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Prevention of cervical cancer

Diploma thesis

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Written Declaration

I declare that I completed the submitted work individually and only used the mentioned sources and literature. Concurrently, I give my permission for this diploma/bachelor thesis to be used for study purposes.

In Prague on March 2, 2010 Ingvild Berland

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Contents

Introduction

I chose the theme of my diploma thesis, prevention of cervical cancer not based on my long-term interest in this subject, but after my clinical practise during 5th year of medicine. I was fortunate enough to be accepted to do parts of my practical training in a hospital in Molde, Norway. My consultant there was an experienced gynaecologist that thought me as much as possible in few weeks. In particular he thought me about cervical cancer and ways how it is possible to prevent it. I also saw many patients affected by the cancer and took part in prevention of some that might suffer from the cancer if they would not get this treatment.

To see the outcome without sufficient prevention was sad, but also very inspiring, it was an excellent method of learning how important prevention can be and that the best way how to treat disease is in fact to find ways how to prevent it. Cervical cancer and its prevention programme is an excellent example of how medicine has succeeded and I hope that reading this diploma work will help the reader understand the degree of its value.

Review of current knowledge on the topic based on the literature research[1].

Cervical carcinoma

Despite dramatic improvements in early diagnosis and treatment, cervical carcinoma is one of the major causes of cancer related deaths in women, especially in the developing world.

After the papanicolaou (pap) smear was introduced 50 years ago, the incidence has dropped a lot. The pap smear remains the most successful cancer screening test ever developed. In areas where screening is regularly, the cancer mortality has reduced as much as 99%!!

But as a concequence the incidence of CIN has increased, but this is because the pap smear detect these precursor lesions at an early stage- permitting discovery of these lesions while curative treatment still is possible.

Cervical intraepithelial neoplasia CIN and squamous cell carcinoma

Nearly all invasive cervical carcinomas arise from precursor epithelial changes referred to as CIN.

It is also important to note that only a fraction of cases of CIN progress to invasive carcinoma.

CIN can be graded as follows:

-CIN I: mild dysplasia (flat condyloma, koilocytic changes in the superficial layers of epithelium)

-CIN II: moderate dysplasia (maturation of keratinocytes delayed in the middle third of the epithelium, with some variation of cell and nuclear size, heterogeneity of nuclear chromatin and mitoses above the basal layer)

-CIN III: severe dysplasia and carcinoma in situ. (More variation in cell and nuclear size, disoriented cells and mitoses- affect all layers of epithelium.

The next stage is invasive cancer.

The higher the grade, the more likely is the risk of invasive carcinoma, and action plan is therefore also directed on what grade CIN is found in screening.

<u>Pathogenesis</u>

Risk factors:

- Early age at first intercourse
- Multiple sex partners
- A male partner with multiple previous sexual partners
- Persistant infection by high-risk papillomaviruses. (HPV 16,18).
- Smoking
- Endogenous or exogenous immunodeficiency.

Other associated risk factors: higer incidence in lower sosioeconomic groups, the rarity among virgins, and the association with multiple pregnancies- these point to sexual transmission as a causative agent, in this cas HPV, which can be detected in all precancerous lesions and invasive neoplasms. Especially type HPV 16, 18, 45 and 31.

Condylomas (genital warts) are benign lesions, associated with HPV types 6,11,42 and so on.. These low risk HPV types does not integrate into the host genome, remaining in the free episomal form, by contrast to the HPV 16 and 18 which usually integrate into to host genome and express latge amounds of proteins that block and inactivate tumor supressor genes p53 and RB. This results in a transformed cell phenotype, which grows autonomously, being susceptible for new mutations.

Invasive carcinoma of the cervix.

The most common cervical carcinomas are squamous cell carcinomas (75%), followed by adenocarcinomas and adenosquamous carcinomas (20%) and small cell neuroendocrine carcinomas (5%).

The peak incidence is at about 45 years, 10-15 years after detection of their precursors, the interval may be shorter in some with very aggressive intraepithelial changes. The only reliable way to monitor the course of the disease is with careful follow up and repeat biopsies.

The adenocarcinomas in proportion to squamous cell carcinomas has been increasing, glandular lesions are not detected well by pap smear and other screening, but the squamous cell carcinoma is becoming less frequent.

What is pap smear?

The **Papanicola test** (also called **Pap smear**, **Pap test**, **cervical smear**, or **smear test**) is a screening test used in gynecology to detect premalignant and malignant (cancerous) processes in the ectocervix. Significant changes can be treated, thus preventing cervical cancer. The test was invented by and named after the prominent Greek doctor Georgios Papanikolaou. An anal Pap smear is an adaptation of the procedure to screen and detect anal cancers.

In taking a Pap smear, a tool is used to gather cells from the outer opening of the cervix of the uterus and the endocervix. The cells are examined under a microscope to look for abnormalities. The test aims to detect potentially pre-cancerous changes (called cervical intraepithelial neoplasia (CIN) or cervical dysplasia), which are usually caused by sexually transmitted human papillomaviruses (HPVs). The test remains an effective, widely used method for early detection of pre-cancer and cervical cancer. The test may also detect infections and abnormalities in the endocervix and endometrium.

In general, it is recommended that females who have had sex seek regular Pap smear testing. Guidelines on frequency vary, from annually to every five years. If results are abnormal, and depending on the nature of the abnormality, the test may need to be repeated in three to twelve months. If the abnormality requires closer scrutiny, the patient may be referred for detailed inspection of the cervix by colposcopy. The patient may also be referred for HPV DNA testing, which can serve as an adjunct to Pap testing.

1.2.1 Whom to screen

Guidelines on whom to screen vary from country to country. In general, screening starts at age 20 or 25 and continues until about age 50 or 60.[2] There is probably no benefit screening women aged 60 or over whose previous tests have been negative.[3]

There is little or no benefit to screening women who have not had sexual contact. HPV can be transmitted in sex between women, so women who have only had sex with other women should be screened, although they are at somewhat lower risk for cervical cancer.[4]

Screening should begin a few years (e.g., three) after first sex, since most women who contract HPV do so soon after becoming sexually active, but it takes an average of a year for their immune systems to control the initial infection, and may take up to four years. Screening during this period may show this immune reaction and repair as mild abnormalities, which are usually not associated with cervical cancer, but could cause the woman stress and result in further tests and possible treatment. Cervical cancer usually takes time to develop, so delaying the start of screening a few years does not pose much risk of missing a potentially precancerous lesion.

Guidelines on frequency of screening vary, typically every three to five years for those that have not had previous abnormal smears, though some guidelines recommend testing as frequently as every year.

Pap smear screening is still recommended for those who have been vaccinated against HPV, since the vaccines do not cover all of the HPV types that can cause cervical cancer.

1.2.2 Procedure

For best results, a Pap test should not occur when a woman is menstruating. However, Pap smears can be performed during a woman's menstrual period, especially if the physician is using a liquid-based test; if bleeding is extremely heavy, endometrial cells can obscure cervical cells, and it is therefore inadvisable to have a Pap smear if bleeding is excessive.

The patient's perception of the procedure ranges from no discomfort at all to severe discomfort (especially in women with cervical stenosis). Many women experience spotting or mild cramping afterward.

The physician or operator collecting a sample for the test inserts a speculum into the patient's vagina, to allow access to the cervix. Samples are collected from the outer opening or **os** of the cervix using an Aylesbury spatula and an endocervical

brush, or (more frequently with the advent of liquid-based cytology) a plastic-fronded broom. The broom is not as good a collection device, since it is much less effective at collecting endocervical material than the spatula and brush.[5] The cells are placed on a glass slide and checked for abnormalities in the laboratory. The sample is stained using the Papanicolaou technique, in which tinctorial dyes and acids are selectively retained by cells. Unstained cells cannot be visualized with light microscopy. The stains chosen by Papanicolaou were selected to highlight cytoplasmic keratinization, which actually has almost nothing to do with the nuclear features used to make diagnoses now.

In some cases, a computer system may pre-screen the slides, indicating some that do not need examination by a person, or highlighting areas for special attention.

1.2.3 Effectiveness

Prior to the introduction of the Pap test, carcinoma of the cervix was a leading cause of cancer death in women. Since the introduction of the Pap test, deaths caused by carcinoma of the cervix have been reduced by up to 99% in some populations wherein women are screened regularly.[6]

Failure of prevention of cancer by the Pap test can occur for many reasons, including not getting regular screening, lack of appropriate follow up of abnormal results, and sampling and interpretation errors.[7] In the US, over half of all invasive cancers occur in women that have never had a Pap smear; an additional 10 to 20% of cancers occur in women that have not had a Pap smear in the preceding five years. About one-quarter of US cervical cancers were in women that had an abnormal Pap smear, but did not get appropriate follow-up (woman did not return for care, or clinician did not perform recommended tests or treatment).

Adenocarcinoma of the cervix has not been shown to be prevented by Pap tests.[8] In the UK, which has a Pap smear screening program, Adenocarcinoma accounts for about 15% of all cervical cancers[9]

Estimates of the effectiveness of the United Kingdom's call and recall system vary widely, but it may prevent about 700 deaths per year in the UK. A medical practitioner performing 200 tests each year would prevent a death once in 38

years, while seeing 152 women with abnormal results, referring 79 for investigation, obtaining 53 abnormal biopsy results, and seeing 17 persisting abnormalities lasting longer than two years. At least one woman during the 38 years would die from cervical cancer despite being screened.[10] HPV vaccine may offer better prospects in the long term.

1.2.4 Human papillomavirus testing

The presence of HPV indicates that the person has been infected; the majority of women that get infected will successfully clear the infection within 18 months. It is those that have an infection of prolonged duration with high-risk types[11] (e.g. types 16,18,31,45) that are more likely to develop Cervical Intraepithelial Neoplasia due to the effects that HPV has on DNA. Studies of the accuracy of HPV testing report:

- sensitivity 88% to 91% (for detecting CIN 3 or higher)[12] to 97% (for detecting CIN2+)[13]
- specificity 73% to 79% (for detecting CIN 3 or higher)[12] to 93% (for detecting CIN2+)[13]

By adding the more sensitive HPV Test, the specificity may decline. However, the drop in specificity is not definite.[14] If the specificity does decline, the result is increased numbers of false positive tests and, for many women that did not have disease, an increased risk for colposcopy[15] and treatment. A worthwhile screening test requires a balance between the sensitivity and specificity to ensure that those having a disease are correctly identified as having it and those without the disease are not identified as having it. Due to the liquid based pap smears' having a false negative rate of 15-35%, the American College of Obstetricians and Gynecologists and American Society for Colposcopy and Cervical Pathology[16] have recommended the use of HPV testing in addition to the pap smear in all women over the age of 30.

Regarding the role of HPV testing, randomized controlled trials have compared HPV to colposcopy. HPV testing appears as sensitive as immediate colposcopy while reducing the number of colposcopies needed.[17] Randomized controlled

trial have suggested that HPV testing could follow abnormal cytology[12] or could precede cervical cytology examination.[13]

1.2.5 Summation of pap smear- do we also need HPV testing and vaccination?

- The fact that Pap smear is a successful way how to detect precancerous lesions is already established. No further studies is needed and a conclusion has been made. The aim in this case could be to increase the number screening in the developing world.
- HPV testing compined with Pap smear has been suggested to decrease the amount of false negative results. American College of Obstetricians and Gynecologists and American Society for Colposcopy and Cervical Pathology[16] have recommended the use of HPV testing in addition to the pap smear in all women over the age of 30.
- The HPV vaccine Gardasil has been included in the child vaccination programme in norway since 2006. The hypothesis is that this will decrease the amount of infected women of high risk HPV 16, 18 and HPV low risk 6 and 11 (which do not cause invasive carcinoma but genital warts). I will look at numbers in France where this vaccine has been available for a longer period of time.

"There are challenges for countries in terms of cost and so on, but this vaccine is unique and offers tremendous possibilities."

Dr Teresa Aguado, WHO's coordinator for the Initiative for Vaccine Research, Product Research and Development team.

1.2.6 Conclusion of pap smear testing

Although HPV testing can identify the pool of women at risk for cervical cancer, most sexually active women will contract cervical HPV infections at some point in their lifetime. This limits their usefulness of HPV testing as a screening tool for cervical cancer. Thus, cervical cytology and cercival examinations (colposcopy) remain the mainstays of cervical cancer prevention. Nevertheless, women who

test HPV negative with the use of molecular probes for HPV DNA are at extremely low risk for harbouring a CIN.

With the advent of the Pap smear, an increasing proportion of cervical carcinomas are diagnosed early in their course. The vast majority of cervical neoplasms are diagnosed in the preinvasive phase and appear as white areas on colposcopic examination after application of dilute acetic acid. More advanced cases of cervical carcinoma are invariably seen in women who either have never had a Pap smear or have waited many years since the prior smear. Such tumors may be symptomatic, called to attention by unexpected vaginal bleeding, leukorrhea, painful coitus (dyspareunia) and dysuria. Mortality is most strongly related to tumor and extent and in some cases to cell type (as in neuroendocrine tumors). Detection of precursors by cytologic examination and their eradication by laser vaporizaton of cone biopsy is the most effective method of cancer prevention. However, once cancer develops, the outlook hinges on stage, with 5 year survivals as follows:

Stage 0 (preinvasive), 100 %, Stage 1 90%, stage 2 82%, stage 3 35 %, stage 4 10%.

Because tumor spread is gradual, 5 year survival of women even with positive pelvic nodes approaches 50%, chemotheraphy may improve survival in advanced cases.

2. The introduction of the vaccine in Norway- what kind of recommendations has been considered?

2.1 This is the HPV vaccine Gardasil [19]

All Norwegian 12 year old girls are getting this autumn offer for HPV vaccine Gardasil as part of the childhood vaccination program. According to WHO; No vaccine that is introduced has been better tested than Gardasil.

In autumn 2008 the politicians in Norway decided to introduce HPV vaccine in the childhood vaccination program. The department of Public Health, the National Council for the quality and priority, Cancer Registry, Cancer Society and Norwegian gynecological association were all clear in their recommendation of the vaccine. In May 2009, selected the Norwegian health authorities HPV vaccine Gardasil for vaccination. Nine out of ten doctors in Europe and the rest of the world choose Gardasil when they prescribe HPV vaccine.

2.1.1 Norwegian girls are not trying rabbits

Gardasil is distributed in 50 million doses worldwide of which three million doses are given to 12-year-old girls. The vaccine is approved by drug authorities in 116 countries and is recommended by both WHO, U.S., European and Norwegian health authorities. The vaccine has been approved in the U.S. since 2006 for the age group 9-26 years and more than 3 million doses are set for girls aged 12-13 years worldwide. In Europe, the HPV vaccine is a part of childhood vaccination program or refund scheme in 17 countries, including our neighbour Denmark and Sweden. No other vaccine has been so thoroughly evaluated before the

implementation of the childhood vaccination program in this country.

2.1.2 Vaccination is no study

HPV vaccine is an approved drug and has been through the necessary studies to obtain approval for a vaccine. Vaccine safety and what side effects it may cause, is already well documented. There are no reports of any deaths or serious side effects that can be linked to the vaccine. In this context it is important to respect that coincide in time is not proof of causation. Norwegian health authorities have initiated their own compliance program in Norway as is always done when a new vaccine is taken into the vaccination program.

2.1.3.Good experiences from France

1.1 million French girls received a total of 2.7 million doses of Gardasil. The number of reported cases of autoimmune reactions / diseases is below the level of the non-vaccinated proportion of the population and shows no causal relationship with vaccination. 70 of the French girls were or became pregnant shortly after vaccination. There are no signals suggesting that the vaccine has had any impact on pregnancy.

2.1.4. Helps prevent sex warts and cervical cancer

Gardasil prevents sex warts and is pre-cancerous and helps to prevent cervical cancer and vulva-/vaginal cancer. Cervical cancer is one of the most aggressive forms of cancer we have, and among the most common forms of cancer for young women under 35 years. Every year about 300 Norwegian women get cervical cancer. Around 80 of these die from the disease. In addition, about 3,000 women each year gets a conisation. Conisation is a surgical procedure to remove pre-cancerous parts of the cervix. Norwegian researchers have shown that conisation

increases the risk of early childbirth and that the HPV vaccine can prevent this.

2.1.5 HPV vaccination and screening

HPV vaccine is not a substitute for the screening program. While the HPV vaccine prevents cervical cancer by preventing HPV infection, cervical dysplasia and cancer screening program can reduce the risk of cancer at the pre stage and be treated before cancer develops. Experience from other countries shows that support for the screening program increases when HPV vaccine is introduced, as awareness increases.

2.1.6 Good effect

The longest follow-up of any HPV vaccine is now nearly ten years, and one sees no signs of waning effect during this period. Already one year after the HPV vaccine was an option for girls / women aged 12-28 years in Australia, reported that about the number of warts on genitalia has been reduced to half. The effect on cervical cancer will come later.

2.1.7 Safe vaccine

There are no reports of any deaths or serious side effects that can be linked to the vaccine. Both the Norwegian health authorities and the manufacturer of Gardasil has initiated its own compliance program in Norway, independently of each other. Health personnel reported in all possible side effects to the Norwegian health authorities, in the same way as it has been done by the introduction of other vaccines.

3. The HPV vaccine- myths and facts19[19, 20]

Myth: There is no documented association between infection with the HPV virus and the development of cervical cancer
Fact: HPV is the cause of almost 100% of cervical cancer, 90% of vaginal cancers, 80% of anal cancers, 50% of penile cancer, 40% of vulvacancer and 24% of ENT cancer. In Norway we have today a lot of research on cervical cancer (screening) based on cell samples. There are plans to replace these cell samples with the HPV test because the HPV test will catch more women with risk of developing cervical cancer than Pap smears do.

Myth: Although there is evidence that the HPV vaccine has an effect on the precursors of cervical cancer, we can not know whether the vaccine will reduce the incidence of cervical cancer
Fact: There is evidence that the precursors (cervical dysplasia) can develop into cervical cancer. In New Zealand it was a doctor who allowed women with cervical dysplasia go untreated for years. Approximately 30% of those with cervical dysplasia had cancer. Today's screening programs against cervical cancer will pick up women with cervical dysplasia so that they can get treatment before cancer develops.

Myth: There should be a proper study where we see it developed more cancers in the placebo group than in the vaccine group
Fact: It is completely unethical to allow women in the placebo group, to develop cancer. All women with cervical dysplasia should be treated regardless of whether they are in the placebo group or in the vaccine group. Most people who had cell changes were in the placebo group. The difference between the two groups was so large that the study had to be canceled because they could no longer allow women to be participants without being offered HPV vaccine. HPV vaccine is so effective that there no longer is allowed to do such studies with a placebo group.

Myth: There is only women at risk who will benefit from HPV vaccine
Fact: Approximately 70-80% of all women (and men) are infected with HPV one or more times during their lifetime. All sexually active women who have more than one partner during their lifetime, or have a partner who has had one or more partners in the past, are at risk for HPV infection.

Myth: The vaccine is not tested on the age group it is intended, 11-12 years old girls
Fact: There are also studies on children aged 9-12 år. The vaccine provides particularly good immune response in this age group which is a sign of good long-term efficacy of the vaccine. Of the 50 million doses that have been given the HPV vaccine so far, three million doses has been given to 12-year-old girls.

Myth: The vaccine is not good enough tested. We know too little about the side effects of long-term
Fact: The vaccine trials are conducted with about ten-year follow-up without having seen waning effect of the vaccine or long-term side effects. For most vaccines, the side effects comes in a few weeks.

Myth: The vaccine will be tested in Norway before it is approved in the U.S.
Fact: The vaccine has been approved in the U.S. since 2006 for girls / women ages 9-26 years. Total 116 countries have approved the HPV vaccine. Health authorities in Norway have recommended that all girls aged 12-16 years should be offered free HPV vaccine, but so far only set aside money for the state budget to vaccinate 12 year old girls.

Myth: It is better for the body to undergo a natural HPV infection than to get vaccine
Fact: Even if an HPV infection is very common, and it goes by itself untreated in most cases have no body any benefit from such an HPV infection. About 10% have sex warts (condylomas) and 10% develop high-grade cervical dysplasia that are pre-cancerous. Lifetime risk of developing cervical cancer in Norway is 1.2%.

Myth: A natural undergone HPV infection provides better immune responses than HPV vaccine

Facts: An undergone HPV infection gives little or no protection against future HPV infections. While most other infectious diseases provides a powerful immune response in two weeks, it will often take many months before the body gives the immune response against the HPV virus. HPV vaccine is designed to provide a good immune response that will protect the body against future HPV infection. The immune response caused by the HPV vaccine is 10 to 10,000 times more potent than the naturally undergone HPV infection.

Myth: HPV vaccine against HPV 16 and 18 provide little protection when there are 14 high-risk HPV types

Facts: HPV type 16 and 18 is the cause of 70% of cervical cancer. It is also shown that the vaccine provides partial protection (cross protection) against any of the other HPV types.

Myth: If the vaccine prevents infection with HPV types 16 and 18, other HPV types take over and cause as much cancer as before

Fact: There is no competition between different types of HPV. They live peacefully side by side. The same woman may be infected with multiple HPV types at once, and the different HPV types can each cause cell changes. Women who are vaccinated against HPV 16 and 18 will rarely be able to get the cancer caused by these two types, but like other women they can get cancer caused by other more unusual HPV types.

Myth: It is unnecessary to take HPV vaccine if you take cell samples regularly

Fact: If you take cell test every three years as it is recommended, the risk of cancer is reduced by 60-80%. The effect of taking cell samples on a regular basis is about the same as to take the HPV vaccine. But the risk of cervical cancer is reduced further if you both take Pap smears regularly and are vaccinated.

Myth: It is unnecessary to take cell samples if you have taken HPV vaccine
Facts: HPV vaccine protects against high-risk types of HPV (types 16 and 18). These are the cause of 70% of cervical cancer. You can still get cervical cancer caused by other HPV types. By taking a cell sample regularly of other HPV types detected causing cancer, the development of cancers be prevented.

Myth: If a woman has had sex is it too late to take the HPV vaccine
Fact: It is best to take the vaccine before the woman has been exposed to HPV infection. In the first vaccine studies was the requirement that women should have fewer than four sexual partners. In later studies was the requirement that women should have a maximum of eight partners. The latest studies have shown that although the HPV vaccine has not an effect on established cell changes, the risk of new cell changes after treatment will be reduced if one takes HPV vaccine.

Myth: Boys and men have no advantage of taking HPV vaccine
Facts: HPV infection is the cause of gender warts, penile cancer, cancer of the rectum (anal cancer) and certain types of ear / nose / throat cancer. When all these types of cancer will be summed together it cause as much as cervical cancer in women. Women are, however, a double hit since they have anal cancer, cancer of the vulva, vagina, and ear / nose / throat cancer in addition to cervical cancer. Cost / benefit of the vaccine is higher in women than in men. The exception is the homosexuals who have higher risk of HPV-induced anal cancer than the risk of cervical cancer in women. It is also important to vaccinate heterosexual men not to infect women who are not vaccinated. In Australia there will be free HPV vaccine to both boys and girls as part of the childhood vaccination program.

Myth: Lesbian women have no advantage of HPV vaccine
Fact: Although HPV primarily transmitted by sexual intercourse, the virus can also spread by other intimate contact. The use of common toys can also spread the infection. Lesbian women often have had heterosexual experiences before they found their lesbian orientation. In general, lesbians are less susceptible to HPV than heterosexual women, but also they can benefit from the vaccine.

Myth: The risk of taking HPV vaccine are greater than the benefits
Fact: In general it is rare that a vaccine will be approved if the risk of death by taking the vaccine are greater than 1 to 1 000 000. According to the WHO this vaccine is the best ever tested. Study up to 10 years of follow-up have shown no increased risk of HPV vaccine than in other vaccines. Lifetime risk for cervical cancer in Norway is 1% and about a third of those who get cervical cancer will die of cancer. HPV vaccine reduces the risk of cancer by 70%. This means that the risk / benefit ratio in terms of death are 1 in 2000. This means that there is a risk when taking the the vaccine, but the risk of death is 2000 times higher if you do not take the vaccine.

Myth: Since only 1% of Norwegian women get cancer, only 1 in 100 women will benefit from the vaccine
Fact: The vaccine protects not only against cervical cancer. It also protects against sex warts, cervical dysplasia and other type of HPV-induced cancer. Approximately 1 in 10 have sex warts during their lifetime, and about 1 in 10 treatment-intensive cell changes. In 2008, it was treated 3 700 women for cervical dysplasia in Norway. Treatment of cervical dysplasia can lead to increased risk of abortions and premature births. The vaccine also has value for those who never have sex warts or cervical dysplasia, because if a person is vaccinated, HPV infection does not spread further. In this way, even those who have not taken the vaccine have a relative protection due to reduced infection risk.

Myth: Although HPV type 16 and 18 is the cause of 70% of cervical cancer in other countries, we do not know much about the incidence of the different types of HPV in Norway
Fact: It is the period 2005 - 2008 taken HPV test on over 30,000 women in Norway in connection with the mass investigation against cervical cancer. HPV type 16 and 18 is the cause of at least 70% of cervical cancer in Norway.

Myth: HPV vaccine may increase the risk of blood clots in women using oral contraceptives

Fact: There were as many women who had blood clots in the vaccine group as in the placebo group. The issue is not so relevant in Norway since very few 12 year old girls are using oral contraceptives.

Myth: HPV vaccine can cause spontaneous abortion and fetal damage in pregnants

Fact: In general, one is careful with the medicines and vaccines for pregnant women. There was still somone in the study that was pregnant when they got the HPV vaccine placebo. There was no difference in the incidence of spontaneous abortion or fetal damage between these groups. 1.1 million French girls received a total of 2.7 million doses of Gardasil. 70 of the French girls were or became pregnant shortly after vaccination. There are no signals suggesting that the vaccine has had any impact on pregnancy.

Myth: HPV vaccine contains mercury

Fact: Although thiomersal (an organic mercury compound) has been a commonly used preservative in vaccines in 70-80 years without seing adverse effects of this, it is no longer any of the vaccines in the childhood vaccination program in Norway that contains mercury, nor the HPV vaccine Gardasil.

Myth: There is no reason to take the HPV vaccine now because a few years there will be a vaccine that is even better

Fact: The current HPV vaccine against HPV type 16 and 18 can reduce the risk of cervical cancer by 70%. It has been tested the vaccines with seven high-risk HPV viruses, which together can reduce the risk of cancer by 85%. Even if you take Gardasil now, there is nothing in the way that you can also take the new vaccine later. It would be foolish to wait to vaccinate if you get the HPV infection in the meantime.

Myth: There will be no measurable effect of the HPV vaccine before about 20-30

years

Fact: Even one year after the HPV vaccine was an option for girls / women aged 12-28 years in Australia, it was reported that about of the number of sex warts was halved. It is already seen effects on pre-cancer vaccine trials, and it is expected to see such a decline in Australia within the next few years. The effect on cervical cancer and another type of HPV-induced cancer comes later.

Myth: HPV vaccine will lead to more unprotected sex

Fact: A survey of 12 year old girls in Manchester who have been vaccinated show that they have become more aware that unprotected sex can lead to infection of diseases.

Myth: HPV vaccine will cause that fewer will take the cell test

Fact: The support of screening program has increased in all the countries where HPV vaccine has been introduced because people generally are becoming more aware of the link between HPV, cervical dysplasia and cancer.

Myth: It is an assault against 12 year old girls to let their parents decide that they should take the HPV vaccine

Fact: A survey from Manchester, where 12 year old girls were asked about attitudes to HPV vaccine showed that parents and children in most cases have agreed if they will accept the HPV vaccine or not. One in ten girls took the vaccine because parents wanted it when they didn't want it themselves. Four out of ten girls told that when their parents refused them the vaccine, they still wanted to take the vaccine.

Myth: It is unnecessary to take HPV vaccine if you always use a condom

Fact: Studies show that women who always use condoms have 60-70% reduced risk of HPV infection. If you take both the HPV vaccine, and always use condoms, you reduce the risk of HPV infection by 90%. Using the condom is inconvenient if you want to get pregnant.

Myth: It is unnecessary to use a condom if you have taken HPV vaccine
Fact: Although the HPV vaccine reduces the risk of HPV infection, the vaccine does not reduce the risk of pregnancy or risk of infection by other STDs.

Myth: HPV vaccine protects against all gynecological cancers
Fact: Although the HPV vaccine reduces the risk of cervical cancer, cancer of the vagina and vulva, it has no effect on cancer of the uterus (endometrial cancer) or ovarian cancer because these types of cancer are not caused by HPV.

Myth: It is unnecessary to take HPV vaccine if you wait to have sex until you marry
Fact: Even if you are a virgin on the wedding night it is not sure that your partner is. You have no guarantee that your spouse is always true to you. Half of all marriages end in divorce. The risk of HPV infection is 10% for each new partner.

Myth: It is better that the state spend money on campaigns for sexual abstinence than on HPV vaccine
Fact: The Bush administration spent millions of dollars on campaigns for sexual abstinence that seemed counterproductive. The average number of sexual partners over a lifetime is eight. It has proven to be very hard to change sexual behavior through attitude campaigns. Instead of trying to change the reality it is more realistic to relate to the way it is, and rather take the consequences of this. Health authorities in Norway have therefore chosen to provide free offer HPV vaccine to 12 year old girls.

Myth: HPV vaccine can lead to sterility
Fact: There is nothing to suggest this.

Myth: HPV vaccine can cause Guillain-Barré syndrome
Fact: Guillain-Barré syndrome is a very rare disease. There were no cases of Guillain-Barré syndrome in vaccine studies, neither in those who received Gardasil and or in those who received placebo. It is so far not shown that the risk of Guillain-Barré syndrome is greater in women who have taken the vaccine, compared with women who have not taken the vaccine. 1.1 million French girls received a total of 2.7 million doses of Gardasil. The number of reported cases of autoimmune reactions / diseases is below the level of the non-vaccinated proportion of the population and shows no causal relationship with vaccination.

Myth: HPV vaccine may cause autism
Fact: Autism is a developmental disorder that particularly affects the development of social function, language and communication. Autism is usually present from birth, and symptoms of autism are usually visible during a child's first three years of life. It is impossible that a well-functioning 12-year-old develop autism after receiving HPV vaccine.

Myth: HPV vaccine can cause the mucous membranes to be more vulnerable to other infections
Fact: There is nothing to suggest this. Immune system has unlimited capacity in terms of recognizing various microorganisms. If you take a vaccine against rubella it does not increase the risk of getting chickenpox. Are you vaccinated against HPV, the risk for other STDs is as great as for non-vaccinated. You can also get cervical cancer caused by other HPV types than those included in the vaccine (HPV types 16, 18).

Myth: Although the efficacy of HPV vaccine are well documented for cervical dysplasia in the cervix, we know little about the effect on the rest of the body
Fact: Vaccine Study follow-up for about 10 years has not shown long-term side effects. It is not seen negative effects of the vaccine to other parts of the body. However, there is reason to believe that the vaccine will also prevent other types of HPV-induced cancer than cervical cancer, vaginal cancer and vulval cancer.

There are currently undergoing studies to investigate this.

Myth: HPV vaccine contains mutant HPV virus with known cancer risk
Facts: HPV vaccine does not contain viruses or genetic material from viruses, but virus-like particles (empty shell) that the immune system perceives as a real virus. The body produces antibodies against the virus-like particles that will later be able to neutralize authentic HPV virus. The vaccine contains no carcinogenic substances and therefore can not cause cancer.

Myth: Health authorities in Norway should have waited a few years before the HPV vaccine was included in the childhood vaccination program
Fact: There are born approximately 60 000 children in Norway every year. That is, there are around 30 000 girls who are 12 years and who now will be offered the HPV vaccine. When the lifetime risk of cervical cancer is 1% that 300 of these 12-year-old girls later will develop cervical cancer if they do not get HPV vaccine. With 80% vaccine coverage, 90% efficacy of the vaccine for 70% of the viruses that can cause cervical cancer, HPV vaccine will prevent 150 of these 12-year-old girls from developing cervical cancer later in life. Since approximately one in three of those who get cervical cancer will die of the disease, the HPV vaccine could prevent 50 deaths each year. It is unwise to let women die unnecessarily when cervical cancer can be prevented by using the HPV vaccine.

CONCLUSION

Prevention of cervical cancer.

- To screen for HPV infection is helping in preventing CIN. http://en.wikipedia.org/wiki/Papanicolaou_smear - cite_note-pmid11966387-16
- To do regular cytology in the right age group help preventing CIN
- HPV is the cause of almost 100% of cervical cancer
- But also most cases of vaginal cancer, anal cancer, penile cancer and vulval cancer are at risk in HPV infection.
- About 70-80 % of all women (and men) will be infected of HPV once or several times in life. [20]
- The effect of the HPV vaccination is so far promising. [21]

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