

Controversial new vaccine to prevent cervical cancer

Trials show that a new vaccine can prevent infection with the human papillomavirus (HPV) that causes cervical cancer. But will the vaccine benefit women in poor countries who — unlike their wealthy counterparts — have limited access to testing and treatment?

Almost half a million women develop cervical cancer every year; more than half of them die as a result of their condition.

More than 80% of the burden of this easily detectable and preventable disease is borne by developing countries, where cervical cancer accounts for 15% of all cancer deaths but which have only 5% of the world's cancer resources.

A woman in the United States has a 70% chance of surviving cervical cancer thanks to relatively easy access to Pap smears or tests to detect early signs of cancer, as well as follow-up treatment.

Not so for her counterpart in Thailand who has a 58% chance of survival, or India, where there is only a 42% chance of beating cervical cancer; in sub-Saharan Africa the survival rate drops to 21%. While 61% of women with cervical cancer in the developed world will survive because they have access to testing and treatment, only 41% of their developing world counterparts will get the treatment they need to survive.

The good news is that cervical cancer has joined a growing list of cancers that can be ascribed to infectious diseases, which can be identified and treated.

Great strides have been made in understanding the crucial role played by the human papillomavirus (HPV), particularly two strains — HPV16 and HPV18 — that between them account for 70% of cervical cancer cases.

Now a vaccine to prevent HPV infection is on the horizon that holds the promise of a radical reduction in the number of women who will be vulnerable to cervical cancer. In October 2005, Merck & Co., Inc. announced the results of its Phase III study on GARDASIL™.

The study comprised over 12 000 women in 13 countries who were given three doses of the vaccine within six months and were monitored for two years. The vaccine prevented 100% of high-grade cervical pre-cancers and non-invasive cervical cancers that were

associated with HPV16 and HPV18.

GlaxoSmithKline's Cervarix™ is undergoing Phase III trials and has produced similarly startling results. Neither product has yet been approved for sale and many fundamental questions, such as the vaccines' cost, long-term efficacy, optimum dosage and age at vaccination, remain unanswered.

Even once the vaccines are on the market, the benefits of widespread vaccination against HPV16 and HPV 18 will take one to two decades to emerge, as vaccination is aimed at protecting girls before they become sexually active and cervical cancer can result from HPV infections that occurred years before they manifest as cancer lesions. In time, however, a vaccine has the power to change the face of cervical cancer prevention.

"Vaccination holds much promise for primary prevention of cervical cancer in the future. It will be well-accepted, but for that to happen the evidence of efficacy has to be firmly established and the cost has to be affordable to developing countries," says Dr Gauden Galea, Regional Adviser on

Noncommunicable Diseases at WHO's Regional Office for the Western Pacific.

Even for developed countries, it is too early to say what impact an HPV vaccine will have on the allocation of resources to combat cervical cancer. In Hong Kong SAR, for example, where over 60% of women have had at least one Pap smear, the potential advent of a vaccine has received a moderate response.

"The impact of the HPV vaccine will depend on the medical profession's and the public's acceptance of it, the timing and cost involved," says Dr Susan Fan, Executive Director of Hong Kong SAR's Family Planning Association, one of the largest providers of cervical cancer screening in the city.

"If there is sufficient evidence to justify the cost-benefit of such a vaccine, and its use is endorsed by relevant authorities such as the Department of Health's Advisory Committee on Immunization, the Association may consider introducing it."

Although the debate about the cost-benefit ratio of HPV vaccination has yet to begin, even further down the line is the potential for ethical or religious objection to a vaccine to prevent a sexually transmitted disease that is targeted at pre-adolescent girls.

HPV can be transmitted in other ways, but in order to cause cervical cancer there must always be contact with the cervix. That means that when HPV causes cervical cancer, it is a sexually transmitted infection (STI).

That's why news of a forthcoming HPV vaccine in the United States was greeted with protest from conservative Christian groups who argued that it would promote sexual promiscuity among children.

No one knows whether there will be objections to the vaccine along similar ethical and religious grounds in developing countries once the public debate reaches them as well.

"We were expecting that reaction from some groups but we don't think it will be a problem generally. It is difficult to say at this stage," says Dr Nathalie Broutet of WHO's Department of Reproductive Health and Research.

"Discussions are needed

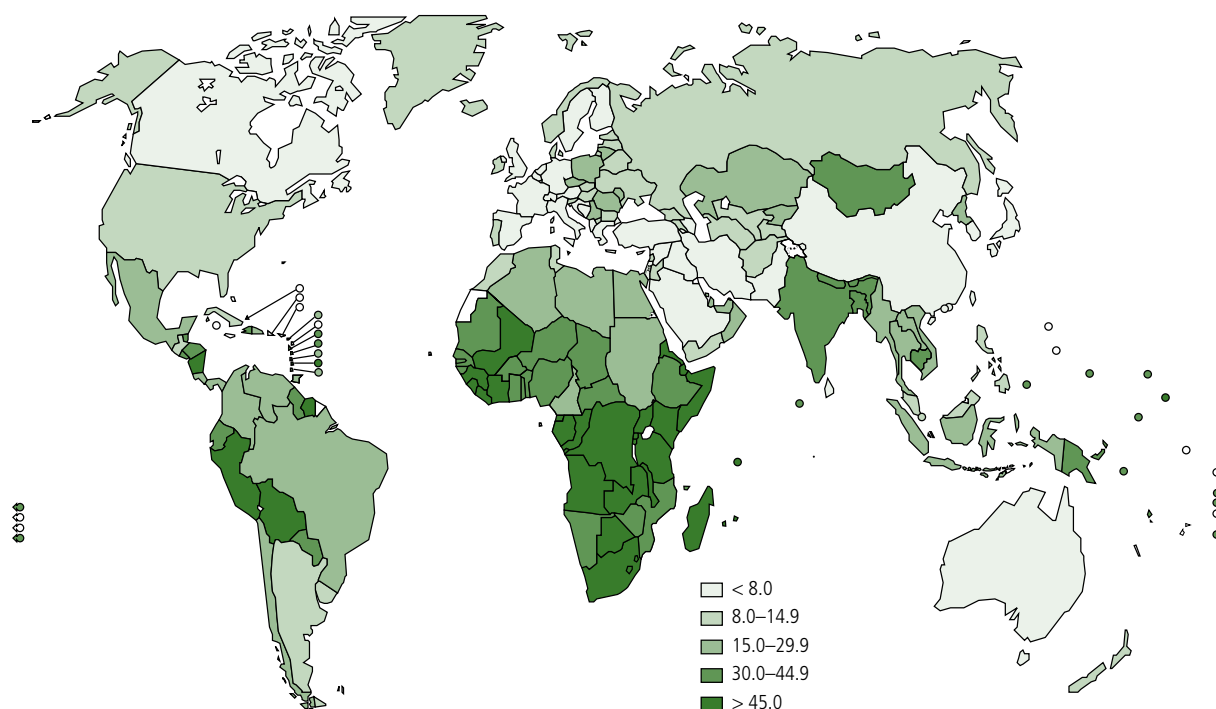
to determine whether this vaccine should be presented as an STI vaccine as well as a cervical cancer vaccine." This is particularly true for the Merck vaccine as it also covers HPV6 and HPV 11, the two strains which account for 90% of all cases of genital warts.

Moreover, clinicians who have worked hard to get women enrolled in screening programmes may be reluctant to bring the stigma of an STI to promotion campaigns for cervical cancer prevention. "There has been a real breakthrough in terms of understanding the virus and its relation to cervical cancer but not in terms of communicating that to the public," says Dr Catherine d'Arcangues Coordinator of

“Vaccination holds much promise for primary prevention of cervical cancer in the future.”

Dr Gauden Galea, Regional Adviser on Noncommunicable Diseases at WHO's Regional Office for the Western Pacific.

Global incidence of cervical cancer, projections for 2005



Source: This map is based on mortality, incidence and burden of disease projections produced for *Preventing chronic diseases: a vital investment*. Geneva: World Health Organization: 2005. http://www.who.int/chp/chronic_disease_report/en.

For a description of the methods used to produce these projections see *Projections working paper* at www.who.int/evidence/bod (select fourth link on page).

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WHO's Department of Reproductive Health and Research.

In many developing countries that breakthrough has been in getting cervical cancer recognized as a serious public health threat that can be effectively averted even in a low-resource setting. For decades the Pap smear test has successfully detected cervical abnormalities and cytological screening has played a vital role in cervical cancer prevention in the developed world. However, the test requires a sophisticated health-care infrastructure, including laboratories and highly-trained technicians to interpret the results, as well as multiple visits for testing, results and subsequent treatment, putting it beyond the reach of many women in the developing world.

"Together with the inconvenience of two or more visits per woman, plus the cost, there is also the issue of unreliable testing which can happen unless there are laboratories that are processing Pap smears in significant numbers. Pap smears are probably not as attractive as going for visual inspection with acetic acid (VIA)," says Galea.

At the JHPIEGO Cervical Cancer Prevention Program conference in

Thailand in December 2005, the key message that delegates took away with them was that VIA followed by immediate cryotherapy — the exposure of tissues to extreme cold to eliminate abnormal cells — can be a viable alternative to cytology in areas where it is prohibitively expensive to set up cytology services.

In Thailand, where cervical cancer accounts for 20.9% of cancer incidence — more than breast cancer at 16.3% — the disease is recognized as a public health problem, but the highest-risk group of women has been left out by Pap smear-based screening programmes.

"We have a shortage of cytopathologists and not enough coverage. Pap smears are done in urban areas and not in the rural areas where most of the high-risk women live," says Professor Khunying Kobchitt Limpaphayom of the Department of Obstetrics and Gynaecology at Chulalongkorn University, Bangkok.

“There is no question that early detection will continue to be a key element even once a vaccine is available.”

WHO is implementing a VIA-based see-and-treat approach in six African countries — Madagascar, Malawi, Nigeria, Uganda, the United Republic of Tanzania and Zambia.

As with other cancers, WHO's recommended approach to cervical cancer is comprehensive, comprising prevention, early detection and screening, treatment and palliative

care. The future addition of vaccine to the armoury in the fight against cervical cancer will be only one component of any successful strategy, says Dr Andreas Ullrich, Medical Officer Cancer Control at WHO's Department of Chronic Diseases and Health Promotion.

"Immunization if available will have to be added [in the area of prevention] to the other components of cervical cancer control. There is no question that early detection will continue to be a key element even once a vaccine is available." ■

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