CERVICAL CANCER FACTSHEET

What is cervical cancer?

ENGAGe

ESGO | European Network of Gynaecological Cancer Advocacy Groups

ENGAGe is releasing a series of factsheets to raise awareness of gynaecological cancers and to support its network to work at a grassroots level.

- Take-up of cervical screening by European women varies from **10 to 79%**[1] and HPV vaccination rates are lower than expected in many countries.[2]
- The chances of being diagnosed with or dying from cervical are highest among women in Eastern Europe.[3]

"Cervical cancer is the easiest gynaecological cancer to prevent through regular screening tests and vaccination, and yet each year over **58,000** women in Europe are diagnosed with cervical cancer and around **24,000** women die of the disease.[3]"

says Professor Vesna Kesic, Former ESGO President.

"Cytology-based screening programmes have achieved large reductions in cervical cancer incidence and mortality; HPV testing alone or combined with cytology-based screening can increase the detection of precursor lesions of cervical cancer. Vaccination can protect against 95% - 100% of HPV infections included in the vaccine but doesn't cure the infection in women who have it (who are HPV DNA positive). However based on the scientific evidence, HPV vaccination is recommended even for women with HPV infection with no upper age limit."

ENGAGe (the European Network of Gynaecological Cancer Advocacy Groups) is a network for all advocacy groups representing gynaecological cancers, especially ovarian, endometrial, cervical, vulvar and rare cancers. ENGAGe was established in 2012 by ESGO, the European Society of Gynaecological Cancer.

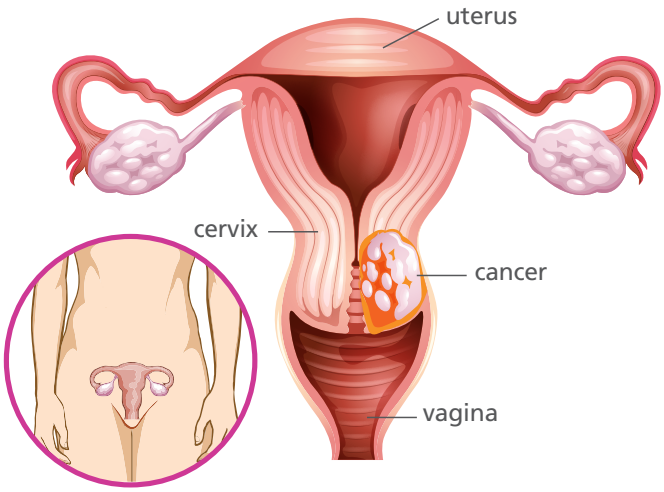
References:

1. Anttila A, et al. Eur J Cancer 2009;45:2649-58
2. European Centre for Disease Prevention and Control. Introduction of HPV vaccines in EU countries—an update. Stockholm: ECDC; 2012
3. Ferlay J, et al. Eur J Cancer 2013;49:1374-403

Cervical cancer

What is cervical cancer?

When cancer starts in the cervix, it is called cervical cancer. The cervix is part of a woman's reproductive system and is the lower, narrow part of the womb (the uterus) that connects with the top of the vagina. Cervical cancer is the second most common cancer in women aged 15-44 years and the fifth most common cancer among European women of all ages.[1,2]



Almost all cervical cancers are caused by human papilloma virus (HPV), which you are at risk of as soon as you are sexually active. HPV is an extremely common virus. At some point in our life most of us will catch the virus. The infection usually clears up without any treatment, but certain types of HPV may persist. Regular screening is needed to detect these persistant or recurrent infections.

HPVs are a large group of related viruses and there are low and high risk HPV types. [8]

Low-risk HPV types

Some types of genital HPV can cause warts on or around the genitals and anus of both men and women. In women, there may also be warts on the cervix and in the vagina. Because these genital warts very rarely grow into cancer, they are called "low-risk" viruses.

High-risk HPV types

Other types of genital HPV have been linked to cancer in both men and women. These types are called"high-risk" because they can cause cancer. Doctors worry more about the cell changes and pre-cancers linked to these types, because they are more likely to grow into cervical cancer over time. Common high-risk HPV types include HPV 16 and 18.

In women who are under increased risk of developing cervical cancer, persistent HPV infection may lead to precancerous changes called cervical intraepithelial neoplasia (CIN) High grade squamous intraepithelial lesion (H-SIL). If untreated, CIN H-SIL eventually develops into cervical cancer that may invade surrounding body tissues. This process, from HPV infection to invasive cervical cancer, usually takes at least 10-15 years.

The grades of CIN are explained under the section *"How are biopsy results reported?"*

How can cervical cancer be prevented?

Cervical screening

Cervical screening is the process of taking a sample of cells from your cervix which are then examined to detect abnormalities that might develop into cancer in the future. If detected early invasive cervical cancer in young women can be treated by conservative surgical approach (conisation, trachelectomy) which enables preservation of fertility.

Cervical screening programmes vary depending on the country, but in general guidelines recommend:[3]

- Start screening at ages 20-30 years, but preferably not before age 25 or 30 depending on cervical cancer rates in the country. (The aim is to avoid unnecessary treatment and possible pregnancy complications because HPV-related changes usually go away by themselves in most younger women.[4]
- Continue screening every three to five years until age 60 or 65.
- Screening can be stopped in older women with three or more recent consecutive normal tests.
- But pay special attention to older women who have never attended screening because they are at increased risk of cervical cancer.

Cervical screening is a way of detecting abnormal cells on the cervix:

• Papanicolau (Pap) testing or liquid-based cytology

In both tests, cells are collected from the cervix and checked under a microscope. Some countries prefer liquid-based cytology because it reduces the need for retesting. An abnormal Pap test result means that other tests will need to be done to find out if a cancer or a pre-cancer is actually present.

• HPV testing

This test is being added to some cervical screening programmes because it helps to identify women who have a higher risk type of HPV. HPV tests can be used for primary screening for women aged 30 and up until the final age of screening, which may vary from 60 – 70 years depending on the country.

HPV testing is used in Three Ways:

Primary cervical cancer screening

Triage: if any Pap or liquid-based cytology test shows early abnormal cell changes, the sample is tested for HPV. If high risk HPV is found (HPV positive result), the woman is offered colposcopy (a detailed look at the cervix using a magnifying instrument called a colposcopy). If there is no HPV (HPV negative result), the woman can return to regular screening every three to five years.

Test of cure: if the cervical screening sample is HPV negative after the abnormal cells have been treated, the woman can return to regular screening. Repeat colposcopy is offered if HPV is found after treatment. Pap testing, liquid-based cytology and HPV testing are only looking to prevent cervical cancer. They do not screen for other gynaecological cancers such as ovarian, uterine, vaginal or vulvar cancers. So even with regular cervical screening, it is important to consult a doctor about any abnormal signs or symptoms (see below).

HPV vaccination

Three vaccines protect against persistent infection caused by different HPV types including two high risk types that cause 70% of all cervical cancers. Therefore, screening will remain critical to protect women against cervical cancer because HPV vaccination reduces the risk of developing cervical cancer but does not eradicate it.

The three HPV vaccines are given as two or three injections over 6-12 months. Girls are best protected if they receive all doses and have time to develop an immune response before being sexually active. Many European countries have now introduced routine HPV vaccination programmes for girls aged 10-14. But in many countries, fewer than expected girls have received the vaccine, and target ages, financing and delivery of the vaccines differ greatly within Europe.[5]

HPV can also cause genital warts and other cancers, including penile cancer and anal cancer. In future, more countries may introduce routine HPV vaccination for boys depending on its effectiveness and cost effectiveness.

Factors that increase the likelihood of HPV persisting and developing into cervical cancer include:[6]

- Smoking
- Other infections including herpes and chlamydia
- HIV and immunosuppression such as following transplantation
- Having several children
- Multiple sexual partners and early age of first sexual intercourse (because they increase the likelihood of HPV infection)
- Personal history of some gynaecological and other cancers
- Family history of cervical cancer
- Older age

How is cervical cancer diagnosed?

The first step in finding cervical cancer is often an abnormal Pap test result. This will lead to further tests which can diagnose cervical cancer.

Cervical cancer may also be suspected if you have abnormal vaginal bleeding (the most common symptom):

- Between periods or during or after sexual intercourse
- Post-menopausal bleeding, if you are not on Hormonal Replacement Therapy or have stopped it for six weeks. Other symptoms include:
- Vaginal discharge that can smell unpleasant
- Discomfort or pain in the pelvis including during sex
- Lower back pain

These symptoms can be caused by cervical cancer, but they can be caused by other conditions as well. Whatever the cause, you should immediately consult a doctor if you have any of these symptoms.

Tests to confirm the diagnosis include:

- Internal pelvic examination to check the cervix
- Colposcopy
- Biopsy of the cervix
- Scans to assess how far the cancer has spread.

Pre-cancerous cells and early stage cervical cancer usually do not cause any symptoms, and can be detected only by Pap or liquid-based cytology testing or colposcopy. Diagnosis is definitely confirmed by a biopsy (taking a small sample of tissue to check under a microscope).

How are biopsy results are reported?[9]

Pre-cancerous changes on a biopsy are called cervical intraepithelial neoplasia (CIN), while on a Pap test they would be called squamous intraepithelial lesion (SIL). CIN is graded on a scale of 1 to 3 based on how much of the cervical tissue looks abnormal when viewed under the microscope. In CIN1, not much of the tissue looks abnormal, and it is considered the least serious cervical pre-cancer. In CIN2 more of the tissue looks abnormal, and in CIN3 most of the tissue looks abnormal. CIN3 is the most serious pre-cancer.

Sometimes the term dysplasia is used instead of CIN. CIN1 is the same as mild dysplasia, CIN2 is the same as moderate dysplasia, and CIN3 includes severe dysplasia as well as carcinoma in situ, which has not started to invade the normal tissues. The terms for reporting cancers (squamous cell carcinoma and adenocarcinoma) are the same for Pap tests and biopsies.

How is cervical cancer treated?

Abnormal cells can be removed before they become cancerous using surgery to surgically remove or electrosurgery to destroy the lesion. Full removal is preferred because it provides histopathological assessment. Treatment of invasive cancer may involve a combination of:

- Surgery can cure cancers limited to the cervix and surrounding tissues. It may be performed by laparotomy (open surgery) or laparoscopy ("minimally invasive" surgery).
- Radiotherapy can cure cancers, limited to the cervix, and it also used to destroy any remaining cancer cells after surgery or to relieve symptoms. It is also highly effective against advanced cancers with or without chemotherapy.
- Chemotherapy is given to shrink advanced cancers and relieve symptoms. It is also sometimes used before surgery or radiotherapy.

Most locally advanced cervical cancer treatments will be a combination of both chemotherapy and radiotherapy. In these cases, there is a higher risk of tumor regrowing locally with appearance of pain in the backbone and lower abdomen, urinary problems, swollen legs, vaginal infections and sometimes bleeding. A good collaboration among all the physicians already involved in the treatment is important.

Further Information

- European Cervical Cancer Association (ECCA): http://www.ecca.info/
- Jo's Cervical Cancer Trust: http://www.jostrust.org.uk/
- World Health Organization. Human papilloma virus and cervical cancer: www.who.int/mediacentre/factsheets/fs380/en/#
- European Cancer Observatory: http://eu-cancer.iarc.fr
- EUROCARE: http://www.eurocare.it
- ENGAGe: http://engage.esgo.org/en
- Women's silent cancers - The state of gynaecological cancers in Europe. Updated September 2013: http://engage.esgo.org/sites/default/files/atoms/files/2013_facts_figures_brochure-print-final.pdf
- ENGAGe network members: http://www1.esgo.org/esgomaps/
- ESGO: http://esgo.org
- RAIDs (Rational molecular Assessments and Innovative Drugs selection): This dropbox was created in order to understand the needs and concerns of cervical cancer patients. All cervical cancer patients from all countries are invited to ask their questions. http://www.raids-fp7.eu/a-question.html

References:

1. European Commission DG Health & Consumers: http://ec.europa.eu/health/sti_prevention/hpv/index_en.htm (last accessed 21 October, 2014)
2. GLOBOCAN. http://globocan.iarc.fr (last accessed 1 September 2014)
3. Arbyn A, et al. Ann Oncol 2010;21:448-58
4. Kyrgiou M et al. Lancet 2006;367:489-98
5. European Centre for Disease Prevention and Control. Introduction of HPV vaccines in EU countries—an update. Stockholm: ECDC; 2012
6. Boyle P, Lewin B. World cancer report. International Agency for Research on Cancer 2008
7. Cancer Research UK. Cervical cancer risk factors. http://www.cancerresearchuk.org/cancer-info/cancerstats/types/cervix/
8. American Cancer Society (ACS) http://www.cancer.org/cancer/cancercauses/othercarcinogens/infectiousagents/hpv/hpv-and-cancer-info (last accessed 21 October 2014)
9. American Cancer Society (ACS) http://www.cancer.org/cancer/cervicalcancer/detailedguide/cervical-cancer-diagnosis (last accessed 21 October 2014)

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