## Thoughts on HPV vaccines

'The appearance of the two human papilloma virus (HPV) vaccines is a very exciting development but there is a lot of hard work and hurdles to overcome before we will be able to start using them,' says Professor Lynette Denny of the Department of Obstetrics and Gynaecology and the Gynaecology Oncology Unit at Groote Schuur Hospital.

*Professor Lynette Denny.*

Some 70% of cervical cancers are caused by infection of the cervix with HPV types 16 and 18 and cervical cancer is the leading cancer among women in developing countries. Denny says that the vaccine would be of particular value in poor countries due to the failure to initiate or sustain Pap smear-based screening programmes for the prevention of cervical cancer.

The vaccine is a prophylactic vaccine and therefore must be administered prior to infection. HPV is transmitted sexually and the ideal time to administer the vaccine is prior to the onset of sexual activity, which means administering the vaccine to adolescents and even girls of 12 years and younger – to prevent a disease that may occur only in their 50s.

'This is going to be a hard sell, particularly to politicians, who prefer to see immediate "returns" on their actions, as the public health benefits are only going to become apparent many years into the future,' says Denny. 'And since one is vaccinating against a sexually transmitted infection there may be objections from religious groups and others that it will encourage promiscuity.'

Another key issue is that it is going to require a new level of infrastructure, Denny says, since in developing countries in particular, adolescents are not traditionally part of vaccination programmes. Coupled with this is that the vaccine is very temperature dependent and requires the maintenance of a cold chain, which is another challenge in many developing countries.

Then there is the question of whether or not boys should be vaccinated, since they are the vector for the HPV infection. 'My view is that we should start with girls and as the resources increase, then expand the programme to include boys and older women,' says Denny.

### Trials

So far, Denny says, while there have been some trials of the vaccines in developing countries there have been none in Africa, and accordingly she and a group of colleagues have an 'application in process' to investigate a number of issues, including barriers, community perceptions and logistical issues in the local setting.

'It is critical we get some country-specific data and we expect the project to take about a year to unravel these issues.'

Also Denny says she is working with a hospital group in Dakar, Senegal designing a protocol to undertake a trial in that country, and that is expected to start later in the year.

A further trial in preparation is to undertake a study of the vaccine in HIV-positive women, as it is expected that between 30% and 40% of HIV-positive women who don't have HPV are expected to be able to benefit.

But perhaps the biggest issue to be overcome, Denny says, is whether the public health system will 'buy in' to the vaccines, since the current costs are 'prohibitive'.

'There is little doubt the vaccines will be available in the private sector, but we need to establish their affordability and feasibility in the public sector,' says Denny, adding that both of the manufacturers have committed themselves to assisting with a tiered pricing programme for developing countries.

### HPV vaccines

The two HPV vaccines are Gardasil from Merck & Co., Inc, and Cervarix from GlaxoSmithKline.

Both vaccines are developed from DNA-free virus-like particles (VLPs), synthesised by self-assembly of fusion proteins of the major capsid antigen L1. Merck's vaccine is a quadrivalent vaccine containing L1 VLPs of types 6, 11, 16 and 18 expressed in *S. cerevisiae* yeast. Inclusion of types 6 and 11 in the vaccine is expected to prevent more than 90% of cases of genital warts and to protect against the early cervical dysplasia seen with types 6 and 11. GSK's vaccine contains VLPs of types 16 and 18 and is based on recombinant baculovirus technology.

Results from large studies of the 2 vaccines, with about 2 – 5 years of follow-up, showed almost 100% protection against cervical cancer precursor lesions related to the vaccine genotypes. For Gardasil, protection against genital warts was 95 – 99%. However, because of the heterogeneity of HPV genotypes in different parts of the world, the impact of the 2 vaccines may vary across regions. Gardasil was registered in a number of countries, including the USA and European countries in 2006, while the first registrations for Cervarix are expected early this year.