

MINISTRY OF HEALTH PROTECTION OF UKRAINE  
NATIONAL MEDICAL UNIVERSITY

Faculty of Medicine No. 1,  
Department of Obstetrics and Gynecology No. 1

**METHODOLOGICAL INSTRUCTIONS ON THE DISCIPLINE  
"OBSTETRICS AND GYNECOLOGY"**

**"DISEASES OF THE ORGANS OF THE FEMALE REPRODUCTIVE  
SYSTEM. FAMILY PLANNING.  
Industrial medical practice in the obstetrics and gynecology department »**

**Topic "Risk factors, early diagnosis and prevention of malignant neoplasms  
of female genital organs and mammary glands"**

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## **Topic "Risk factors, early diagnosis and prevention of malignant neoplasms of female genital organs and mammary glands"**

### **I. Relevance of the topic**

Early diagnosis of malignant tumors of the female external genital organs and mammary glands is one of the urgent problems, due to the fact that in 75% of cases the disease is detected in advanced stages, although this localization of cancer refers to visual forms, where it is possible to establish a diagnosis in the early stages and carry out treatment. Malignant tumors detected in the early stages are curable in almost 100% of cases. However, the five-year survival rate of vulvar cancer is only 47.3% (according to the International Federation of Obstetricians and Gynecologists), which is due to a patient's untimely referral to a doctor. Usually, patients explain this by the fact that at menopausal age it is no longer necessary to visit the doctor for a preventive examination (let young people go), and they are ashamed. But the disease begins mainly in women aged 45-50 years and evolves through the stages of dystrophy of the vulva, dysplasia of the vulva, pre-invasive and invasive cancer. Therefore, prevention and treatment of background diseases and dysplasia of the vulva are most relevant. It is necessary to pay attention to the appearance of dysplasia of the external genitalia in young women, which is due to the high level of infection of this age group with viral infections, namely the human papilloma virus and herpes viruses

### **II. Learning objectives**

Familiarize yourself ( $\alpha=1$ ),

- with the frequency of background and precancerous conditions of female genital organs and mammary glands.

Learn ( $\alpha=2$ ) :

- Causes and pathogenesis of background and precancerous conditions of the cervix and endometrium and mammary glands

- Risk factors of background and precancerous conditions of the cervix and endometrium and mammary glands

- Classification of background and precancerous conditions of the cervix and endometrium and mammary glands.

- Diagnosis of background and precancerous conditions of the cervix and endometrium and mammary glands.

- Clinic of background and precancerous conditions of the cervix and endometrium and mammary glands

- Medical tactics of background and precancerous conditions of the cervix and endometrium and mammary glands

- Methods of treatment of background and precancerous conditions of the cervix and endometrium and mammary glands

- Methods of preventing background and precancerous conditions of the cervix and endometrium and mammary glands

Master and improve skills ( $\alpha=3$ ):

- Collect gynecological history

- Perform a gynecological examination.

- Evaluate the results of additional research methods (laboratory, ultrasound, endoscopic, instrumental, histological).

Be able to ( $\alpha=4$ ):

- Collect the anamnesis and highlight the signs characteristic of background and precancerous conditions of the cervix and endometrium and mammary glands.

- Make an examination plan for the diagnosis of background and precancerous conditions of the cervix and endometrium and mammary glands.

- To evaluate the results of the main and additional examination for background and precancerous conditions of the cervix and endometrium and mammary glands.

- To diagnose background and precancerous conditions of the cervix and endometrium and mammary glands.

- To determine the risk factors for background and precancerous conditions of the cervix and endometrium and mammary glands.

o. No	Disciplines	Know	Be able
<b>Providing disciplines</b>			
1.	Human anatomy	Anatomy of external and internal genital organs	To describe the structure of the female genital organs
2	Histology	Histological structure of the uterus and mammary glands	Evaluate the results of histological examination
3	Pathological anatomy	Histological structure background and precancerous conditions of the cervix and endometrium and mammary glands	Evaluate the results of histological examination
	Topographic anatomy	Interposition of the female genital organs with the organs of the urinary and digestive systems.	Differentiate formation of pelvic organs
	Surgery	Clinic and diagnosis of "acute" abdomen, hemorrhagic shock	Provide emergency care for bleeding, determine treatment tactics for acute abdomen
<b>Provided disciplines</b>			
1	Family medicine	Clinic, diagnostics, methods of treatment background and precancerous conditions of the cervix and endometrium and mammary glands	Diagnose and make a plan for examination and treatment at background and precancerous conditions of the cervix and endometrium and mammary glands
<b>Intra-subject integration</b>			
1.	Research methods in gynecology	Basic and additional methods of examination in gynecology	Carry out a gynecological examination. Evaluate the results of clinical and laboratory studies and additional examination methods

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•To determine the management tactics of a patient with background and precancerous conditions of the cervix and endometrium and mammary glands.

•Prescribe treatment for background and precancerous conditions of the cervix.

- Prescribe treatment for background and precancerous conditions of the endometrium.

- Prescribe treatment for background and precancerous conditions of the mammary glands

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- Make a plan for the rehabilitation of patients with background and precancerous conditions of the cervix

- Make a plan for the rehabilitation of patients with background and precancerous conditions of the endometrium

- Make a plan for the rehabilitation of patients with background and precancerous conditions of the mammary glands

- Draw up a plan for the rehabilitation of patients with trophoblastic diseases

### III. Educational goals

- Educational (to teach students responsibility and consistency in work, sensitivity and tolerant attitude towards pregnant women, women in labor, women in labor, gynecological patients);

- Scientific (to teach students logical clinical thinking based on new diagnostic and treatment methods for him);

- Creative (give the student the opportunity to independently solve an atypical problem with an independent choice of the solution path);

- Responsible (to develop in students a sense of responsibility for the correctness of professional actions).

### IV. Interdisciplinary integration:

### V. Content of educational material

The widespread prevalence of malignant tumors of the female genital area, which occupy a leading place in the structure of oncological morbidity in women, as well as the continuous improvement of methods of their diagnosis and treatment, make it necessary to acquaint not only practicing doctors, but also students with modern achievements in

this area. Doctors of various specialization profiles now more often than before have to solve the issue of not only early diagnosis, but also the prevention of these diseases. Since even complex treatment of malignant processes does not give the desired result, especially in advanced cases, prevention and early detection of oncopathology come first. As a rule, the development of oncological diseases is preceded by background and precancerous processes, which are effectively curable with timely diagnosis. Thus, the earliest possible diagnosis of background, precancerous and malignant diseases is very important in order to preserve the health and life of patients.

High-risk groups for cancer of the female genital organs:

I - women who are at risk of cervical cancer, kraurosis, leukoplakia, erythroplakia of the vulva and vagina.

II - women who are at risk of uterine cancer, ectopy, eroded ectropion, leukoplakia, and uterine dysplasia.

III – women who are at risk of developing cancer of the uterus, complicated oncological history, neuroendocrine disorders, ovulation disorders, endometrial hyperplasia, hormonally active ovarian tumors, uterine fibroids.

IV – women at risk of ovarian cancer, ovarian surgery, ovarian cysts, chronic inflammation of the appendages, ovarian dysfunction, benign ovarian tumors

V - women who are at risk of fallopian tube cancer, chronic recurrent inflammation of the uterine appendages

The risk factors for the occurrence of cancer of the external genital organs include: early age at the onset of menstruation (up to 12 years and earlier), early onset of sexual life, infertility, the presence of chronic sexually transmitted infections, especially human papillomaviruses and herpes viruses, a large number of childbirths ( more than three), the age of onset of menopause (up to 40 years) and its duration of more than 11 years, concomitant diseases: cardiovascular, chronic diseases of the liver and gastrointestinal tract, diseases of the thyroid gland/

What patients should pay attention to. The first and widespread symptom of vulva diseases is itching, which occurs at any time of the day, but mainly at night. Its intensity can be different, in severe cases it can drive a woman to insanity. Itching can be disturbing in case of background diseases of the vulva, i.e. those that, like a "trigger", start the entire cascade of transformation of cells into cancer cells and the formation of a malignant tumor. Also, itching can bother a woman with diseases of the liver and biliary tract, pancreas, stomach, intestines, kidneys, with diabetes, parasitic invasions (infection with worms), hormonal disorders and other diseases. The second symptom is pain syndrome. Pain can occur independently at any time of the day, can accompany sexual intercourse. The third symptom that should be paid attention to is the nature of discharge from the genital tract: purulent watery discharge with an unpleasant odor and dirty discharge should alert a woman. Dysuria (painful and frequent urination) can also bother a woman. When carrying out daily hygiene procedures, you should pay attention to the appearance of dryness of the skin and mucous membranes, cracks, the presence of white and red spots, tumors, blisters.

### **Cervical cancer risk factors**

- Human papilloma virus (HPV) infection. HPV DNA is determined in 75 - 100% of cases of cervical cancer, in 77 - 94% of cases of cervical intraepithelial neoplasia (dysplasia) of various degrees, and in 30 - 70% of cases with a normal cytological picture.

Currently, more than 150 types of HPV are known, almost 40 of which infect the anogenital area. They are divided into 2 large groups: highly oncogenic viruses that cause cancer in multilayered flat and cylindrical epithelia (15 types of them are already known: 16, 18, 31, 33, 35, 39, 45, 51, 56, 68, 73, 82, 26, 52, 53rd), and low-oncogenic, which most often lead to tumor and precancerous diseases in multilayered flat epithelium. Currently, 14 types have been studied in detail: 6, 11, 34, 40, 42, 43, 44, 54, 55, 61, 62, 70, 71. The highest risk of developing cervical cancer is associated with types 16, 18, 31, as well as 33, 35, 45 HPV. At the same time, the number of people infected with HPV is much higher compared to the frequency of precancerous diseases and cervical cancer.



Tens and hundreds of millions people infected with HPV are registered in the world every year, and in most cases, the virus is eliminated on its own without any treatment. Cervical intraepithelial neoplasia of the II and III degree appears only in a small part of women.

- Early onset of sexual life (up to 16 years). It is believed that at a young age, the epithelium of the vaginal part of the cervix is more susceptible to carcinogenic factors, primarily due to the increased amount of glycogen. It is possible that a longer exposure to carcinogenic factors on the cervix is important. However, this risk factor is not recognized by all researchers.

- **A large number of sexual partners.** The frequency of invasive cervical cancer is directly proportional to the number of sexual partners during the patient's lifetime.

- **The male factor.** A high prevalence of HPV in men is noted in those countries where the largest number of invasive cervical cancers are found. It was noted that in patients with cervical cancer, men were more likely to get sexually transmitted infections, were prone to risky sexual behavior, and had contact with prostitutes.

- **A large number of pregnancies.** With an increase in the number of pregnancies, the risk of developing cervical carcinoma also increases: in women who have had 4 or more pregnancies, the risk of developing cervical cancer is on average 2 times higher, and in the presence of 4 or more deliveries, it is 3 times higher than in women who have not were pregnant.

- **Low socio-economic status.** About 80% of all oncological pathology of the cervix occurs in developing countries, which is associated with both the lack of funds for screening and the low cultural level of the population in these countries. In addition, HPV of oncogenic strains are more often detected in cervical mucus in women of low social status.

- **Smoking**, including the passive. In women who smoke, as well as in those who do not smoke, but are surrounded by tobacco smoke for at least 3 hours a day, nicotine, continin and tobacco-specific N -nitrosamines, which cause damage to cervical DNA, are determined in the cervical mucus. epithelium and disrupt the local cellular immune

response. It has been proven that such women have a 3-8 times higher incidence of cervical cancer compared to the general population.

- **HIV infection.** Invasive cervical cancer is included in the list of conditions characteristic of acquired immunodeficiency syndrome (AIDS). In HIV-infected people, the frequency of cervical pathology is higher than in people without HIV infection. HIV is also a cofactor of HPV in the development of cervical pathology, although the mechanism of their interaction is not completely clear.

- Taking immunosuppressants. Immunosuppressants (glucocorticoids, cytostatics) inhibit the cellular immune response and contribute to the occurrence and progression of cervical cancer.

-**Contraception.** The use of barrier methods, especially in combination with spermicides, reduces the risk of cervical cancer. The effect of taking combined oral contraceptives (COC) on the frequency of the disease has not been proven.

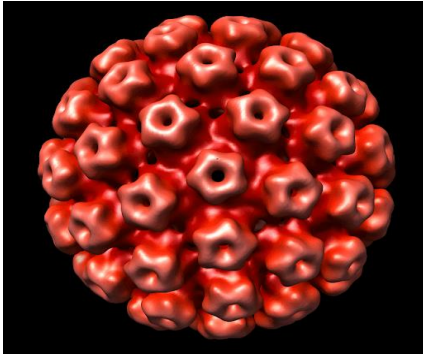
-Race. People from Africa and Latin America get this disease twice as often as Europeans. Representatives of the peoples of Asia have morbidity with the same frequency as Europeans or less often.

It should be noted: the connection between cervical neoplasia and infection with Chlamydia trachomatis, Herpesvirus type 2, and Cytomegalovirus has not been proven.

**Human papilloma virus-** this is a common infection of the genital tract. This pathogen is found in almost every sixth inhabitant of the planet. When infected, the pathogen enters the epithelial cells, disrupting the process of division, activates the development of various diseases. Mostly, the virus affects the organs of the genitourinary system, the anorectal region. Diseases that occur when infected with HPV:

1. Formation of acute condylomas.
2. Development of papillomatosis of the respiratory tract.
3. Damage to the genitals with the development of a tumor process.

Almost 70% of the population are carriers of the pathogen without clinical manifestations of the disease. Re-infection is also possible during life. Because not all patients with papillomavirus infection develop resistance to the virus.



## Types of HPV

Currently, more than 150 types of HPV are known. Some of them are relatively safe for human health, others can activate the development of oncological processes. Most often, clinical signs of the disease are not manifested in the first stages. Usually, the first symptoms appear after the action of provoking factors.

According to oncological activity, such viruses are classified into:

1. Strains with a high oncogenic risk (18, 16, 31, 33, etc.)
2. Strains with a low oncogenic risk (6, 11, 32, 40-44, 72)

Low oncogenic strains of viruses lead to warts and skin papillomas on the surface of the body.

Highly oncogenic strains cause the formation of warts in the anogenital area, on the surface of the cervix in women and the penis in men.

Long-term effect on the body of 16,18, 31,33 types of virus can lead to cervical dysplasia and a more dangerous disease - cervical cancer.

However, even with the presence of high oncogenic risk HPV in the body, oncological pathology does not always develop. Timely referral to experienced doctors for diagnosis, correctly selected treatment, will allow you to never encounter dangerous clinical manifestations of the human papilloma virus.

Female and male patients are affected by this pathogen equally often.

The main way of transmission is considered to be sexual. Usually, HPV is infected after the first sexual contact, but there are also other ways of transmission of infection:

1. Vertical. That is, during the passage through the birth canal of a woman infected with HPV, the newborn can become infected.
2. Autoinoculation. Self-infection (transfer from one part of the body to another) during epilation or shaving is possible.
3. Contact household. The human papilloma virus remains viable in the environment for some time. Therefore, you can get infected with it after visiting public places (bath, gym, swimming pool).
4. Contact. Infection is possible through a wound surface on the skin or mucous membranes (abrasions, wounds, bruises).
5. Sexual. The most common route of infection.

Anyone can get a viral infection. In order to diagnose it in a timely manner, it is necessary to undergo preventive examinations by a doctor to determine the first symptoms of the pathology.



### **The main manifestations of infection**

The presence of papillomavirus infection may not have clinical manifestations for a long time. The incubation period of the disease can last several years, during which the patient can be infected with different types of the virus. Only after exposure to provoking factors (immunodeficiency, hypothermia, stressful situations) can one observe signs of HPV infection. In most cases, self-treatment of this infection occurs within 1-2 years, but in some patients the pathology becomes chronic.

The disease can be manifested by the following formations:

1. **Genital warts** (acute condylomas). Externally, these are papilla-like growths that resemble cauliflower or a comb in shape. They have flesh or pink color, can be single or multiple. They can form anywhere, but are most often found on the skin and mucous membrane of the genitals. Formations are characterized by low oncogenic potential. They rarely turn into malignant neoplasms, usually do not cause discomfort to the patient.



2. **Flat condylomas**. They have a characteristic structure - they do not protrude above the surface of the mucous membrane of the affected organ. Such formations have a high oncological potential, so they require a more thorough diagnosis. They are usually located on the mucous membrane of the walls of the vagina, urethra, and cervix. To diagnose the nature of the condyloma, a biopsy is required.



3. Dysplasia. It is characterized by a violation of the differentiated structure of the tissue. There is often the presence of atypical cells that can cause the development of oncological pathology. It requires careful observation and, if necessary, surgical correction.



Each of the forms of pathology must be carefully monitored by a doctor. To reduce the risk of developing an oncological process, it is recommended to remove such growths on the skin and mucous membranes.

### Diagnosis of HPV

It is necessary to diagnose the presence of HPV in stages, for this a number of physical, laboratory and instrumental studies are used.

1. Examination by a doctor. With its help, you can detect the presence of warts. When condylomas are detected in the anogenital area, a cervical examination is mandatory. Urethroscopy is also possible.

2. Colposcopy. Conduct specific tests with acetic acid and Lugol's solution. With their help, you can determine the presence of atypical cells, signs of HPV infection and cervical cancer.

3. Cytological research. Pap smears of the cervical mucus are taken. This is a screening test for the presence of precancerous and oncological cells in the wall of the vagina or cervix.

Histological examination of tissues, detection of sexually transmitted diseases with which HPV infection is often associated can also be carried out. The PCR method has a high diagnostic value. It can be used to identify the HPV strain.

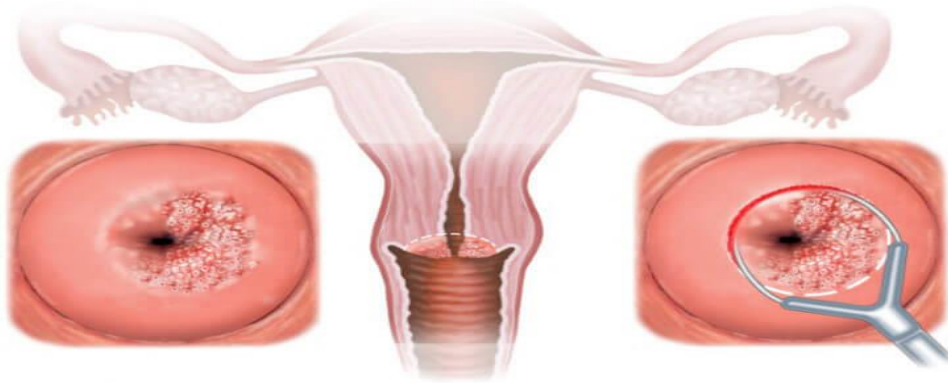
### HPV treatment

It is impossible to completely eliminate the virus from the patient's body. The doctor can fight only with the consequences of the vital activity of the infectious agent. Symptomatic agents, antivirals, and drugs that stimulate immune processes can be used as general therapy.

To combat various types of warts, the following can be used:

1. Cryodestruction, electrocoagulation, cauterization with a laser or chemical substances. Such methods are effective in getting rid of acute condylomas.

2. Electrosurgical treatment methods are used to remove the affected area on the surface of the cervix (dysplasia, condyloma).



### Prevention of HPV

In order to prevent the development of the disease, various methods are used. The most effective are:

1. Monogamous relationships. You have sex only with a person for whom you are the only sexual partner. This method will allow you to protect yourself from all sexually transmitted infections, including HPV.

2. Use of barrier contraception. It is easy, affordable, but not always 100% to prevent infection. The patient can become infected with the virus, even when coming into contact with an area of damaged skin.

3. Periodic preventive examinations. Girls need to be regularly examined by a gynecologist. In this way, the first signs of the disease can be detected and its treatment can be started in time.

4. Vaccination. This is an effective and convenient preventive method. Vaccination can be carried out in both men and women. There are the following vaccines:

Cervarix (bivalent against type 16 and 18).

Gardasil (tetraivalent 16, 18, 6, 11 type).

Vaccination is most effective before the onset of sexual life (application is allowed from 9 years of age). Or individuals live a sexual life in the absence of contraindications

## **Cervical cancer screening**

Translated from English, the word screening means selection, sifting or securing from something unpleasant. Screening in oncology is understood as a system of secondary prevention measures aimed at diagnosing precancerous and early stages of cancer.

The ACS recommends that women start cervical cancer screening at age 25 and have initial human papillomavirus (HPV) testing every 5 years until age 65 (preferred). If primary HPV testing is not available, individuals aged 25 to 65 should have cotesting (HPV testing combined with cytology) every 5 years or cytology alone every 3 years (acceptable). (Strong recommendation). Cotesting or cytology alone are acceptable cervical cancer screening options because access to an FDA-approved primary HPV test may be limited in certain settings. As the United States transitions to primary HPV testing, the use of both cotesting and cytology for cervical cancer screening will not be included in future guidelines.

Often screening should be once a year. If there are 3 consecutive negative results, the frequency may be 1 time in 3 years.

### **Methods of detecting precursors of cervical cancer.**

What to do if a pathological type of smear is detected?

You should consult a gynecologist for a detailed examination. The fact is that the result of a cytological screening test is not a basis for establishing a diagnosis, let alone prescribing treatment!

What additional examinations does the doctor perform to make an accurate diagnosis?

**1) Colposcopy** is an examination of the cervix using an optical device with additional lighting and magnification. The method makes it possible to detect precancer and initial cancer of the cervix, which are not visible during a routine gynecological examination. Tasks of colposcopy:

- an adequate examination of the transformation zone - the meeting point of the multilayered flat nonkeratinized epithelium of the vaginal part of the cervix and the single-layered cylindrical epithelium of the cervical canal, which is the source of 90% of oncological pathology of the cervix



- clarify the topography of the process
- choose a place for targeted biopsy.

The use of colposcopy as a screening procedure is not recommended!!!

**2) Targeted biopsy**— with the help of forceps, a sample of cervical tissue is taken from the pathological focus for histological examination and diagnosis.

**3) Scraping of the cervical canal (curettage) and uterine cavity (according to indications)** is a scraping of tissue from the cervical canal for histological examination to determine the extent of the cervical lesion. All these procedures are practically painless and do not require anesthesia.

- Material from the vaginal part of the cervix is taken with an Air spatula of the appropriate size, and from the cervical canal with an endocervical brush; cells from the transformation zone must be present in the material;

- Taking the material must be done on the 10th - 18th day of the cycle (from the 1st day of the last menstruation);

- Do not douche within 48 hours before the test;

- Do not use tampons, vaginal creams 48 hours before the test;

- Refrain from sexual contact for 48 hours before the test. The recommendations of the American Society for Colposcopy and Cervical Pathology, which were approved in 1988 and revised and supplemented in 2001, are currently used for the interpretation of PAP smears (Table 2).

#### **4) Determination of oncogenic strains of HPV**

It is established that from 30 to 70% of all sexually active women are infected with the human papilloma virus, which is associated with the majority of cases of CIN II, CIN III, as well as pre-invasive and invasive carcinoma. The mechanism of the oncogenic effect of HPV is not fully understood, however, studies have shown that the DNA of the virus, embedded in the host's genome, blocks the E2 gene and begins to reproduce the so-called oncoproteins E6 and E7, which inhibit natural tumor suppressors, leading to the activation of cell growth (Figure 1).

The HPV test is used:

- during primary screening in women aged over in combination with cytological examination in countries with organized cytological screening;
- as an independent test in those countries where there is no cytological screening or not organized;
- in case of an uncertain result of a cytological examination;
- for monitoring after treatment of CIN 2–3 and initial forms of RSM.

Primary screening using HPV self-testing. Pilot and cohort studies of a new method of obtaining cellular material for HPV testing are being conducted in many countries (especially in Sweden). Screening on the basis of a "self-smear" taken at home, followed by a cytological examination carried out in a medical institution, turned out to be cost-effective. However, these techniques require clinical confirmation of the expected results.

#### **Methods of determining HPV in cervical mucus:**

- Blot
- hybridization in situ
- liquid phase hybridization (hybrid capture). Sensitivity 59 - 86% for the determination of CIN in women with a cytological picture of nonspecific atypical squamous cell changes and mild PIP.
- polymerase chain reaction (PCR). In determining CIN, sensitivity reaches 98-100%, specificity - no more than 10%. The positive prognostic value in relation to CIN II, CIN III, carcinoma in situ is also no more than 10%.
- tests for the determination of the E7 protein in cervical mucus are under development, which will allow us to find out the depth of the introduction of HPV into the host's cell and, perhaps, will serve as a more reliable test for detecting HPV-dependent changes in the cervix.

#### **Prevention of cervical cancer**

In Ukraine, vaccination against cervical cancer (CRC) is recommended for women and girls from 9 years of age. The program was developed in cooperation with the European Cervical Cancer Association (ECCA).

Prevention of oncological diseases caused by HPV is compliance with the rules of sexual behavior, use of barrier methods of contraception, regular gynecological examinations and cytological examination (PAP test) even in the absence of complaints and, of course, VACCINATION.

There is currently no effective treatment for HPV. Under the age of 25, the virus often disappears on its own, thanks to the work of the immune system.

### **TYPES OF PAPILOMAVIRUS VACCINES:**

- **"Cervarix"**– a recombinant vaccine made from highly purified non-infectious virus-like particles (HPV) of the main capsid protein (L1) of the HPV type 16 and 18 envelope;

- **"Gardasil-4"**– adjuvant non-infectious recombinant quadrivalent vaccine that protects against HPV types 6, 11, 16 and 18;

- **"Gardasil-9"**- adjuvant non-infectious nine-valent recombinant vaccine against human papilloma virus (protects against 9 types: 6, 11, 16, 18 31, 33, 45, 52, 58).

### **VACCINATION WITH THESE VACCINES PREVENTS THE FOLLOWING DISEASES:**

- Maca cervical cancer. If a woman was not infected with HPV and was vaccinated before the age of 25, the effectiveness of protection is 98-100%;

- precancerous conditions and malignant neoplasms of vulva and vagina;

- anal cancer in women and men;

- genital warts, precancerous or dysplastic conditions;

- cervical intraepithelial neoplasia of the vulva, vagina, anal canal of various degrees, etc. However, we remember that the mentioned HPV vaccines protect against a maximum of 9 types of HPV, namely, 15 types are highly oncogenic.

### **VACCINATION AGAINST HPV IN UKRAINE**

"Gardasil-4", "Cervarix" can be vaccinated on the territory of our state.

There is no "Gardasil-9" yet.

### **VACCINATION AGAINST HPV**

In order to achieve the greatest effect, vaccination against the papillomavirus should be done before the start of sexual life. Studies prove that immunity lasts for about 10 years. Ideally, during this time, a person finds a permanent sexual partner and creates a family. So, after that, even with reduced immunity, the risk of HPV infection will be minimal. The vaccine is administered intramuscularly in the shoulder. Vaccination is repeated once or twice. Gardasil — with an interval of six months, Cervarix — after 1 and 6 months. If the vaccination was carried out only once, it is necessary to re-vaccinate at least until the age of 26

**Secondary prevention of oncological diseases** consists in the implementation of screening programs to detect precancerous conditions or early stages of cancer, in which effective treatment is possible. Screening for cervical cancer, breast cancer, and colorectal cancer has proven its effectiveness at the population level [8, 9].

Cervical screening is the main component of secondary prevention of cervical cancer. Data obtained in recent years regarding the role of cofactors in the development of cervical cancer against the background of HPV persistence (chlamydial infection, violation of vaginal biocenosis, smoking) make it possible to consider their influence as a component of secondary prevention in the future [10, 11].

**Tertiary prevention of RSHM** aims to prevent disease recurrence and improve prognosis/survival in such patients [6, 7]. Tertiary prevention involves treatment according to the stage of disease development and rehabilitation [6, 7].

A Pap test by the method of liquid or traditional cytology is a study that is used in the screening for PCM. Risk factors and prevention of breast cancer.

All women over the age of 18 who receive care from a general practitioner/family medicine must be entered in the register, undergo a questionnaire to assess genetic risk. The primary task for a general practitioner /family medicine is to explain to the female population the feasibility of participating in screening and involving as many women as possible aged 50–69 years, without complaints and without genetic risk of breast cancer (BC), to mammography. Age is the biggest risk factor for most women.

Prevention of breast tumors is divided into primary, secondary and tertiary.

**Primary prevention** consists in providing information on avoiding risk factors for the prevention of smoking, excessive alcohol consumption, excess weight, hypodynamia, stressful situations, and excessive sun exposure.

**Secondary prevention** consists in the early detection of benign dyshormonal diseases of the mammary gland and the timely correction of hormonal disorders, which are a prerequisite for the development of tumors. As well as regular monthly self-examination starting from the age of 20. Clinical examination of the mammary gland (MG) at a general practitioner/family medicine doctor once every three years (all age groups).

The "gold standard" of prophylactic examination of MG is bilateral mammography in the screening program for breast cancer, which is due to the high efficiency of diagnosing asymptomatic malignant tumors: in 85-90% of cases.

**Tertiary prevention.** Specific tertiary prevention consists in the appointment of hormonal therapy for women in menopause for a period of up to 5 years, leads to a decrease in the possibility of recurrent tumors (in the case of hormone-dependent tumors), but can provoke thromboembolic complications and endometrial cancer.

The high-risk group includes individuals with a combination of certain genetic, phenotypic factors and lifestyle features.

The main factors that increase the risk of breast cancer are:

- age (over 40 years);
- hereditary and family predisposition (women whose mothers or sisters suffered from breast cancer have a much higher chance of developing this disease);
- late menopause;
- early onset of menstruation (up to 12 years);
- the birth of the first child over the age of 30;
- termination of pregnancy;

- in women who have never given birth;
- the presence of fibrocystic mastopathy and other proliferative diseases of the mammary glands;
- obesity (over 40% of normal weight);
- diabetes, hypertension;
- systematic smoking and alcohol consumption. Breast cancer in women under the age of 25 practically does not occur.

### **Breast cancer screening**

All women over the age of 18 attached to a general practitioner/family medicine must:

- 1) to receive information on the risk factors of breast cancer related to lifestyle;
- 2) be educated of the methods of breast self-examination from the age of 20 (monthly from the 7th to the 14th day of the cycle);
- 3) to receive information about cases of familial cancer and the possibility of counseling regarding genetic factors.

There is no evidence regarding MG.

There is evidence of the decisive impact of national screening programs on reducing mortality from breast cancer.

1. Informing patients about breast cancer screening and the expediency of participating in it for people aged 50–69.
2. A clinical examination of the MG is carried out once every 3 years by a general practitioner / family medicine, a paramedic, a nurse (who has received special training) before referral for a mammographic examination.

### **BREAST CANCER SCREENING PROGRAM**

## The main tasks of a general practitioner/family medicine doctor

1. Keeping a register of the female population receiving care from a general practitioner/family medicine doctor.

2. Completion of the "Anamnesis Questionnaire" by all women who receive the care of a family doctor, in order to identify "familial" breast cancer.

3. Explaining to the female population the feasibility of participating in screening for breast cancer and involving as many women as possible aged 50-69, without complaints about breast cancer and without a genetic risk of breast cancer to mammography. Age is the most important risk factor for most women.

4. Provision of information to all women regarding the method of self-examination of MG, which is carried out monthly starting from the age of 20 (on days 7-14 of the cycle).

5. A clinical examination of the mammary glands is carried out once every three years by a general practitioner/family medicine doctor, a paramedic, a nurse who has undergone special training, in primary health care facilities, before referral for a mammographic examination.

6. Organization of a general practitioner/family medicine doctor to refer a woman to a regional diagnostic center or dispensary for mammography (by phone or other forms of personal invitations).

7. Entry of data by a family doctor into the register of the female population regarding a woman's mammographic screening.

The main task of oncologists and radiologists is to provide high-quality mammography with the provision of a written conclusion to all women who have contacted them regarding the mammographic screening program.

8. Carrying out mammography:

- do not prescribe mammography to women under the age of 35, if there are no convincing reasons for this (use ultrasound examination);

- if there is a family history of breast cancer - mammography is recommended once every 1-2 years (regularly examining the breasts independently and in the doctor's office), starting at the age of 35;

- in the age range of 35-40 years, all women undergo a one-time primary mammography to determine the structure of the mammary gland tissue;

- at the age of 40-49, it is suggested to carry out mammography depending on the indications (clinical examinations and self-examinations);

- at the age of 50-69, mammography is performed once every 2 years, taking into account the results of previous examinations, self-examinations and clinical examinations.

9. Regular provision of information to the family doctor regarding lists of women who have undergone mammographic screening.

## **GENERAL ALGORITHM OF DIAGNOSTICS AND DIFFERENTIAL DIAGNOSTICS**

1. Mandatory studies:

1. Examination (pay attention to the color of the skin, symmetry of the MG, changes in the areas of the axillary, supraclavicular and subclavian lymph nodes.

2. Physical examination: 1. Clinical examination of mammary glands;

2. Measurement of blood pressure and pulse.

3. Laboratory studies: 1. Detailed blood analysis with formula;

2. Biochemical blood analysis (protein, bilirubin, urea, creatinine, glucose, electrolytes, alkaline phosphatase, Ca<sup>2+</sup>, ALT, AST, albumin);

3. Urine analysis

4. Instrumental studies: 1. Ultrasound examination of: both mammary glands and regional lymph nodes, organs of the abdominal cavity, retroperitoneal space and pelvis;

2. X-ray of the chest;

3. Mammography of both mammary glands in 2 projections;



4. Fine-needle biopsy or trepan biopsy of tumors with cytological, morphological and immunohistochemical examination of a punctate of mammary gland lesions, lymph nodes, a biopsy of mammary glands and lymph nodes;

5. Consultations of related specialists: 1.5.1. an oncologist surgeon, a radiation therapy doctor, a gynecological oncologist, if necessary, an anesthesiologist, a cardiologist.

6. According to the indications: 1. CT of the chest, abdominal cavity, retroperitoneal space and pelvis with intravenous contrast;

2. Cytological examination of secretions from the nipple and from ulcerative tumors; postoperative material;

3. MRI of mammary glands, brain;

4. Bone scanning and other radioisotope examinations (in the case of advanced disease, the presence of pain in the bones and an increase in alkaline phosphatase in blood serum);

Breast self-examination

### Review



Stand in front of a mirror first with lowered, and then with raised arms

**Pay attention to the following signs:**

- retraction or protrusion of the skin;
- nipple retraction;
- a change in the usual shape or size of one of the MG;
- the presence of yellowish or bloody discharge from the nipple;

- redness and swelling of skin areas of the MG.

### **Probing**

It is performed in a supine position. Under the scapula on the side being examined, place the roller in such a way that the chest is slightly raised. Palpate each breast with the opposite hand. Avoid rough palpation and grasping of a large area of breast tissue, as this may give the impression of a lump that is not there.

The examination is carried out in three positions:



- the hand on the examined side is directed along the body;
- the hand is directed upwards behind the head;
- the hand is directed to the side.

With the fingers of the second hand, the MG is palpated in the following way: you can choose circular movements (Fig. 1); linear movements up and down (Fig. 2); wedge-shaped movements (Fig. 3). Always palpate the mammary glands in the same sequence. This will help you not to miss a single area, as well as remember what your mammary glands usually feel like. The nipple is examined separately. It is squeezed between the fingers, starting from the edge of the areola, in order to make sure that no discharge appears from the nipple (Fig. 4).



Fig. 1



Fig. 2



Fig. 3



Fig. 4

**It should be remembered that when changes are detected in the mammary glands** it is necessary to consult a mammologist, who will conduct a clinical examination of the mammary glands and, if necessary, refer the patient to ultrasound of the mammary glands or mammography.

**Effectiveness of early detection.** Retrospective studies on the effectiveness of self-examination of MG in early detection of breast cancer show different results. However, it has been proven that if a woman conducts regular self-examinations, she has less chance of detecting cancerous growths of 2 cm or more or the transition of metastases to the lymph nodes.

### **Clinical examination of the mammary gland**

The clinical examination is carried out by a doctor, a paramedic, a nurse who has undergone training on the topic "Nursing in oncology" in health care institutions - once every 3 years, taking into account the data of previous self-examinations and examinations of the MOH.

Examinations are carried out according to the following plan:

**During the clinical examination of the mammary glands, the principle of cancer prevention is decisive.**

### **Clinical signs of malignancy are as follows**

- a tumor that is detected during palpation;
- retraction of the nipple or nipple skin;
- nipple asymmetry;
- nipple erosion;
- pain in the MG;
- axillary lymphadenopathy;
- edema of the upper limb;
- swelling of the skin - "lemon skin";
- pain in the axillary region.

**Review:** assess the symmetry of the glands and nipples, changes on the skin - local dilatation of veins, redness, "lemon peel" symptom, "flat" symptom, wrinkling of the skin and its retraction, retraction of the nipple and areola. MG is examined in the upright position of the patient with his head and hands down.

**Palpation:** start palpation symmetrically from the supraclavicular and subclavian areas with both hands at the same time, then move the hands down to the nipples with sliding stroking movements. The nipples are slightly squeezed and when secretions appear, slides are applied to them and swabs are prepared for cytological examination. Fix the color of discharge. Palpation of each MG is continued separately: placing the gland on the palm of one hand and supporting it from below, the fingers of the other hand feel from above the entire thickness of its tissues. To examine the regional lymph nodes, the doctor places the folded fingers of one of his palms to the armpit area (the woman's hand is raised up), and places the other on the upper arm. The woman slowly lowers her hand, and the doctor carefully palpates the armpit with slippery vertical movements. Similarly, everything is repeated from the opposite side. Next, they offer the woman to lie down on the couch and continue to palpate the MG spread out on the chest. Carefully, consistently palpate all areas of the gland in a circle, starting from the perimeter and ending with the area around the areola. They once again check the presence of discharge from the nipples, palpate the axillary, supraclavicular and subclavian areas. After

completing the physical examination, the doctor describes its results in the medical documentation (ambulatory chart, medical history): notes the quadrant of the MG where the pathology was detected, the size of the neoplasm, its consistency, contours, surface, mobility, fixation to the skin or adjacent tissues, soreness, asymmetry of the glands, the condition of the nipples and areolas, the nature of discharge from the nipples, the size of the lymph nodes — all symptoms are compared with the opposite gland.

During the examination of the mammary glands and the management of a woman when pathology of the MG is detected, the rule of "seven positions" (B) is used: 1) position - the examination of the woman is first carried out in a sitting position, then - standing, after that - lying down with raised arms; 2) size - turn attention to the asymmetry of the size of the glands; 3) palpation - performed "clockwise" with the pads of the fingers; 4) pressure - note the density of the mammary gland, if there is a formation - its density and displacement; 5) the examination method - must correspond to the accepted algorithm; 6) feedback - provides consistency and continuity of actions of specialists of various specialties; 7) dispensary observation

**When pathology is detected** during the screening, a further examination of the state of the mammary gland is carried out, which is carried out using the "triple test", which includes:

- ⊙ Clinical examination;
- ⊙ Bilateral mammography;
- ⊙ In the presence of bulky formations - fine-needle aspiration biopsy under ultrasound control with subsequent cytology.

**Women are younger than 40 years old** in order to reduce the radiation load on a woman's body, when palpation of a bulky neoplasm in the mammary gland is detected, it is advisable to use ultrasound of the mammary glands instead of mammography for diagnosis.

It is also possible to determine tumor markers and genetic factors:

**Oncomarker Ca 15-3.** Indications for appointment: differential diagnosis of breast cancer and benign mastopathy (hormonal); monitoring the effectiveness of breast

carcinoma treatment, early detection of relapses and metastases. The normal range is up to 25.0 Units/ml. It is used in combination with the cancer-embryonic antigen (CEA). Serum concentration may double during menstruation, endometriosis, and pregnancy (1st trimester).

**Cancer - embryonic antigen REA.** The determination of CEA in blood serum cannot be used to diagnose the initial stages of breast cancer due to its low specificity, but it can be used to detect recurrences and metastases in the distant period after surgery, to assess the effectiveness of treatment. Normal range: non-smokers (aged 20-69 years) up to 3.8 Units / ml, smokers (aged 20-69 years) up to 5.5 Units / ml.

**BRCA-1 and BRCA-2 genes** are the suppressor genes that encode proteins that inhibit cell growth. Women who carry a mutant form of the BRCA gene have approximately 90% chance of developing breast cancer during their lifetime. At the same time, the risk of developing ovarian cancer is about 40%. Breast cancer associated with BRCA-1 and BRCA-2 gene mutations in many cases has a higher degree of malignancy (mostly G3) compared to sporadic breast cancer.

#### **Diagnostic criteria — a tumor in the mammary gland**

Cancer (nodular form of breast cancer) is a dense, bumpy tumor of an irregular shape, limited mobility, progressive growth, painless in most cases. If the skin is involved in the process, the symptoms of "flat", "lemon peel", and umbilication appear. Hyperemia of the skin over the tumor is a sign of specific lymphangitis; thickening of the folds of the areola (Krause's symptom) is a local lymphostasis due to damage to the lymphatic plexus of the subareolar area.

Prybram's symptom: when the nipple is pulled, the tumor moves behind it.

König's symptom: when pressing with the palm of the hand on the MG, the tumor is felt under the palm and does not move; in the case of a benign tumor, it moves beyond the palm. Most often, a cancer lesion is localized in the upper outer quadrant. When the tumor is localized under the nipple, retraction, deformation or deviation of the nipple, pathological secretions are noted. A tumor of medium or large size deforms the contour

of the MG. Enlarged lymph nodes of dense and elastic consistency can be palpated in the axillary, subclavian, and supraclavicular regions.

Fibroadenoma is a benign tumor of dense elastic consistency, oval (elliptical) or rounded shape with a smooth surface and clear contours, relatively mobile, sometimes painful when palpated. Sizes: from 5 mm to several centimeters. A long history of growth.

A cyst is a benign tumor of a rounded shape, smooth, elastic, elastic, mobile. History: lactation period, injuries, cystic changes of the ovaries. A cyst has a less than 1.0% chance of turning into cancer.

Nodular mastopathy is a benign formation of a soft-elastic consistency with areas of compaction without clear boundaries, painful on palpation. Depending on the phase of the menstrual cycle, the consistency and sensitivity of the node changes. Nodular mastopathy is the most dangerous in terms of malignant transformation.

Lipoma is a benign tumor of soft consistency, oval shape, without clear contours, painless, with a long history of growth; in the case of fibrolipoma, the borders of the tumor are well contoured. In the case of breast cancer, discharge from the nipples is noted in 3% of women and in 20% of men. In most cases, secretions indicate benign changes (fibrocystic mastopathy, intraductal papilloma, etc.). Milk-like secretions are characteristic of galactorrhea, purulent — for an infectious-inflammatory process, sticky and multicolored — for intraductal ectasia, bloody — for intraductal papilloma (Mint's disease). However, discharge in women over the age of 50 is more likely to be malignant. Serous secretions signal breast cancer in only 5% of cases, blood-tinged secretions in 15%, bloody secretions in 20%, and watery secretions are a 50% sign of a malignant process. In the presence of malignant growth, carcinoma cells are often detected during the cytological examination of secretions. Diffuse forms of breast cancer.

Edema-infiltrative cancer: the affected MG is enlarged, the skin is tense, has a characteristic "lemon peel" appearance, palpation shows diffuse edematous swelling of the gland, pastiness.

Pancer-like cancer: characterized by tumor infiltration of the skin and chest wall. Over time, the skin becomes dense, pigmented, the skin thickens, decreases in size, pulls up, becomes motionless and, together with infiltrative-indurative damage to the adjacent tissues, covers the chest wall like a shell. Among the diffuse forms, only shell cancer has a torpid course.

Urticaria: on the skin of the MG, there are areas of intense hyperemia with uneven contours that resemble the erythematous stage of urticaria. Redness is caused by cancerous infiltration of capillaries and lymphatic vessels of the skin (carcinomatous lymphangitis). This form of cancer is characterized by an acute onset, high malignancy and rapid metastasis.

Mastitis-like cancer: MG is enlarged, dense, hyperemia of the skin and local temperature rise are noted. Diffuse seals can be palpated in the thickness of the gland. Infiltration quickly covers the entire gland and spreads to adjacent tissues, regional and distant metastases appear.

Paget's carcinoma clinically resembles unilateral nipple and areola eczema. Primary multiple breast cancer is characterized by simultaneous damage by several tumors of one or both breast cancer.

Sarcomas make up less than 1% of all malignant tumors of the MG. Angio-, lipo-, fibrosarcomas and malignant fibrous histiocytomas are most often found among soft tissue sarcomas.

### **Breast cancer treatment**

The solution to the issue of treatment in the case of malignant neoplasms of the MG is carried out only in the oncology institution at the place of residence. The choice of the method of treatment of breast cancer is determined by the stage of the disease, the clinical form of the tumor, age and general condition, as well as additional data characterizing the specific properties of the tumor. Before prescribing treatment, morphological verification



of the diagnosis and the most accurate determination of the stage of the disease are mandatory.

Specialized assistance to cancer patients is provided exclusively in oncology institutions.

Patients with breast cancer are treated by a surgeon-oncologist. In the treatment of breast cancer, depending on the stage of the disease, the presence of concomitant pathology, the age and severity of the patient's condition, all methods known in oncology are used: surgical, radiation, systemic therapy like hormonal, chemotherapy, targeted and immunotherapy. Combined treatment of breast cancer is carried out from the standpoint of biological ethics in the interests of the patient according to the principles of rational radicalism and organ preservation to create conditions for full rehabilitation.

Follow-up, including medical examination

After special treatment, patients are registered by the oncologist.

There is evidence for the need for various forms of psychological support for women undergoing treatment for breast cancer.

### **Trophoblastic disease of pregnancy**

Trophoblastic disease of pregnancy is a collective term that includes a group of benign and malignant neoplasms of the trophoblast. The disease belongs to rare tumors (1-2.5% among malignant neoplasms of female genital organs) and develops mainly in women of childbearing age. The most common form of trophoblastic tumors is cystic cysts. Even in the IV century. B.C. Cystic pregnancy was described by Hippocrates, calling it dropsy of the uterus. The term "bubble drift" was first used by Smellie W. in 1700.

It was only in 1947 that drift was classified as a neoplastic disease of the bladder. based on the results of 200 observations Hertig A. and Sheldon W. An attempt to characterize the incidence of blisters is associated with certain difficulties.

The problem of accumulating reliable data on the spread of the disease is related to the lack of consistency in the description of clinical cases, inadequate characteristics of the population categories that are in the risk group, an insufficient number of qualitatively selected control groups, and the rarity of this disease. However, the biggest problem in all European countries, including Ukraine, is the lack of centralized databases, which does not allow assessing the significance of the problem in the country and timely diagnosing malignant trophoblastic tumors initiated by bladder drift.

### **Risk factors of malignant trophoblastic tumors**

- Pregnancy at the age of more than 40 years is associated with a 7-fold increase in the risk of developing an apparent snowdrift, compared to a younger age. If there is a pregnancy at the age of 35, this risk increases by 2 times. After 40 years, the risk of progression of cystic entrainment in chorionepithelioma also increases. There are data on an increase in the frequency of finding bubble snow at the beginning of the reproductive age (16-18 years). The age of the father does not influence the development of trophoblastic disease.

It should be noted: the age of the mother does not affect the risk of partial PP.

- Belonging to the Mongoloid race increases the risk of developing trophoblastic disease by 3-10 times, compared to other peoples. The reason for this is not fully known, however, there are assumptions about the effect of a lack of animal fats and beta-carotene in the food of representatives of this race.

- Spontaneous abortions. In case of involuntary termination of previous pregnancies, the risk of developing gestational trophoblastic disease increases significantly. One spontaneous abortion in the anamnesis increases the risk of developing vesicular sleet by 2-3 times, and two consecutive spontaneous abortions increases this risk by 10 times. The risk is reduced if there is a history of a live birth during a full-term pregnancy.

- Bubbly blizzard during a previous pregnancy increases the probability of the appearance of this pathology in the future by 10 times: 0.6-1.5% of women with complete PP have a risk of repeating PP during the next pregnancy. For partial PP, this risk is unknown

**Gestational trophoblastic disease (GTH)**— lesions caused by pregnancy and characterized by abnormal trophoblast proliferation. This group of diseases consists of benign, non-neoplastic lesions, including hydatidiform mole, placental site nodule, and exaggerated placental site.

Gestational trophoblastic neoplasia (GTN) — includes a group of true tumors. These are malignant tumors due to the possibility of local invasion and metastasis. Unlike other more frequent malignant neoplasms, GTNs are curable in 85–100% of cases, even in the presence of widespread disease.

GTNs include: choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and invasive mole. In the absence of material for histological diagnosis, the disease diagnosed as a result of a persistent increase in human chorionic gonadotropin (hCG) after the evacuation of a molar pregnancy is called HTN. Most of these tumors produce the beta subunit of hCG, which is used as a tumor marker and as a screening test to monitor the effectiveness of treatment.

Bubble snow is the most common form of gestational trophoblastic disease (GTD) — 80%.

### **Classification of MH**

MH can be:

1. Full (80%)
2. Partial (or incomplete) (10%)
3. Invasive (10%).

- Complete and partial MH, although benign, are considered precancerous diseases because they can turn into malignant neoplasms.

- The development of malignant gestational trophoblastic neoplasia usually occurs after complete MZ (15–20%), not partial MZ (1–5%) and consists of invasive mole — 75%, choriocarcinoma — 25%.

- Invasive MH refers to HTN and is a malignant tumor

The cause of development (etiology) of bladder drift remains unstudied. Accumulated facts give reasons to believe that the development of the disease can be affected by a violation of the immune status in women with a large number of pregnancies

and a short interval between them; deficit of animal fats and fat-soluble vitamins (in particular, vitamin A); smoking; action of ionizing radiation and herbicides.

The reason for such errors is that the informativeness of the traditional morphological study of cystic fibrosis decreases significantly during pregnancy (up to 8 weeks), and it is usually very difficult to morphologically distinguish miscarriage from partial cystic fibrosis.

In some cases, differential diagnosis requires auxiliary research methods, such as the determination of P57kip2, in situ hybridization, or flow cytometry, which allow to determine the ploidy of the scraped tissue and, therefore, to diagnose clinically more favorable partial cystic fibrosis.

In today's practice, the difficulties of the morphological diagnosis of cystic fibrosis at these terms dictate the need for careful control of the chorionic gonadotropin (pregnancy hormone) level after the termination of any pregnancy.

It should be emphasized that the structure of the chorionic gonadotropin molecule is different in patients with trophoblastic tumors and in pregnant women.

Therefore, secondary prevention, the prevention of the development of widespread forms of malignant trophoblastic tumors, involves the use in clinical practice of test kits with high sensitivity for the determination of chorionic gonadotropin in human serum ( $< 2$  IU/l), which allow for the determination of altered chorionic gonadotropin molecules.

**Treatment of cystic fibrosis-** surgical and consists in the removal of tumor masses from the uterus by vacuum aspiration followed by curettage (scraping) of the uterine walls.

Spontaneous separation (expulsion) of the bladder drift is possible up to the 16th week and is occasionally observed after the 28th week of pregnancy.

Surgical treatment of cystic fibrosis with uterine size  $> 16$  weeks of pregnancy should be performed only by doctors who have experience in treating such patients.



Рис. 4.А. Повний міхуровий занос (макропрепарат).



Рис. 4.Б. Повний міхуровий занос (фрагмент пухлинної тканини).

Surgical evacuation of partial cystic fibrosis is recommended if it is technically possible (short term of pregnancy). The presence of a fetus, as a rule, requires the use of a medicinal method (introduction of prostaglandin E2 into the uterine cavity through an extra-amniotic Foley catheter).

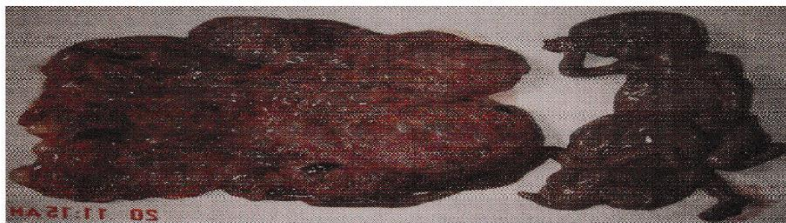


Рис. 5. Частковий міхуровий занос

Today, there are no standard protocols that determine the indications for repeated scraping of the uterine walls. At the moment, indications for repeated curettage are considered to be the level of chorionic gonadotropin in the serum of women  $>5000$  IU/l and residual tumor tissue in the uterine cavity confirmed by U3D.

Such pregnancies are extremely rare - 1 in 20,000, 1 in 100,000 pregnancies and are associated by most practitioners with an increased risk of developing malignant trophoblastic tumors initiated by bladder drift. It is not necessary to terminate such pregnancies if the woman wishes and there are no abnormalities in the development of

the fetus, since in 35.0% of cases, the birth of healthy children is possible. According to the literature and the experience of the Ukrainian Center for Diagnosis and Treatment of Trophoblastic Tumors, the risk of developing malignant trophoblastic tumors initiated by cystic fibrosis after such pregnancies is about 30.0%.

**Secondary prevention** of malignant trophoblastic tumors in this group of women requires a mandatory histological examination of the fetus and adequate observation after the end of pregnancy according to the algorithm of observation of patients after the evacuation of the bladder.

All patients after removal of cystic fibrosis should be under the supervision of an oncologist with a primary examination of the serum level of chorionic gonadotropin.

With a favorable course of the disease, after the removal of a complete cystic drift, the normalization of the chorionic gonadotropin level occurs approximately on the 78th day, with a partial one - on the 63rd day.

Strict adherence to the monitoring algorithm of patients after the evacuation of cystic drift is the main prerequisite for the secondary prevention of malignant trophoblastic tumors initiated by cystic drift. The diagnosis of "Malignant trophoblastic tumor" after the evacuation of cystic drift is determined according to the criteria of FIGO-WHO (2002): 1) a plateau level of chorionic gonadotropin during a four-time study during 3 weeks (on 1, 7, 14 and 21 days) after evacuation of the cystic drift

2) an increase in the level of hCG by 10.0% or more during a three-time examination within 2 weeks (on the 1st, 7th, 14th day) after the evacuation of the bladder drift;

3) diagnosis of chorionic gonadotropin in blood serum 6 months after the evacuation of cystic drift;

4) histologically confirmed choriocarcinoma initiated by cystic drift.

**Management tactics of patients with malignant trophoblastic tumors**

-consultation of an oncologist;

- monitor the level of chorionic gonadotropin in blood serum every week (with test kits with a sensitivity < IU/l);

- consult the micropreparations of the removed tumor at the Ukrainian Center for diagnosis and treatment of trophoblastic tumors at the National Cancer Institute;

- perform radiography of the chest cavity organs after removal of cystic drift;

- perform an ultrasound examination of the organs of the abdominal cavity and pelvis (dopplerography).

There are no special precautions for patients after cyst removal.

After the examination, you can continue your normal lifestyle and diet. Restoration of menstrual function is usually observed 4 weeks after removal of the tumor, but long-term (up to 3 months) amenorrhea (absence of menstruation) is possible.

## VI.Lesson plan and organizational structure.

o	The main stages of the lesson, their functions and content	o	Control and training methods	Methodological support materials	ime
\n	2		4	5	
Preparatory stage					
ND	Organizational measures				%
I	Setting educational goals and motivation			See item 2 "Educational objectives" See item 1 "Relevance of the topic"	%
II	Control of the initial level of knowledge, skills, abilities: -Causes and pathogenesis of background	$\alpha=2$ )	- individual theoretical survey - test control	- a question for a theoretical survey - tests	5%

<p>and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</p> <ul style="list-style-type: none"> <li>- Classification of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> <li>-Clinic for background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> <li>- Diagnosis of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> <li>-Medical tactics for precancerous and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> <li>- Methods of treatment of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> <li>- Methods of preventing background and precancerous conditions of the cervix and endometrium, mammary glands and</li> </ul>		<ul style="list-style-type: none"> <li>- solving typical problems</li> </ul>	<ul style="list-style-type: none"> <li>- typical tasks</li> <li>-structural and logical schemes, tables</li> <li>- dummies</li> </ul>	
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	trophoblastic diseases				
The main stage					
V	<p>Formation of professional skills:</p> <ul style="list-style-type: none"> <li>- Collect gynecological history</li> <li>- Perform a gynecological examination.</li> </ul> <p>Formation of professional skills:</p> <ul style="list-style-type: none"> <li>-Collect anamnesis and identify signs characteristic of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> <li>- Draw up an examination plan for the diagnosis of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> <li>-Evaluate the results of the main and additional examination for background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> <li>- Conduct diagnosis of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</li> </ul>	<p><math>\alpha=3</math>)</p> <p><math>\alpha=4</math>)</p>	<p>Skill formation method: practical training</p> <p>Method of formation of skills: training in solving typical and atypical situational problems - real clinical, simulated, test</p>	<p>Algorithm of examination methods gynecological patients, dummies for training, gynecological instruments, Thematic patients, medical histories;Ultrasound - pictures or ultrasound in real time,results of other additional examination methods situational tasksIVlevel, interactive tasks.</p>	5%

	<p>- To determine the management tactics of a patient with various forms of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</p> <p>-Prescribe treatment for background and precancerous conditions of the cervix and endometrium.</p> <p>-Determine indications for surgical treatment in precancerous conditions of the cervix and endometrium, mammary glands</p> <p>- Draw up a plan for the rehabilitation of patients with background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases</p>				
Final stage					
	<p>Control and correction of the level of practical skills.</p> <p>Control and correction of the level of professional skills</p> <p>Summary of the lesson: Theoretical, practical, organizational</p> <p>Homework</p>	<p><math>\alpha=3</math>)</p> <p><math>\alpha=4</math>)</p>	<p>Individual control of practical skills</p> <p>Analysis of the results of students' clinical work, solutions to problems and tests of the IV level</p> <p>Final evaluation of students</p>	<p>Thematic patients, dummies Gynecological tools</p> <p>Results of clinical work, non-typical tasks and IV level tests</p> <p>An indicative map for independent work with literature.</p>	<p>0%</p>

I			according to the criteria of knowledge, skills, and abilities	Recommended literature (basic, additional, electronic sources)	
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## VII. Materials for methodological support of the lesson

### 7.1. Control materials for the preparatory stage of the lesson

Question ( $\alpha=2$ ):

- Causes and pathogenesis of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases
- Classification of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases
- Clinic of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases
- Diagnosis of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases
- Risk factors of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases
- Medical tactics for precancerous and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases
- Methods of treatment of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases

### **Test tasks**

1. A 40-year-old patient, on examination of the cervix, a 2x2 cm mass of pale yellow color, the contours are uneven, the borders with the healthy cervical mucosa are clear. On the surface - minor papillomatous growths. The body of the uterus has no pathological changes, parameters are free on both sides. On the left, close to the walls of the pelvis,

there is a dense immobile formation of 3x4 cm. What is the most appropriate method of examination to clarify the diagnosis?

1. Targeted biopsy
2. Cytology of cervical smears
3. Extended colposcopy
4. Laparoscopy
5. Smears on microflora

2. A 42-year-old woman turned to a gynecologist with complaints of contact bleeding from the external genital tract. During the examination - hypertrophy of the vaginal part of the cervix, the surface is eroded. What diagnostic method is most indicated for verifying the diagnosis?

1. Colposcopy
2. Wasserman's reaction
3. Biopsy of cervical tissue
4. Cytological examination of a smear from the surface of the cervix
5. Cervicoscopy

3. Benign pathological processes of the cervix include the following pathological processes:

1. In which normoplasia of the epithelium is preserved
2. In which there is a violation of differentiation, maturation and rejection of epithelial cells, while the process does not go beyond the boundaries of the basement membrane.
3. In which there is a violation of differentiation, maturation and rejection of epithelial cells, while the process goes beyond the boundaries of the basement membrane.
4. In which cells with varying degrees of atypia appear

4. Benign (background) pathological processes of the cervix include:

1. Fields of dysplasia

2. Ectopia of the cylindrical epithelium
3. Simple leukoplakia.
4. Proliferating leukoplakia

5. Preclinical cervical cancer includes:

1. Exo- and endocervicitis.
2. Cervical endometriosis
3. Ectopia of cylindrical epithelium
4. Pretumor zone of transformation

6. Patients cured of benign pathological processes can be removed from dispensary supervision only:

1. After a final examination using colposcopic and cytological methods one and a half to two months after treatment

2. After a final examination using colposcopic and cytological methods six months after treatment

3. After a final examination using colposcopic and cytological methods one year after treatment

4. After the final examination using colposcopic and cytological methods two years after treatment

7. Deregistration of patients with precancerous processes of the cervix after radical treatment is permissible only:

1. With complete endoscopic, cytological recovery two years after treatment

2. With full endoscopic, cytological recovery one year after treatment

3. With complete endoscopic, cytological recovery six months after treatment

4. With complete endoscopic, cytological recovery three years after treatment

8. A 55-year-old patient complains of an increase in the size of the abdomen, constipation, asthenia, the appearance of smearing discharge from the vagina after 4 years, after the onset of menopause. What research method should be used to verify the diagnosis?

1. Separate diagnostic scraping of the uterine cavity and cervical canal
2. Ultrasound
3. X-ray examination of the gastrointestinal tract
4. Metrosalpingography
5. Laparoscopy

9. A 33-year-old patient with complex atypical hyperplasia of the endometrium underwent a diagnostic curettage of the uterine cavity after 3 months of conservative hormonal therapy. Upon repeated histological examination, complex atypical hyperplasia of the endometrium was again revealed. What is the further treatment strategy?

1. Appointment of progestogens.
2. Appointment of gonadotropin-releasing hormone agonists.
3. Endometrial ablation.
4. Supravaginal amputation of the uterus.
5. Extirpation of the uterus.

10. A 62-year-old woman approached the doctor with complaints of vaginal bleeding. Menopause is 12 years old, I haven't had a gynecologist for 10 years. During the examination, the uterus is not enlarged, painless, the appendages are not palpable. The doctor's tactics?

1. Fractional diagnostic scraping.
2. Hemostatic therapy
3. Hormonal hemostasis.
4. Operative treatment.
5. Puncture of the posterior vault.

11. A 58-year-old patient with complex atypical hyperplasia of the endometrium underwent a diagnostic curettage of the uterine cavity after 6 months of conservative hormonal therapy. Upon repeated histological examination, complex atypical hyperplasia of the endometrium was again revealed. What is the further treatment strategy?

1. Appointment of progestogens.
2. Appointment of gonadotropin-releasing hormone agonists.
3. Endometrial ablation.
4. Supravaginal amputation of the uterus.
5. Extirpation of the uterus.

12. At an appointment with the district obstetrician-gynecologist, the 28-year-old patient L. was diagnosed with simple leukoplakia. Cytological findings: anucleated surface cells with hyperkeratosis were obtained. What are the medical tactics?

1. Hormonal therapy.
2. Cryodestruction.
3. Observation.
4. Anti-inflammatory therapy.
5. Electroeczesia.

13. Which of the listed tumor-associated antigens should be used in patients with breast cancer:

1. SA 15.3
2. SA 19.9
3. SA 125
4. CA 72.4

14. Among the listed factors, single out the most important one with regard to the risk of developing breast cancer in women:

1. Metabolic disorders (obesity)
2. Exogenous factors (smoking, high-calorie food)
3. Genetic factors of VRCA
4. Endocrine disorders (diabetes, hypothyroidism)

15. A sentinel or signal lymph node is:

1. An enlarged solitary regional lymph node, which can be palpated
2. One of the first lymph nodes on the way of outflow of lymph from the primary tumor
3. Solitary lymphogenic micrometastasis in the area of regional lymph drainage, diagnosed histologically.
4. Lymphogenic regional metastasis, diagnosed on the basis of immunohistochemistry.

### **Situational problems ( $\alpha=2$ )**

1. Patient K., 19 years old, turned to the doctor with complaints that she has been experiencing abundant light mucous discharge for a long time. Menstruation without deviations from the norm. When examined in mirrors, a bright pink area is found on the cervix. Colposcopically, a bright pink area with a grainy surface resembling a bunch of grapes was found in zones I and II, partially III. Changes on the part of the uterus, appendages, parameters were not detected. Make a preliminary diagnosis. What modern methods of treatment can be used for this pathology?

2. In patient A., 36 years old, during a preventive examination in the mirrors, deformation of the cervix due to old postpartum tears was revealed. During the colposcopic examination on the back lip in zone II at 16:00, fields of dysplasia were detected. Preliminary diagnosis. What should be done to clarify the diagnosis?

3. A 46-year-old patient has obesity and disorders of the menstrual cycle. Over the past 3 years, separate scraping of the cervical canal and uterine cavity was performed 5 times for therapeutic and diagnostic purposes. The result of histological examination after



each scraping is endometrial polyposis. Conservative treatment is ineffective. Diagnosis. Plan for further treatment.

4. A 35-year-old patient turned to a gynecologist with complaints of heavy and frequent menstruation. Before that, I did not consult a gynecologist. History: two deliveries and 2 artificial abortions. Bimanual examination revealed no pathology. Ultrasound: the body of the uterus and appendages are of normal size, the structure has not changed. M - echo 25 mm. Diagnosis. Examination and treatment plan..

5. A 59-year-old patient complains of vaginal bleeding that appeared after 8 years of menopause. The general condition is satisfactory. 2 childbirths, 3 abortions. She has not consulted a gynecologist in the last 2 years. Objectively: external genitalia without pathology, cervix atrophic, clean. The body of the uterus is of normal size, slightly soft, mobile, painless. The vaults are deep. The appendages are not defined, their area is painless. Parameters are free. The secretions are serous and bloody. Diagnosis? What shall I do?

6. A 30-year-old patient underwent a cytological examination at the regular professional examination, the result of which was smear type IIIa. Make a preliminary diagnosis. What should be done to clarify the diagnosis?

7. A 43-year-old patient complains of bloody discharge from the genitals for two weeks. Menstruation from the age of 14, for 4–5 days, after 26 days, moderate, painless. The last menstruation began with a delay of two weeks and lasted 14–15 days. During the examination, it was established: the cervix is cylindrical, the eye is closed, the body of the uterus is of normal size, movable, painless. The vaults are deep. The appendages are not palpable. Parameters are free. The secretions are bloody, in moderate amounts. What shall I do?

8. A 45-year-old patient turned to the doctor of the regional oncology dispensary with complaints about the presence of painful swellings in the left breast gland. It is known from the anamnesis that she gave birth 1 month ago, the lactation period lasts a month. During the last two days, the patient has a hectic fever. During examination and palpation, sharp soreness and swelling in the left breast gland in the area of the lower

inner quadrant are determined, the skin over this area is hyperemic. Regional lymph nodes are not enlarged.

Preliminary diagnosis? What treatment should she be prescribed?

9. A 48-year-old patient, unmarried, complained about the presence of an ulcer on the outer edge of the areola of the right mammary gland, which did not heal for 4 months. Objectively: an ulcer up to 3 cm in diameter, with uneven edges, a purulent bottom, an inflammatory ridge around the ulcer. What was your previous diagnosis? Your first diagnostic measures? What is the treatment plan in this case?

10. A 63-year-old patient complained of a tumor in the left mammary gland to the clinic of the dispensary. She noticed the neoplasm more than a year ago, so she notes that the tumor has increased in size. On palpation, a 3 by 5 cm tumor is noted, dense, painless, immobile, without clear contours. Enlarged left axillary nodes. What additional diagnostic methods are shown to be used? What disease occurs in this situation?

11. Patient M., 45 years old, turned to the doctor with complaints of dull pain in the right mammary gland, swelling, a feeling of heaviness and discomfort, especially before menstruation. She has been sick for 3 months. There are no pathological discharge from the nipple, the areola has not changed. Palpation: in the outer upper quadrant, a tumor measuring 3 by 2 cm, movable, dense-elastic consistency is determined. The skin over it is not changed. What is the most favorable diagnosis for this patient? What is your further diagnostic strategy?

12. Patient N., 31 years old, consulted a mammologist with complaints about a mass in the left mammary gland, which appeared suddenly during the last day. Clinically, during the examination, the mass is subareolar, round in shape with a smooth surface, dense and elastic consistency. measuring 2 by 2 cm. Axillary lymph nodes are not enlarged. What is your previous diagnosis? What tests should be performed? What treatment options are possible in this case?

## **7.2. Materials for methodical support of the main stage of the lesson**

### **Tasks for the formation of skills ( $\alpha=3$ ):**

1. Collect complaints and gynecological history.
2. Carry out the main methods of gynecological examination: examination of the external genitalia, examination in mirrors, bimanual examination

### **Tasks for the formation of skills ( $\alpha=4$ )**

1. Collect the anamnesis and highlight the signs inherent in background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases

2. Draw up an examination plan for the diagnosis of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases

3. To evaluate the results of the main and additional examination for background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases

4. To carry out the diagnosis of background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases. To determine the risk factors for the occurrence of background and precancerous conditions of the cervix and endometrium.

5. Prescribe treatment for background and precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases

6. Determine indications for surgical treatment in precancerous conditions of the cervix and endometrium, mammary glands and trophoblastic diseases

6. Interactive task ( $\alpha=4$ ):

1. The group of students should be divided into 3 subgroups, tasks for the formation of skills should be given to each subgroup

2. Divide the group of students into 3-4 subgroups, provide each group with different images of ultrasound studies with various forms of precancerous conditions of the cervix and endometrium, on the basis of which it is suggested to establish a diagnosis.

3. Divide the group of students into 2 subgroups:

Subgroup 1 – conducts an analysis of the management of the thematic patient based on the provided medical history

Subgroup 2 - evaluates the correctness of the conducted analysis

7.2. Materials for methodological support of the final stage of the lesson

a. Evaluate the results of the provided interactive tasks c subgroups of students.

### **7.3. Materials for methodical support of students' independent work.**

#### **Literature.**

##### ***Educational.***

##### ***Main:***

1. Gynecology: a textbook (edited by B.M. Ventskivskyi, G.K. Stepankivskyi, V.P. Lakatosha). - K.: VSV Medicine, 2012. - 648 p.
2. Obstetrics and gynecology (in 2 books): textbook (edited by V.I. Hryshchenko, M.O. Shcherbyny)// Book I Obstetrics.-K.: Medicine, 2011.- 422 p.; Book II Gynecology. - K. Medicine, 2011. - 375 p.
3. Zaporozhan V.M., Chaika V.K., Markin L.B. Obstetrics and gynecology (in 4 volumes): national textbook: 2013

##### ***Auxiliary:***

1. Norwitz Yerrol R., Shorge John O. Obstetrics and Gynecology (translated from English). - M.: GEOTAR - MED, 2003.-141 p.
2. Senchuk A.Ya., Vdovichenko Y.P., Ventskovsky B.M., Shunko E.E. Guide to practical skills in gynecology, obstetrics and neonatology. - K.: Gidromax, 2006. - 368 p.

##### **Methodical**

3. Midwifery: a textbook (University III — IV year) / B. M. Ventskivskyi, I. B. Ventskivska and others; under the editorship B. M. Ventskivskyi, G. K. Stepankivskyi, M. E. Yarotskyi. "Medicine". 2012. — 648 p.
4. Zhabytskaya L.A. Cystic prolapse: clinical aspects, management tactics / Reproductive health. Eastern Europe. Appendix. — 2018. — 44–46 p.
5. Ross S Berkowitz, MD. Hydatidiform mole: Management / Ross S Berkowitz, MD, Donald Peter Goldstein, MD, Neil S Horowitz, MD // Sep. 2017.

6. Ross S Berkowitz, MD. Hydatidiform mole: Epidemiology, clinical features, and diagnosis / Ross S Berkowitz, MD, Donald Peter Goldstein, MD, Neil S Horowitz, MD. — Sept. 2017.

7. Rebecca N Baergen, MD. Gestational trophoblastic disease: Pathology. — Sept. 2017.

8. Obstetrics and gynecology. / Current Obstetric & Gynecologic Diagnosis & Treatment. Eleven Edition / Lauren Nathan, Alan H. DeCherny. 2012.

9. <https://almostadoctor.co.uk/about><https://geekymedics.com/category/medicine/og/>