Summary

Expert Group on Papillomavirus Disease Prevention. Report of the study by the Expert Group on Papillomavirus Disease Prevention appointed by the National Institute for Health and Welfare. National Institute for Health and Welfare (THL). Report 28/2011. 121 pages. Helsinki, Finland 2011.

Task of the Working Group

In spring 2008 the National Institute for Health and Welfare (THL, formerly the National Public Health Institute) appointed a working group to survey the burden of human papillomavirus (HPV) disease in Finland and to propose the best possible measures for further reduction of the disease burden from cervical cancer and other HPV diseases. In its proposal the working group was expected to include, in particular, a stand on the most effective screening method for cervical cancer and a stand on the inclusion of an HPV vaccine in the national vaccination programme.

In addition to assessment of the burden of HPV diseases and assessment of organised screening, the working group assessed the extent of Pap smear testing outside the screening programme. The working group also compiled data on the efficacy and safety of vaccine preparations in use, and carried out a cost-effectiveness analysis.

Burden of Disease

There are more than 100 papillomavirus types, of which 14 are considered high-risk HPV types causing cervical cancer. HPV infection is mainly sexually transmitted and is very common. Approximately one in four young women about 20 years of age carries a high-risk HPV type. Most HPV infections clear up on their own within two years of transmission. Sometimes, however, HPV infection is prolonged and proceeds to a premalignant condition or to cancer. The period between detection of HPV infection to the development of cancer in general is at least seven years, usually longer.

About 150 cases of cervical cancer are diagnosed in Finland each year, approximately one-third of which are fatal. Screening for cervical cancer is done to find developing premalignant conditions by means of Pap smear testing and further histological analysis. Detected premalignant conditions that are at least moderately serious (cervical intraepithelial neoplasia, CIN 2+) are treated surgically. Each year a little under 500,000 Pap smear tests are performed in Finland for screening purposes; about two-thirds of them are done outside the organised screening programme. About 2,800 premalignant conditions are detected per year, of which approximately 2,000 are at least moderately severe. It is estimated that screening can prevent about 80% of cervical cancer cases. The healthcare costs caused by cervical cancer and its premalignant conditions at present are 9.3 million euros a year.

In addition, HPV is the underlying cause of a share of cancer, inter alia, of the tonsil, penis, anus and female external genitalia. Screening for these cancer types is not done in Finland. The working group assessed the disease burden of these cancers at a rough level. Aside from cancer, HPV causes over 6,000 condyloma cases per year in Finland.

Vaccines

At present, two vaccine preparations for HPV are available. They protect against HPV infection and the subsequent premalignant conditions and cancers. So far, the scientific evidence of the efficacy of these vaccines against cancer is the indirect evidence obtained concerning efficacy against HPV infection and premalignant conditions. Both vaccines protect against the two most serious HPV types (16, 18) causing cancer. The

prophylactic efficacy of both vaccines against HPV types causing at least moderately severe premalignant conditions is nearly 100%. In addition, one of the two protects against the two most common HPV types (6, 11) causing condyloma. Both vaccines also provide some protection against infection from other HPV types, one of them slightly more broadly than the other.

Enough data on the safety in widespread use of two preparations currently on the market have accumulated to be able to make a recommendation. On the basis of the HPV vaccine studies reported, there is no reason to suspect that the vaccines would be associated with any significant adverse immunological effects. So far, however, the risk of extremely rare autoimmune diseases cannot be excluded, although several million vaccines of each type have been administered; one of the two has even been administered to tens of millions of people.

Conclusions and Recommendations

Screening of those not vaccinated

On the basis of the extensive study and mathematical modelling, the working group determined that reducing Pap smear testing outside organised screening and optimising the screening programme can prevent more cases of cervical cancer with less adverse effects and at substantially lower costs, when compared against the current practice. This can be accomplished by reducing overtesting and excess treatment among young women, by continuing the screening of HPV-positive women past the current screening age and by developing screening by means of HPV testing in a controlled and planned manner.

The working group recommends that organised screening be started at the age of 25 years and continued to the age of 65 years so that, from the age of 35 years, a test for the human papilloma- virus (HPV) would be used as the primary screening test. In addition, if the test result at the age of 65 years is positive, screening should be continued until the age of 85 years or until the HPV test result on the next test round is negative.

At present, aside from organised screening, extra screening tests are performed, inter alia, in the private sector and in primary healthcare. The costs of these extra screening tests are about three times the costs of organised screening. Moreover, Pap test screenings of very young women outside the organised screening easily lead to unnecessary treatments, as most changes clear up without treatment. The working group suggests that measures be taken to reduce unnecessary Pap test screening, inter alia by providing guidelines for primary healthcare and eliminating health insurance reimbursement for opportunistic Pap smear tests.

Vaccination of girls

Significant health benefits are achieved with HPV vaccines. On the basis of cost-effectiveness analysis, from the perspective of cervical cancer and HPV disease burden, a vaccination programme for young girls about 12 years of age is cost-effective in the long term and, depending on the price of the vaccine, even saves healthcare costs. Vaccination would probably cost about two to three million euros a year. According to the modelling, the effects of the vaccination programme begin to surface in less than ten years from launching of the programme, in all vaccinated age classes. The working group recommends the inclusion of an HPV vaccine in the vaccination programme for 11–12 year-old girls. Furthermore, the working group recommends that, during the initial stage, a so-called catch-up programme be implemented among girls of upper-level comprehensive school age, i.e. that 13–15 year olds would be offered the vaccine the year the vaccination programme is started.

Screening of those vaccinated

Screening for cervical cancer must be done also among vaccinated age classes because the vaccines do not protect against cancers caused by all HPV types. Screening among the vaccinated age classes must be optimised further. Continuation of the current massive Pap smear testing of the vaccinated population outside organised screening is extremely expensive in view of the benefits achieved.

Vaccination of boys

Vaccination of boys would seem to be cost effective if other HPV-based cancers are considered in the analysis. For the time being, however, the working group does not recommend the vaccination of boys. The situation should be reconsidered in the coming years because among boys, HPV causes cancer, e.g. of the penis, tonsil and anus. Additional data are required about the aetiological fraction of HPV in these cancers and the prophylactic effect of the vaccine against them. These data will probably be obtained in the near future.