other complications for people living with HIV (Palefsky, Gillison & Strickler, 2006).

IS HPV VACCINATION EFFECTIVE IN HIV POSITIVE WOMEN?

There are concerns among researchers that current HPV vaccines will be less effective in protecting against cervical cancer in HIV positive women, than in HIV negative women. This is because a number of recent studies have analysed HPV genotypes in HIV positive women with pre-cancerous cervical cell

changes or cervical cancer. The findings have been contradictory. Studies in Zambia and Kenya have found that the HPV genotypes involved in cervical cancer are the same for HIV positive women and HIV negative women (Ng'andwe et al, 2007; De Vuyst et al, 2008). However, a global analysis of HPV genotypes in HIV positive women with abnormal cell changes and/or cervical cancer, and a second study in Zambia, suggests that HPV genotypes, other than HPV 16 and 18, may frequently be associated with cervical cancer in HIV positive women (Clifford et al, 2006; Sahasrabudde et al, 2007).

So, while vaccination may provide protection against HPV 16 and 18 to HIV positive women not yet exposed to these genotypes, the range of HPV types causing disease in HIV positive women is likely to mean the benefits of vaccination are reduced. The effectiveness of HPV vaccination is also likely to depend on the timing, with more benefits if it is given once HAART has been successfully initiated (Palefsky, Gillison & Strickler, 2006). Against this backdrop, some researchers have called for the development of new, 'polyvalent' vaccines, which would protect against numerous HPV genotypes, increasing the protection available for HIV positive women (Sahasrabudde et al, 2007; Chaturvedi & Goedert, 2006).

VACCINATING BOYS AND MEN

Current WHO guidelines do not include vaccination of boys. However, the exclusive focus on vaccinating girls and women has gender implications, and adds to the health-seeking burden on women, who may already face difficulties in accessing sexual and reproductive health services (Harries et al, 2008).

CONTINUED NEED FOR CERVICAL SCREENING

Even if HPV vaccination is in place, it will not eliminate cervical cancer. It will continue to be important for women to receive regular screening (whether by Pap smears or 'test-and-treat' techniques, such as VIA). This is especially important for HIV positive women, in whom cervical cancer can be particularly aggressive and fast-developing. Continued advocacy to improve screening policy and implementation is needed.

POSSIBLE NEXT STEPS

Research is urgently needed to fill a number of gaps in current knowledge. These include:

- How to implement effective and accessible HPV/cervical cancer prevention, screening and treatment in low-resource, high HIV-prevalence settings
- Safety of HPV vaccination for HIV positive women
- HPV genotypes in HIV positive women

with invasive cervical cancer

- How to ensure that the existence of HPV vaccines does not increase gender and health inequalities (including more research on the usefulness of vaccinating boys and men, vaccination pricing policies, acceptability issues, etc)

Any research on this issue must be responsible, and sensitive to ethical issues including:

- HIV and HPV testing of research participants
- Power dynamics between healthcare professionals/researchers seeking research participants, and women seeking healthcare

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References

ACCP, Alliance for Cervical Cancer Prevention. 2004. *Planning and Implementing Cervical Cancer Prevention and Control Programmes: A Manual for Managers*, Seattle, ACCP.

Chaturvedi, A.K. & Goedert, J.J. 2006. 'Human papillomavirus genotypes among women with HIV: Implications for research and prevention'. In: *AIDS*, 20(18), pp2381-2383. [Online]. [www.aidsonline.com]

Clifford, G. et.al. 2006. 'Human papillomavirus types among women infected with HIV: A meta-analysis'. In: *AIDS*, 20(18), pp2337-2344. [Online]. [www.aidsonline.com]

Danso, D., Lyons, F. & Bradbeer, C. 2006. 'Cervical screening and management of cervical intraepithelial neoplasia in HIV-positive women'. In: *International Journal on STD & AIDS*, 17, pp579-586. [Online].

De Vuyst, H. et.al. 2008. 'Human papillomavirus type in women with invasive cervical carcinoma by HIV status in Kenya'. In: *International Journal of Cancer*, Volume 122, pp244-246. [Online]. [www3.interscience.wiley.com].

Harries, J. et.al. 2008. 'Preparing for HPV vaccination in South Africa: Key challenges and opinions'. In: *Vaccine*, 27(1), pp38-44. [Online].

Khan, J.A. et.al. 2007. 'Personal meaning of human papillomavirus and Pap test results in adolescent and young adult women'. In: *Health Psychology*, 26(2), pp192-200. [Online].

Moodley, J.R. et.al. 2006. 'HIV and pre-neoplastic and neoplastic lesions of the cervix in South Africa: A case-control study'. In: *BMC Cancer*, 6(135) [Online].

National Center for Infectious Diseases Division of HIV/AIDS et.al. 1992. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults. In: *Morbidity and Mortality Weekly Report*, December 18, RR-17 [Online]. [www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm]

Ng'andwe, C. et.al. 2007. 'The distribution of sexually-transmitted Human Papillomaviruses in HIV positive and negative patients in Zambia, Africa'. In: *BMC Infectious Diseases*, Volume 7 (77). [Online].

PAHO (Pan American Health Organisation) (2003) *Visual Inspection of the Uterine Cervix with Acetic Acid (VIA): A Critical Review and Selected Articles*. Washington: D.C. PAHO [Online]. [www.paho.org/English/AD/DPC/NC/cc-via.pdf]

Palefsky, J.M., Gillison, M.L. & Strickler, H.D. 2006. 'HPV Vaccines and Screening in the Prevention of Cervical Cancer'. In: *Vaccine*, 24 (3), pp140-146. [Online].

PATH (2007) Preventing cervical cancer: Unprecedented opportunities for improving women's health. In: *Outlook*, Volume 23, Number 1, June. [Online] [www.rho.org/files/PATH_outlook23_1_web.pdf]

PlusNews. 2007. 'SOUTH AFRICA: Cervical cancer vaccine offers distant hope', 19 June 2007 [Online]. [www.plusnews.org/Report.aspx?ReportId=72809]

Sahasrabudde, V.V. et.al. 2007. 'Prevalence and distribution of HPV genotypes among HIV-infected women in Zambia'. In: *British Journal of Cancer*, 96, pp1480-1483 [Online].

Sankaranarayanan, R. et.al. 2004. 'Initial results from a randomized trial of cervical visual screening in rural south India'. In: *International Journal of Cancer*, 109(3), pp461-467. [Online].

Stevens, M. & Bomela, N. 2008. 'Cervical cancer – is vaccination the way to go?'. In: *Nursing Update*, May, p37. [Online]. [www.hst.org.za/publications/745]

World Health Organization & United Nations Population Fund. 2006. *Preparing for the introduction of HPV vaccines: Policy and programme guidance for countries*. Geneva: WHO. [Online] [www.who.int/reproductive-health/publications/hpvpvaccines/]

World Health Organization. 2007. *Human papillomavirus and HPV vaccines: Technical information for policy-makers and health professionals*. Geneva: WHO. [Online]

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