Ministry of Health of the Republic of Belarus
Educational Institution
“Gomel State Medical University”

Department of Pathological Anatomy

Author:
Grigorii V. Tishchenko, Associate Professor of the Department of Pathological Anatomy, Candidate of Medical Sciences (Ph.D. in Medicine)

METHODICAL GUIDELINES

for conducting a practical class
in the academic discipline “Pathological Anatomy”
for students
of the 3rd year, Faculty of International Students (instruction in English),
enrolled in the specialty
7-07-0911-01 “General Medicine”

Topic: “Female reproductive system pathology”

Duration: 3 hours

Approved at the meeting of the Department of Pathological Anatomy
(Minutes No. 1 dated 30.08.2025)

2025

EDUCATIONAL AND INSTRUCTIONAL GOALS, OBJECTIVES, AND MOTIVATION FOR MASTERING THE TOPIC

Educational Goal:

- To study the definition, classification, etiology, pathogenesis, morphology, clinical presentation, complications, and outcomes of diseases of the female reproductive system. To analyze pathology of the vulva: Bartholin cyst/abscess, lichen sclerosus, squamous cell carcinoma (associated with HPV and lichen sclerosus), Paget disease of the vulva. To examine pathology of the vagina: vaginitis (bacterial, candidal, trichomonal, atrophic), vaginal adenosis (associated with diethylstilbestrol – DES exposure, risk of clear cell adenocarcinoma). To analyze pathology of the cervix: cervicitis (acute, chronic), cervical ectropion, cervical intraepithelial neoplasia (CIN 1, 2, 3 – squamous dysplasia and carcinoma in situ), koilocytotic atypia (HPV effect – perinuclear halo, wrinkled nuclei), squamous cell carcinoma (most common, HPV types 16, 18, 31, 33), adenocarcinoma (less common). To discuss the role of Pap smear screening and HPV testing. To examine pathology of the uterus: endometrial hyperplasia (simple, complex, with/without atypia – risk of progression to endometrioid adenocarcinoma), endometritis (acute, chronic, plasma cells), endometriosis (endometrial glands and stroma outside the uterus – pelvis, ovaries, peritoneum; causes pain, infertility), adenomyosis (endometrial glands within myometrium), endometrial polyps, endometrial carcinoma (endometrioid – most common, serous, clear cell – associated with Tamoxifen, unopposed estrogen), uterine leiomyomas (fibroids – benign smooth muscle tumors, most common female neoplasm, whorled appearance), uterine leiomyosarcoma (malignant, necrosis, atypia, mitotic figures). To examine pathology of the fallopian tubes: salpingitis (acute, chronic, hydrosalpinx, pyosalpinx), ectopic pregnancy (tubal pregnancy, rupture, hemoperitoneum), paratubal cysts. To analyze pathology of the ovaries: functional cysts (follicular, corpus luteum, theca lutein), polycystic ovary syndrome (PCOS – subcapsular cysts, stromal hyperthecosis), ovarian tumors: surface epithelial-stromal tumors (most common: serous cystadenoma/cystadenocarcinoma (psammoma bodies), mucinous cystadenoma/cystadenocarcinoma (pseudomyxoma peritonei), endometrioid carcinoma, clear cell carcinoma, Brenner tumor), germ cell tumors (mature cystic teratoma (dermoid cyst) – most common ovarian neoplasm in young women; immature teratoma, dysgerminoma, yolk sac tumor (endodermal sinus tumor – Schiller-Duval bodies), choriocarcinoma), sex cord-stromal tumors (granulosa cell tumor – Call-Exner bodies, produces estrogen; thecoma; fibroma; Sertoli-Leydig cell tumor – produces androgens). To discuss tumor markers: CA-125 (epithelial ovarian cancer), AFP (yolk sac tumor), hCG (choriocarcinoma), inhibin (granulosa cell tumor).

Instructional Goal:

- Within the framework of the educational process for this academic discipline, the student must acquire not only theoretical knowledge, practical skills and

abilities in the specialty but also develop their personal potential. They should cultivate qualities of responsibility and patriotism, be prepared to actively participate in the economic, socio-cultural, and public life of the country, recognize the social significance of their future professional activity, understand the norms of medical ethics and deontology, and learn to observe academic and labor discipline. In the course of studying the educational material, students should realize the importance of maintaining a healthy lifestyle and, as an example in the future, when performing professional duties, set an example for those around them and their patients.

Objectives: Upon completion of the practical session, the student must:

Know:

- The morphology of CIN (cervical intraepithelial neoplasia) and koilocytotic atypia;
- The classification and morphology of endometrial hyperplasia and endometrial carcinoma;
- The gross and microscopic features of uterine leiomyoma and leiomyosarcoma;
- The definition and morphology of endometriosis and adenomyosis;
- The classification of ovarian tumors (epithelial, germ cell, sex cord-stromal);
- The morphological features of common ovarian tumors (serous cystadenocarcinoma, mature cystic teratoma, granulosa cell tumor);
- The role of tumor markers in ovarian cancer.

Be able to:

- Identify koilocytes in HPV-associated cervical lesions;
- Distinguish leiomyoma from leiomyosarcoma;
- Recognize psammoma bodies in serous cystadenocarcinoma;
- Identify Schiller-Duval bodies in yolk sac tumor;
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body.

Master:

- Basic techniques for working with a microscope;
- Skills in clinical-anatomical analysis;
- The fundamentals of synthetic generalization of morphological diagnostic signs of diseases and their correct interpretation in cause-and-effect relationships.

Motivation for Mastering the Topic:

Diseases of the female reproductive system are extremely common in clinical practice and include benign conditions (leiomyomas, endometriosis, functional cysts) as well as malignant neoplasms (cervical, endometrial, ovarian cancer). Cervical cancer is a leading cause of cancer death in women in developing countries, despite being largely preventable through screening (Pap smear, HPV testing). Ovarian cancer is the most lethal gynecologic malignancy due to late diagnosis. Understanding the morphological features of these diseases is essential for

gynecologists, pathologists, oncologists, and primary care physicians for accurate diagnosis, treatment, and prevention.

QUESTIONS

1. Pathology of external female genital organs. Examples. Morphology. Complications and outcomes.
2. Cervicitis. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations.
3. Cervical ectropion (cervical erosion). Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations. Complications and outcomes. Colposcopy.
4. Squamous cervical precursor lesions: CIN, SIL. Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.
5. Endometritis. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations. Complications and outcomes.
6. Endometrial hyperplasia. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations. Complications and outcomes.

COURSE OF THE SESSION

Embryology

The development of the female reproductive system begins in the early stages of embryonic life. The **genital ridge**, which is the precursor to the ovaries, uterus, and fallopian tubes, is formed during the first few weeks of gestation.

This ridge develops into the **mesonephros**, which is then transformed into the permanent kidneys. The ovaries then form on the posterior aspect of the mesonephros as the primitive sex cords extend and differentiate into the ovarian follicles.

The **paramesonephric ducts**, which are also known as the **Müllerian ducts**, begin to develop near the genital ridge at around the same time. The ducts will eventually fuse in the midline and form the uterus, fallopian tubes, and upper part of the vagina.

The formation of the female reproductive system is a highly coordinated process that is vulnerable to disruptions at different stages of development. **Environmental factors** such as exposure to certain chemicals or drugs, as well as **genetic factors**, can cause **abnormalities** in the development of the system.

Anatomy

The female reproductive system is a complex network of organs that work together to facilitate the production and fertilization of ova, support the development of a fetus, and provide for the birth of a healthy baby. The system consists of both **internal** and **external organs**. The internal organs include the **ovaries**, **fallopian tubes**, **uterus**, **cervix**, and **vagina**. The external organs, collectively known as the **vulva**, include the **mons pubis**, **labia majora** and **minora**, **clitoris**, and **vestibular glands** (aka Bartholin's glands).

The ovaries are two small almond-shaped organs located on either side of the uterus. They are responsible for producing ova or eggs and hormones such as estrogen and progesterone.

The fallopian tubes are narrow tubes that extend from the ovaries to the uterus. They provide a passage for the ova to travel from the ovaries to the uterus and are the site of fertilization.

The uterus is a muscular organ that supports fetal growth during pregnancy. It is divided into three layers: the endometrium, myometrium, and perimetrium.

The cervix is the lower portion of the uterus that connects it to the vagina.

The vagina is a muscular canal that connects the cervix to the external genitalia.

Bartholin's gland cyst (BGC) is a common condition in women that occurs when one or both of the **Bartholin's glands**, located on either side of the vaginal opening, become **blocked or infected**. BGC usually occur as a result of an **obstruction** in the gland duct. This can be caused by **trauma**, **infection**, or **inflammation**, and may also be associated with **hormonal changes**.

The clinical manifestations of Bartholin's gland cysts can vary depending on the size and location of the cyst. In some cases, the **cyst may be asymptomatic** and only detected during a routine pelvic exam. However, larger cysts can cause **pain, discomfort**, and **swelling** in the vulva area. In some cases, the cyst may become infected, leading to the development of an **abscess**. This can cause severe pain, fever, and difficulty walking or sitting.

The morphology of BGC varies depending on the stage of development. Early cysts may appear as small, fluid-filled sacs located near the Bartholin's gland. As the cyst grows, it may become more palpable and firm to the touch. Eventually, the cyst may **rupture** or become infected, leading to the formation of an abscess. The abscess may appear as a red, painful lump on the vulva, and may require **drainage** or **antibiotic treatment** to resolve. In **chronic cases**, the cyst may develop into a firm, fibrous nodule that requires surgical removal.

Colposcopy is a **medical examination technique** used to closely examine the cervix, vagina, and vulva for signs of abnormal cell growth or other abnormalities. During a colposcopy, a specialized instrument called a **colposcope** is used to magnify the tissues of the lower genital tract, allowing for a more detailed examination of the area.

The **purpose of colposcopy** is to detect and diagnose abnormalities in the cervix, vagina, and vulva, including precancerous conditions. It is often performed as a follow-up to an abnormal Pap test or other screening test that has shown abnormal cells. Colposcopy may also be used to diagnose other conditions, such as genital warts or infections. In some cases, a biopsy may be taken during the colposcopy to confirm the diagnosis and guide treatment options. Overall, colposcopy is a valuable tool in the detection and prevention of cervical cancer, as it allows for early identification and treatment of abnormal cells before they can develop into cancer.

Cervicitis

Morphologically, cervicitis is characterized by **inflammation** of the cervix, which can range from mild to severe. Microscopic examination of cervical biopsy specimens may reveal **dilated glands** and **infiltration of inflammatory cells** such as lymphocytes, plasma cells, and neutrophils. In more severe cases, the cervix may appear **ulcerated** and **friable**, with areas of pus-filled discharge.

Chronic cervicitis can lead to cervical fibrosis and scarring, which can cause cervical stenosis and interfere with fertility.

Clinical manifestations of cervicitis can vary depending on the underlying etiology and severity of inflammation. Symptoms may include **vaginal discharge**, pain or **discomfort during intercourse**, **abnormal vaginal bleeding** or spotting, and pelvic pain. Complications of cervicitis can include the spread of infection to other parts of the reproductive tract, such as the uterus and fallopian tubes, leading to pelvic inflammatory disease, chronic pelvic pain, and infertility. Cervicitis is also a risk factor for the development of **cervical cancer**.

Cervical ectropion, also known as cervical erosion, is a benign condition that is commonly seen in **young women**. The exact etiology of cervical ectropion is not fully understood, but it is thought to be caused by **hormonal changes**, particularly during puberty, pregnancy, and the use of hormonal contraceptives. These hormonal changes can lead to the **growth and proliferation of glandular cells from the endocervix onto the ectocervix**, resulting in the appearance of a bright red, granular patch on the cervix.

Cervical ectropion is a relatively **common condition**, with an estimated prevalence of **10-15%** in women of reproductive age. It is more commonly seen in women who are pregnant or taking hormonal contraceptives. Other risk factors for cervical ectropion include a history of sexually transmitted infections, multiple sexual partners, and a weakened immune system. Women who have undergone cervical procedures such as conization or cryotherapy may also be at increased risk of developing cervical ectropion.

Clinical manifestations of cervical ectropion can include abnormal vaginal bleeding, spotting between periods, or bleeding after intercourse. Some women may also experience discomfort or pain during sexual activity. In some cases, cervical ectropion may be asymptomatic and discovered incidentally during a routine pelvic exam. Although cervical ectropion is a benign condition, it can mimic the appearance of cervical cancer, and a biopsy may be performed to rule out malignancy.

Histopathologically, cervical ectropion is characterized by the presence of **columnar epithelium on the ectocervix**, which is normally covered by stratified squamous epithelium. The glandular cells are arranged in **small papillary projections** and may show mild to moderate atypia, which can be mistaken for cervical dysplasia or carcinoma in situ. In some cases, cervical ectropion may be associated with chronic inflammation and infection, leading to the presence of inflammatory cells such as **lymphocytes** and **plasma cells**.

Squamous cervical precursor lesions are histopathologically characterized by the presence of abnormal squamous epithelial cells in the cervix. These lesions are considered to be a precursor to invasive cervical carcinoma and are classified as **cervical intraepithelial neoplasia** (CIN) or **squamous intraepithelial lesions** (SIL) based on their degree of cellular atypia and involvement of the epithelium.

CIN is classified into **three grades** based on the degree of cellular atypia and involvement of the epithelium.

CIN1 is characterized by mild dysplasia involving the lower one-third of the epithelium, while **CIN2** and **CIN3** are characterized by moderate to severe dysplasia involving the lower two-thirds and full thickness of the epithelium, respectively.

SIL is also classified into **low-grade SIL** (LSIL) and **high-grade SIL** (HSIL) based on the degree of cellular atypia.

Squamous cervical precursor lesions

On histological examination, CIN and SIL appear as abnormal squamous epithelial cells that are arranged in various patterns.

These cells may show nuclear abnormalities such as **hyperchromasia**, **pleomorphism**, and **irregular nuclear membranes**. The cytoplasm may also appear abnormal, with increased or decreased staining intensity.

In CIN and SIL, the abnormal cells are confined to the epithelium and **do not invade into the stroma**.

However, these lesions have the potential to progress to invasive cervical carcinoma if left untreated. Therefore, prompt diagnosis and management of CIN and SIL are essential in **preventing the development of cervical cancer**.

Endometritis is an **inflammation of the endometrium**, the inner lining of the uterus. It can be caused by a variety of infectious and non-infectious etiologies.

Infectious endometritis is most commonly caused by **bacterial pathogens**, including Escherichia coli, Streptococcus spp., Staphylococcus spp., and Mycoplasma spp.

Non-infectious causes of endometritis include retained **products of conception, foreign bodies,** and **trauma**. Endometritis can also occur as a complication of gynecological procedures, such as dilation and curettage.

The **epidemiology** of endometritis varies depending on the underlying cause. Infectious endometritis is more common in women with risk factors for bacterial infections, such as sexually transmitted infections, immunocompromised status, or prolonged hospitalization. Non-infectious endometritis is more commonly seen in women who have recently undergone a gynecological procedure or experienced trauma to the uterus. Endometritis can also occur as a complication of pregnancy, particularly after delivery or miscarriage.

The clinical manifestations of endometritis can vary depending on the underlying cause and severity of the inflammation. **Acute endometritis** is often characterized by pelvic pain, fever, and uterine tenderness on examination. Vaginal discharge may also be present and may have a foul odor. **Chronic endometritis** may have milder symptoms, such as abnormal vaginal bleeding or discharge, or may be asymptomatic.

Histopathology of endometritis involves examination of the endometrial tissue to identify the underlying cause of inflammation. In cases of **infectious endometritis**, there will be infiltration of neutrophils and lymphocytes, edema, and vascular congestion. Bacterial colonies may also be present.

Chronic endometritis is characterized by a more diffuse infiltration of lymphocytes and plasma cells within the endometrial stroma, which can form lymphoid follicles. The glands may be dilated, and there may be evidence of fibrosis or scarring within the stroma.

Non-infectious causes of endometritis, such as retained products of conception or foreign bodies, may be identified by the presence of **necrotic tissue**, **granulation tissue**, or **foreign material** within the endometrial cavity. Trauma to the endometrium may result in areas of hemorrhage, necrosis, or ulceration.

Endometrial hyperplasia is a condition characterized by the abnormal proliferation of endometrial glands and stroma. The etiology of endometrial

hyperplasia is multifactorial, with several risk factors contributing to its development. The most common risk factor is an **imbalance of estrogen and progesterone hormones**, which can result from obesity, polycystic ovary syndrome, hormone replacement therapy, or anovulation.

Other risk factors include a family history of endometrial cancer, nulliparity, diabetes mellitus, and tamoxifen therapy.

The epidemiology of endometrial hyperplasia varies depending on the population studied and the diagnostic criteria used. The prevalence of endometrial hyperplasia is estimated to be approximately **1-2% in premenopausal women** and up to **25% in postmenopausal women** with abnormal uterine bleeding. The incidence of endometrial hyperplasia is increasing due to the aging of the population and the rising prevalence of obesity and diabetes mellitus.

The clinical manifestations of endometrial hyperplasia vary depending on the severity and histologic subtype of the lesion. The most common presenting symptom is abnormal **uterine bleeding**, which may be heavy or prolonged, or occur between menstrual periods. Postmenopausal bleeding is a particular concern and warrants immediate evaluation.

Women with endometrial hyperplasia may also experience pelvic pain or pressure, especially in cases of **atypical hyperplasia** or concurrent **adenomyosis**.

Endometrial hyperplasia is typically diagnosed on **endometrial biopsy or dilation and curettage**. Further evaluation may include imaging studies such as transvaginal ultrasound or magnetic resonance imaging to assess the extent of disease and exclude other causes of abnormal uterine bleeding.

Morphologically endometrial hyperplasia is classified into with or without atypia.

Atypical hyperplasia, also known as **endometrial intraepithelial neoplasia** (EIN), is characterized by the presence of abnormal glandular architecture and cytologic atypia, including nuclear pleomorphism, hyperchromasia, and increased mitotic activity. These features suggest a higher risk for progression to endometrial carcinoma compared to non-atypical hyperplasia.

Histopathologic examination of endometrial biopsy or curettage specimens is the gold standard for diagnosis of endometrial hyperplasia and atypical hyperplasia/EIN. Immunohistochemical markers may also aid in the diagnosis and prognostication of atypical hyperplasia/EIN, including **p53** and **Ki-67**.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

1. Pathomorphology : textbook / ed. by I.V. Sorokina, V.D. Markovskyi, D.I. Halata. - 2nd ed. - Kyiv : AUS Medicine Publishing, 2020. - 327 p., [10] col. inserts : tab.

2. Klatt, E. C. Robbins and Cotran Atlas of Pathology : [with Student Consult Online Access] / Edward C. Klatt. - third edition. - Philadelphia : Elsevier, 2015. - 587 p. : il.

3. Robbins Basic pathology / [ed. by] Vinay Kumar, Abul K. Abbas, Jon C. Aster. - 9th ed. - [Philadelphia] : Elsevier ; Saunders. - 910 p. : ill., scheme, tab.

ADDITIONAL LITERATURE

1. Sobotta. Atlas of human anatomy. [V. 1]. General anatomy and musculoskeletal system / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 400 p. : ill., col. ill.

2. Sobotta. Atlas of human anatomy. [V. 2]. Internal organs / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 259 p. : ill., col. ill.

3. Sobotta. Atlas of human anatomy. [V. 3]. Head, neck, and neuroanatomy / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 370 p. : ill., col. ill.

4. Weir & Abrahams' imaging atlas of human anatomy / ed.: J. D. Spratt [and oth.] ; consultant eds.: J. Weir, P. H. Abrahams. – 5th ed. - [S.l.] : Elsevier, 2017. - xvi, 263 p. : ill.

NORMATIVE LEGAL ACTS AND DOCUMENTS

1. Order of the Ministry of Health of the Republic of Belarus No. 111 of 06/01/1993 "On further improvement of the pathological service of the Republic of Belarus"

Access mode: http://patan.by/menyu/administrativnyie-proczeduryi.html - The date fccess: 20.03.2022.

ELECTRONIC DATABASES

1. Physician's consultant. Electronic Medical Library = Consultant of the doctor. Electronic medical library [Electronic resource] / Publishing group "GEOTAR-Media", LLC "IPUZ". – Access mode: http://www.rosmedlib.ru/ . – Access date: 03/15/2022.

2. Springer Link [Electronic resource] / Springer International Publishing AG. – Access mode: https:link.springer.com. – Date of access: 03/15/2022.