HUMAN PAPILLOMAVIRUS FACTSHEET

What is human papillomavirus?

ENGAGe
ESGO | European Network of Gynaecological Cancer Advocacy Groups

This Factsheet was written by Asst. Prof. Murat Gultekin (Turkey) and Mrs. Icó Tóth (Hungary) with the contribution of Prof. Karina Dahl Steffensen (Denmark).

ENGAGe would like to thank the authors, the contributors, and ENGAGe Executive Group members for their work and constant availability.

Foreword

Human Papillomavirus (HPV) is an important topic for healthcare professionals. The fact that a vaccine against HPV exists means we are able to protect ourselves - not only women but men too.

Harald Zur Hausen won a Nobel Prize for showing the relationship between HPV and cervical cancer.

HPV is mostly mentioned as a cause of cervical cancer. Unfortunately, this virus also causes other types of cancers and lesions.

We must discuss HPV and pass our knowledge on to others.

We have weapons to use against HPV, but the problem is not everybody is familiar with these tools, and even more critical, not everyone uses them!

IF WE HAVE THE POSSIBILITY OF PREVENTING A TYPE OF CANCER, WE MUST DO IT!

HPV stands for Human Papillomavirus

HPV is

- The most common sexually transmitted infection (STI).
- A different virus than HIV and HSV (herpes).
- So common that nearly all sexually active people will become infected at some point in their lives. Since limited protection is developed in the body after having been infected, one person can potentially be infected repeatedly.[1]
- The cause of various health problems, including genital warts and cancers.
- A DNA virus capable of inducing a malignant transformation of epithelial cells and of causing cervical, anal, vulvar, vaginal, penile and some oral cancers.
- Capable of affecting both women and men.
- A local virus. HPV doesn't get into the bloodstream.
- Preventable through vaccinations.
- Complicated. There are more than 100 types of HPV, of which at least 13 are cancer-causing (also known as high-risk type).

Low-Risk HPV (LR)	**6, 11, 42, 43, 44/55**
High-Risk HPV (HR)	**16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68**
Non-identified HPV (NA)	

1 https://www.ncbi.nlm.nih.gov/pubmed/?term=castle+PE+lancet+2007

Cervical cancer

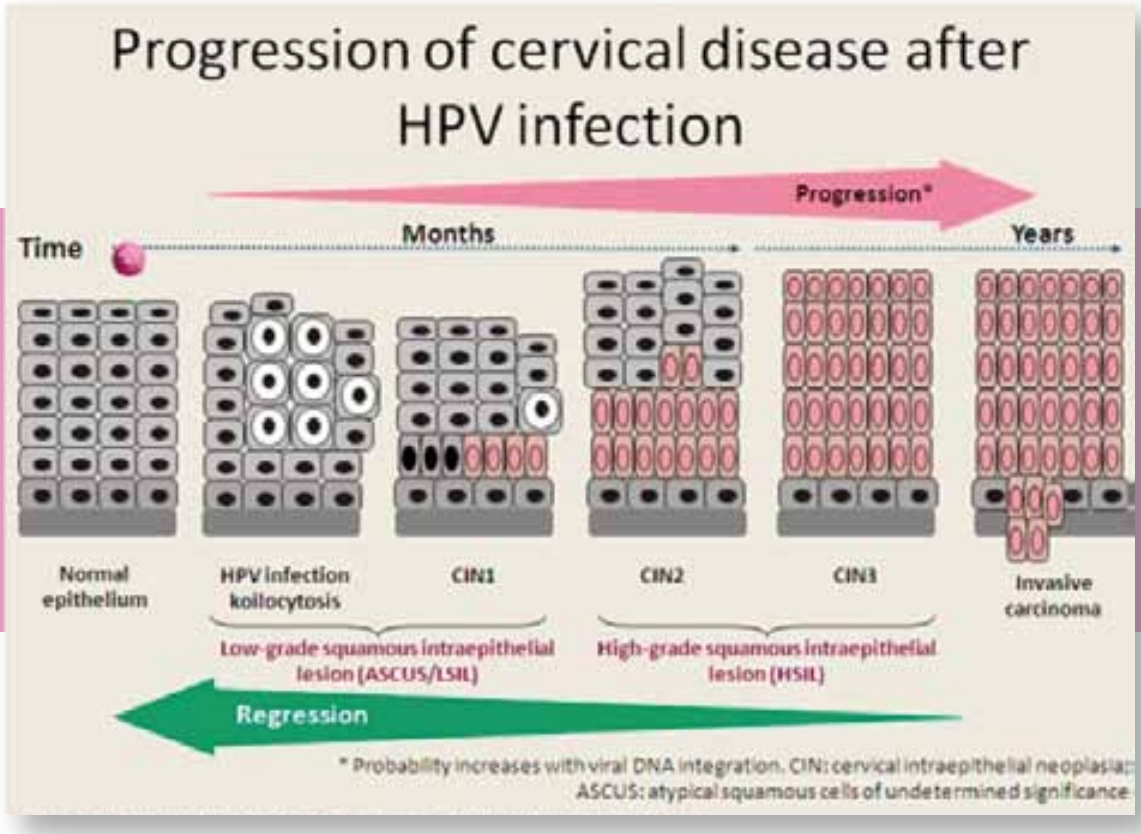
In women with cervical diseases, HPV-16 is the most common type detected, followed by HPV-18. Together, they account for 70% of cervical cancer cases worldwide.

Over 80% of sexually active individuals will be infected by a genital HPV in their lifetime. The high incidence and prevalence rates of HPV infection are found in both females and males soon after the onset of sexual activity.

The majority of genital HPV infections are asymptomatic and usually clear from the body within 1–2 years without consequences if immune function is normal.

Prevention of cervical cancer is possible through screening because progression from infection to cancer is usually slow, sometimes taking decades.

Infection by High-Risk (HR) HPV does not mean that it will turn into a cancerous lesion.



Burd EM. Clin Microbiol Rev 2003; 16:1-17; Solomon D, et al. JAMA 2002; 287; 2114-2119

Signs and Symptoms of Cervical Cancer

The majority of HPV infections do not cause symptoms or disease and resolve spontaneously. However, persistent infection with specific types of HPV (most frequently, HPV-16 and -18) may lead to precancerous lesions. If untreated, these lesions may progress to cervical cancer, but this progression usually takes many years.

Symptoms of cervical cancer tend to appear only after the cancer has reached an advanced stage and may include:

- abnormal bleeding that is irregular, intermenstrual (between periods) or occurs after sexual intercourse;
- pain in the back, leg or pelvis;
- fatigue, weight loss, loss of appetite;
- vaginal discomfort or odorous discharge;
- a single swollen leg

What Does HPV Do?

Genital Warts

More than approximately 30 million people are affected by HPV genital warts globally.[2] Before HPV vaccines were introduced, roughly 340,000 to 360,000 women and men were affected by genital warts caused by HPV every year. Also, about one in 100 sexually active adults in the U.S. has genital warts at any given time. In Europe, it is estimated there are more than 700,000 affected individuals.[3]

Cervical Cancer

Cervical cancer remains an important worldwide public health problem with approximately 530,000 new cases and 265,000 deaths each year.[4]

Vulvar Cancer

Vulvar cancer is a relatively rare disease with two types: 1) basaloid/warty types and 2) keratinising types. The basaloid/warty types are associated with younger women and carry similar risk factors as for cervical cancer and HPV infection of the cervix. The keratinising cancers have a low prevalence of HPV infection, occur in older women, and are frequently associated with the skin disease lichen sclerosus et atrophicus and predisposing factors.

Anal Cancer

HPV DNA is found in a high percentage of cases of anal cancers, over 90% in most cases, with HPV-16 being the most prevalent. Anal cancer is more common in HIV-infected men and women as well as in men who have sex with men.

---

2 https://www.ncbi.nlm.nih.gov/pubmed/23199955
3 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5387299/figure/Fig1/
4 Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359–86.

Head and Neck Cancers - Oropharyngeal Cancers

Overall, head and neck cancer is the sixth most common type of cancer globally, accounting for 650,000 new cases and 350,000 cancer deaths per year. Head and neck cancer is a broad term that encompasses epithelial malignancies that arise in the oral cavity. Most are squamous cell carcinoma and the most important risk factors are tobacco and alcohol.

Oral HPV is transmitted to the mouth by oral sex, or possibly in other ways. Many people are exposed to oral HPV. About 10% of men and 3.6% of women have oral HPV. Most people clear HPV within one to two years, but HPV infection persists in some people and can trigger cancer development.

HPV can infect the mouth and throat and cause cancers of the oropharynx (back of the throat, including the base of the tongue and tonsils). This is called oropharyngeal cancer. HPV is thought to cause 70% of oropharyngeal cancers.[5]

Penile Cancers

Squamous cell cancer of the penis is rare and accounts for around 0.5% of all cancers in men, affecting mostly men over the age of 50. The incidence varies among different geographic regions, and in some areas, penile cancer constitutes 10% of malignant disease in men, especially in Africa, Asia and some countries in South America, with the age-standardised incidence rate ranging from 4.3–4.4/100. Persistent infection with hrHPV types is associated with a subset of men with penile cancer. Globally, HPV is believed to contribute to 40–50% of penile cancers, with HPV-16 being the most frequent type detected. Other risk factors include cigarette smoking, no circumcision, and poor hygiene.

Transmission of HPV

Most people will become infected at some point in their life. Most infections will disappear on their own and not cause serious problems. However, reinfection with the same HPV type is also common, necessitating long-term surveillance for patients once they are found to be HPV-positive.[6] Unfortunately, thousands of women and men get cancer and other diseases from HPV.[7]

Anyone can get HPV by having vaginal, anal or oral sex with someone who carries the virus. This is how it is most commonly spread, and it is important to note that anyone who is sexually active can get HPV, even a person who has had sex with only one other person. Additionally, sexual contact is sufficient for transmission, even without sexual intercourse.

However, there are also reported non-sexual transmissions of HPV. For a proper understanding of the exact natural history of HPV infection acquired via the non-sexual route, long-term prospective studies need to be undertaken.

HPV can be passed even when an infected person has no signs or symptoms. Symptoms may develop years after having sex with an infected partner.[8]

5 EH5 - https://www.ncbi.nlm.nih.gov/pubmed/28937544
6 EH1 - https://www.ncbi.nlm.nih.gov/pubmed/28165175
7 Harper DM, DeMars LR. HPV vaccines - a review of the first decade. Gynecol Oncol 2017;146:196–204.
8 https://www.ncbi.nlm.nih.gov/pubmed/28165175

We have efficient tools for avoiding HPV

HPV Vaccine

The HPV vaccine targets the HPV types that most commonly cause cervical cancer and can cause some cancers of the vulva, vagina, anus, and oropharynx. It also protects against the HPV types that cause most genital warts. The HPV vaccine is highly effective in preventing the targeted HPV types, as well as the most common health problems caused by them.

Primarily, the HPV vaccine is discussed from the perspective of preventing cervical cancer, but in fact, the vaccine protects against additional tumours and precancerous lesions caused by HPV.

There are currently three vaccines which protect against both HPV-16 and -18, which are known to cause at least 70% of cervical cancers. The vaccines may also have some cross-protection against other less-common HPV types that cause cervical cancer. One of the vaccines also protects against HPV-6 and -11, which cause anogenital warts, and the nine-component vaccine protects against nine different HPV types.

CERVARIX	**HPV-16, -18 + cross protection**
SILGARD/GARDASIL	**HPV-4, -6, -16, -18**
GARDASIL9	**HPV-6, -11, -16, -18, -31, -33, -45, -52, -58**

All vaccines work best if administered prior to HPV exposure. Therefore, it is preferable to administer them to young patients, as early as 9 years old.

Based on the recommendations, these vaccines are the most effective before starting sexual life but are effective in approximately 70% of older patients as well (in some countries the recommendation encompasses patients to age 55). It is possible to take the vaccine even with an existing HPV infection. In this case, the vaccine guards against subsequent infections.

The vaccines cannot treat HPV infection or HPV-associated diseases such as cancer.

Clinical trial results show that all current vaccines are safe and quite effective in preventing HPV-16 and -18 infections.

The HPV vaccines have been licensed by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA). The United States CDC (Centres for Disease Control and Prevention) has approved them as safe and effective. The vaccines were studied in thousands of people around the world, and these studies showed no serious safety concerns. Side effects reported in these studies were mild and included pain where the shot was given, fever, dizziness, and nausea. Vaccine safety continues to be monitored by CDC and the FDA. The latest World Health Organisation (WHO) safety reports clearly state that these vaccines are extremely safe.[9]

The vaccines contain individual proteins from HPV virus types, which produce an immune response.

To understand how a vaccine works in the body, imagine a cupboard. The sheath of the HPV molecule is the cupboard. The virus's cupboard usually contains infectious DNA, but in the vaccine this cupboard is empty. The empty cupboard helps the immune system recognise the outside surface of the virus, teaching it to protect the patient in case of future exposure.

Since the vaccination prevents genital cancers in males as well as females, some countries have also started to vaccinate boys. One of the two available vaccines also prevents genital warts in males and females and furthermore prevents other HPV-associated cancer in males as described previously. WHO recommends vaccination for girls aged 9–13 years as this is the most cost-effective public health measure against cervical cancer. Adolescents 9 through 14 years of age should get an HPV vaccine as a two-dose series with the doses separated by six to 12 months. People who start HPV vaccination at age 15 and older should get the vaccine as a three-dose series with the second dose given one to two months after the first dose and the third dose given six months after the first dose. There are several exceptions to these age recommendations. Your healthcare provider can give you more information.

Vaccinations for Boys

Vaccinations for young men and boys are also important due to:

- the protection of males from HPV-associated cancer,
- preventing infection of females from men (community protection)

Equal access to the HPV vaccine is a topic currently being discussed; meanwhile, the incidence of male cancers caused by HPV is rising continually. In addition, HPV-related diseases in men are often diagnosed at a late stage.

Most EU countries have implemented HPV vaccination programmes, usually for girls under 14, but in some countries, HPV vaccination is also implemented for boys.

9 http://apps.who.int/iris/bitstream/handle/10665/255353/WER9219.pdf;jsessionid=71DFCD0

HPV Screening

Recently, screening for HPV DNA has been used in the primary screening of cervical cancers alone for women over age 30. Especially in vaccinated populations, the cervical cancer screening test, also called the Pap smear, has lower sensitivity and positive predictive value due to the fact that there will be fewer abnormal pap-smears and experienced cytopathologists in the vaccinated populations. Screening for HPV DNA has a higher sensitivity for detecting cancers compared to the Pap smear, a higher negative predictive value, and, therefore, the opportunity to increase the screening interval. The test can be done by a doctor or through a self-collection kit.

Treatment Options

There is currently no medical treatment for persistent HPV infections that are not associated with abnormal cell changes. However, genital warts, benign respiratory tract tumours, precancerous changes at the cervix, and cancers resulting from HPV infections can be treated by different treatment modalities, for example, surgery.

When there is an HPV infection that does not cause any clinical disease or genital warts, treatment is to leave the immune system to do its work and include a denser follow-up than normal.

Methods commonly used to treat precancerous cervical changes include cryosurgery (freezing infected and HPV-transformed tissue); loop electrosurgical excision procedure (also called LOOP), which is the removal of cervical tissue using a hot wire loop; surgical conisation (surgery with a scalpel, a laser, or both to remove a cone-shaped piece of tissue from the cervix and cervical canal); and laser vaporisation conisation (use of a laser to destroy cervical tissue).

Treatments for other types of benign respiratory tract tumours and precancerous changes caused by HPV (vaginal, vulvar, penile, and anal lesions) and genital warts include topical chemicals or drugs, excisional surgery, cryosurgery, electrosurgery, and laser surgery. Treatment approaches are being tested in clinical trials, including a randomised controlled trial that will determine whether treating anal precancerous lesions will reduce the risk of anal cancer in people who are infected with HIV.

HPV-infected individuals who develop cancer generally receive the same treatment as patients whose tumours do not harbour HPV infections, according to the type and stage of their tumours. However, people who are diagnosed with HPV-positive oropharyngeal cancer may be treated differently than people with oropharyngeal cancers that are HPV-negative. Recent research has shown that patients with HPV-positive oropharyngeal tumours have a better prognosis and may do just as well on less intense treatment. Ongoing clinical trials are investigating this question.

Cancer treatments also include surgery (which can be extensive in advanced disease), radiotherapy, chemotherapy, and biological and biosimilar therapies.

A new treatment modality for advanced cancer disease is immunotherapy.

ENGAGe Contact:

Web: http://engage.esgo.org/

Email: engage@esgo.org