

ONMedU, Department of Obstetrics and Gynecology. Practical lesson No. 4. Operative laparoscopy in the treatment of female infertility and CPPS.

MINISTRY OF HEALTH OF UKRAINE

ODESSA NATIONAL MEDICAL UNIVERSITY

Faculty international

Department of Obstetrics and Gynecology



CONFIRMED by
Vice-rector for scientific and
pedagogical work
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August 29, 2024

**METHODICAL RECOMMENDATIONS FOR PRACTICAL CLASS
from elective discipline**

Faculty international, 6th course

Elective discipline **"ENDOSCOPIC TECHNOLOGIES IN OBSTETRICS
AND GYNECOLOGY"**

Practical lesson No. 4. "Operative laparoscopy in the treatment of female infertility and CPPS".

Methodological recommendations for a practical lesson, EPP "Medicine", 6th course, Faculty international Elective discipline "Endoscopic technologies in obstetrics and gynecology".

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Approved:

Meeting of the Department of Obstetrics and Gynecology
of Odesa national medical university

Protocol No. 1 dated August 29, 2024

Head of the department _____



(Ihor HLADCHUK)

Developer:

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of department of obstetrics and gynecology



Bykova N.A.

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Practical lesson No. 4

Topic: "Operative laparoscopy in the treatment of female infertility and CPPS".

Aim. Learn the causes of female infertility. Learn the plan of examination of a married couple in case of infertility. Get acquainted with the capabilities of modern endoscopic equipment in the diagnosis and treatment of infertility and CPPS (chronic pelvic pain syndrome). Master the basic technique of endoscopic interventions. Determine the indications and contraindications for laparoscopy in the diagnosis and treatment of CPPS and infertility. Familiarize yourself with determining the main stages of laparoscopic surgery salpingostomy, salpingo-ovariolysis, endometrioid excision heterotopia, chromohydrotubation. To form a clear idea about the examination of patients before operative laparoscopy. Learn the plan for managing patients in the postoperative period.

The main ones concept: Causes of female infertility and CPPS. Salpingovariolysis. Salpingostomy. Endometrioid excision heterotopia. Chromohydrotubation. Preoperative preparation and management of the postoperative period.

Equipment: Professional algorithms, structural and logical schemes, tables, models, video materials, results of laboratory and instrumental studies, situational problems, patients, case histories.

1. Organizational measures (greetings, inspection those present, message of the topic, purpose of the lesson, motivation students of studying the topic).

According to domestic and foreign authors, 10-15% of all marriages are infertile. Hence the relevance of this problem not only in the medical aspect, but also in the social aspect. The social significance of the problem of marital infertility lies in a significant decrease in the birth rate in the country and more frequent divorces in families without children. Timely diagnosis and a correctly developed infertility treatment algorithm are the key to stabilizing the demographic situation in Ukraine.

2. Reference level control knowledge (written work, written testing, online, frontal testing poll etc.).

Requirements for theoretical readiness students to perform practical classes (knowledge requirements, list of didactic units).

- Knowledge requirements: _
- Skills communication and clinical examination the patient
- Ability determine list necessary clinical and laboratory and instrumental research and evaluate their results.
- Ability establish preliminary and clinical diagnosis disease
- Perform medical manipulation

- Ability to conduct medical documentation
- List didactic units:
 - Causes of female infertility and CPPS.
 - Salpingovariolysis.
 - Salpingostomy.
 - Excision of endometrioid heterotopia.
 - Chromohydrotubation.
 - Preoperative preparation and management of the postoperative period.

Questions (test tasks, tasks, clinical situations) for verification basic knowledge on the subject of the lesson.

Question:

1. Classification infertility in marriage.
2. Methods diagnostics female infertility, indications.
3. Modern methods of conservative treatment patients with infertility.
4. Endoscopic methods of treating infertility patients.
5. Operative laparoscopy as a method of diagnosis and treatment of patients with external genitalia endometriosis.
6. Operative laparoscopy as a method of diagnosis and treatment of patients with CPPS.
7. Surgical reconstructive- plastic methods operations on fallopian tubes.
8. Chromohydrotubation as a method of diagnosing the tubo- peritoneal form of infertility.
9. Operations of HF cauterization of ovaries, resection of ovaries in anovulatory form of infertility.

Typical situations tasks

1. To the gynecologist a 29- year -old patient applied with complaints about infertility. Sexual by life has been married for 4 years, from pregnancies are not protected. There were no pregnancies. During the examination women established: development sexual organs without deviations from norms _ Fallopian tubes are not passing in the distal departments Basal temperature during three menstrual cycles two -phase. The most likely cause of infertility ? Treatment.

Answer: Tubo- peritoneal form of infertility. Laparoscopy, salpingoneostomy, chromohydrotubation are indicated.

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- 2. A 25- year -old woman turned to the women's clinic consultation with complaints about absence offensive pregnancy. Married for 2 years, lives regular sexual life, does not use contraceptives. It is known from the anamnesis that repeatedly was treated in the gynecological department department for exacerbations chronic adnexitis. Which diagnostic method is the most appropriate to recommend to the patient?

Answer: Diagnostic laparoscopy. Chromohydrotubation.

Typical tests task

1. The patient is 35 years old complains about the absence pregnancy for 7 years marital life _ During a gynecological examination, the doctor suspected external genitalia endometriosis _ What method is the gold standard for diagnosing external genitalia endometriosis ?
 - A. Culdoscopy.
 - V. Laparoscopy.S. Hysteroscopy.
 - D. _ Colposcopy.
 - E. Ultrasound.
2. Woman T, 27 years old, consulted a gynecologist about the absence of pregnancy after 3 years of marriage. The man was examined, no pathology was found. Polycystic ovary syndrome was detected during the woman's preliminary examinations. Conservative treatment (hormonal, stimulation of ovulation) was carried out - without effect. What is the most appropriate thing to offer the patient in this case?
 - A. Anti-inflammatory therapy.
 - B. Laparoscopy. Ovarian drilling.
 - S. Laparotomy. Wedge resection of the ovaries.
 - D. _ Laparoscopy. Salpingovariolysis.
 - E. Laparoscopy. Ovariectomy.

Answers 1 - B, 2B.

3. Formation of professional abilities and skills (mastery of skills, conducting curation, determining the treatment scheme, conducting laboratory research, etc.).

— **Content tasks (tasks, clinical situations etc.).**

Interactive tasks:

students groups divide into 3 subgroups of 4-5 people each. _ We work in offices female consultations with gynecological patients, we give tasks:

And the subgroup - put previous diagnosis.

second subgroup is to draw up a management plan gynecological the patient

III subgroup - evaluates correctness answers of subgroups I and II and adds his own corrections.

Atypical situational tasks:

Task 1.

The woman is 26 years old turned to to the gynecologist with and complaints about infertility, SCHATB within 3 years. Menstruation from 14 years old, painless, moderate. Cycle 4-5/28, regular. At the age of 16, she underwent an appendectomy complicated by peritonitis. Postcoital test and analysis sperm husband - within the norm. According to the data measurement basal temperature ovulatory, luteal cycles the phase is 12-14 days. According to ultrasound of the pelvic organs, there is a 4x6 cm mass in the area of the right fallopian tube. Define further management plan.

Answer: Therapeutic and diagnostic laparoscopy, chromohydrotubation. Adhesiolysis. Salpingoneostomy.

Task 2.

A gynecological examination of a 29-year-old patient suffering from chronic pelvic pain revealed: the uterus in fixed retroflexio - versio, painful and lumpy sacro -uterine ligaments. It is known from the anamnesis that they have been married for 5 years and no pregnancies have occurred. Previous diagnosis ? Management tactics

Reply: Frivolous genital endometriosis ? To determine the final diagnosis of UTI, the patient is indicated for laparoscopy, excision of endometriosis foci followed by histological examination.

Unusual test tasks:

1. The patient is 32 years old complains about the absence pregnancy within 5 years marital life. The basal temperature is biphasic. Man examined - healthy. During metrosalpingography, the fallopian tubes are filled with contrast to the ampullary one department, in the abdomen there is no contrast in the cavity. Which of the above ? most expedient prescribe for treatment this one sick ?

- A. Laparoscopic fallopian tube plastic surgery
- B. Courses hydraulic tubing
- C. Stimulation ovulation
- D. Extracorporeal fertilization
- E. Insemination with donor sperm

endometrioid cyst of the left ovary 5 cm in diameter, according to clinical examination and pelvic ultrasound. Operative treatment is offered. Determine the expected volume of the operation.

- A. Laparotomy. Extraction of the cyst capsule.
- B. Laparotomy. Adnexectomy.
- S. Laparoscopy. Adnexectomy.
- D. Laparoscopy. Enuclation of the ovarian cyst capsule.
- E. Laparoscopy. Tubectomy.

Correct answers: 1 - A, 2 - D.

— **Recommendations (instructions) for performing tasks (professional algorithms, orienting maps for formation practical skills and abilities etc.).**

Women's barrenness

<p><u>Classification:</u></p> <p>I. Endocrine genesis (infertility associated with a violation ovulation) – 35-40%:</p>	<ul style="list-style-type: none">- hypothalamic-pituitary insufficiency (HGN);- hypothalamic-pituitary dysfunction (GGD) (ovarian and adrenal forms);- primary insufficiency ovaries;- violation functions sexual bodies;
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<p>II. Tubal- peritoneal genesis - 20-30%.</p> <p>III. Uterine genesis - 2-3%:</p> <p>And V. Cervical genesis - 5%.</p> <p>V. Immunological genesis - 20%:</p> <p>V I. Others forms female infertility: WITH</p>	<ul style="list-style-type: none"> - hyperprolactinemia. - absence of a uterus; <ul style="list-style-type: none"> - anomalies development of the uterus; - synechiae in the uterine cavity (Asherman 's syndrome). - availability antisperm blood pressure only in the cervical mucus ; - with availability antisperm BP in the blood women, ova, follicular liquid - - feminine infertility, conditioned urogenital infection; - endometriosis and infertility; - uterine myoma and infertility.
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Male sterility

<p style="text-align: center;"><u>Classification:</u></p> <p>Excretory sterility</p> <p>Secretarial sterility</p> <p>mixed sterility</p> <p>Immunological infertility</p>	<p>(insufficiency secretory functions sexual glands), which is conditioned congenital and acquired pathology.</p> <p>conditioned violation of the transport of sperm through the vas deferens.</p> <p>when secretory insufficiency sexual glands combined with obstructive, immunological and inflammatory process _</p>
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<p><u>Examination women:</u></p>	<p>Gathering somatic anamnesis. Gathering gynecological history. Collection of reproductive anamnesis. General and gynecological review RW, HIV. Schedule basal temperature for 2-3 months. Colposcopy. Urogenital monitoring _ _ infection, cytological examination _ Ultrasound of the pelvic organs. Hysterosalpingography (day 7-11 of the menstrual cycle). Hormonal examination _</p> <p>Immunological tests: - PCT (postcoital test) - allows to evaluate biological compatibility spermatozoa and cervical slime women _ - MAR-test - definition antisperm antibodies in the ejaculate (normally < 30%).</p> <p>Hysteroscopy, laparoscopy. <i>Additional research by signs:</i></p> <ul style="list-style-type: none"> <input type="checkbox"/> Hormonal examination (cortisol, DHEA-c, insulin, T₃, T₄, TSH, THG, antibodies to thyroglobulin, etc.); samples _ <input type="checkbox"/> Examination mammologist, mammography (day 7-10 of the menstrual cycle). <input type="checkbox"/> R - graph Turkish saddles (according to indications). <input type="checkbox"/> CT, MRI (as indicated). <input type="checkbox"/> Ultrasound of the thyroid glands (as indicated).
<p><u>Examination men:</u></p>	<p><u>(carried out jointly and simultaneously with the examination women)</u></p> <p>General clinical methods examination Urogenital examination _ infection Examination ejaculate according to the WHO classification (3-4 dnistrual rest). Consultation of a therapist, geneticist, sexologist (on request). <i>If available pathologies in the spermogram additionally conducted:</i> Tank. seeding of sperm for sterility. Hormonal examination (FSH, LH, prolactin, testosterone). Test capacitance.</p>

	Ultrasound of the prostate glands and scrotums.
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Treatment algorithm different forms of infertility

<u>Treatment algorithm tubal genesis infertility.</u>	Operative laparoscopy - for recovery passability fallopian tubes There is none effect (within 6-12 months) – IVF with PE (transfer embryo). Absence fallopian tubes, impossibility restoration their passability - ECO with PE.
<u>Treatment algorithm female infertility uterine genesis</u>	(absence of the uterus; anomalies development of the uterus; Asherman 's syndrome). Surrogate motherhood. Provided available opportunities - operative reconstructive treatment
<u>Treatment algorithm female infertility cervical genesis.</u>	Insemination with male sperm (ICH) in physiological or induced cycles. Absence effect - IVF with PE.
<u>Treatment algorithm immunological infertility</u>	<i><u>With availability antisperm antibodies only in the cervical mucus - in the</u></i> intrauterine insemination with a man 's sperm. <i><u>With availability antisperm antibodies of a woman's blood, ovum, follicular fluid -</u></i> intrauterine insemination with donor sperm in the background stimulation ovulation.
<u>Treatment algorithm infertility, conditioned male factor.</u>	Oligoasthenospermia 1-2 degrees - treatment by an andrologist and UCI. Grade 3 oligoasthenospermia and azoospermia - donor sperm insemination (ISD) or ICSI Absence effect - IVF with PE with donor sperm.

Chromohydrotubation (Fig. 1)

Any operation for tubal or peritoneal infertility requires the use of intraoperative ascending chromohydrotubation. To do this, before the operation, the external genitalia and vagina are treated with a solution of antiseptics. The cervix is grasped with ball forceps. A uterine cannula is inserted through the external uterine opening. Ball forceps and cannula are fixed to each other. Chromohydrotubation is performed at the beginning of the operation to determine the level of fallopian tube obstruction.

After the laparoscopic intervention on the fallopian tubes, chromohydrotubation confirms the effectiveness of the performed operation. Level obstructions fallopian tube is possible to determine from filling her liquid. Absence filling of the fallopian tube with the injected liquid testifies to it obstruction in the isthmus parts. To conduct chromohydrotubation use isotonic solution sodium chloride, colored methylene blue



Fig. 1. Chromohydrotubation. Stage of the procedure. Effusion of methylene blue into the abdominal cavity.

Salpingoneostomy (Fig. 2)

It is performed in the presence of hydrosalpinx. After chromopertubation with the use of methylene blue dye (for better visualization of the fallopian tube), a cross-shaped incision is made through the scar tissue at the distal pole of the hydrosalpinx to form four flaps. The cut edges of the pipe are carefully grasped with an atraumatic tool clamp and produce coagulation of the serous lining of the fallopian tube for their eversion.

With a correctly performed operation, the fimbrial part of the fallopian tube is formed anew, which is also called salpingostomy according to Bruis.

According to the alternative method, two atraumatic clamps are used, with the help of which the distal part of the tube is everted for 2-3 cm. Some surgeons prefer to apply 1-2 sutures to support the tube in the given position.

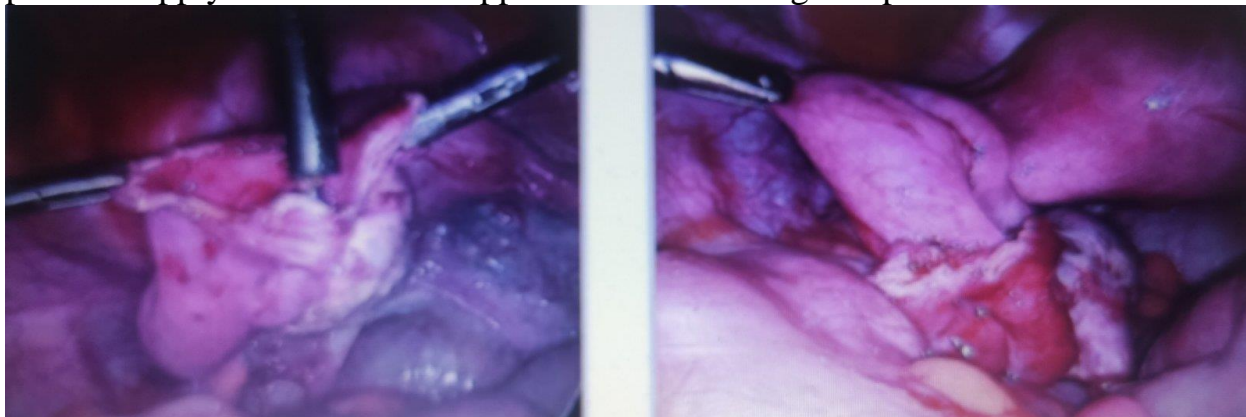


Fig. 2. Salpingoneostomy. Stages of the operation.

Ovarian diathermocauterization (drilling) (Fig. 3)

It is performed as a surgical stimulation of ovulation in polycystic ovary syndrome and is a more gentle method compared to ovarian resection. The technique consists in creating perforation holes on the surface of one or both ovaries using thermocoagulation. If necessary, additional hemostasis is performed.



Fig. 3. Type of ovaries after diathermocauterization monopolar coagulator.

Surgical treatment of endometriosis.

Stages of surgery for excision of endometriosis foci on the peritoneum of the pelvis (Fig. 4)

1. Detailed examination of the peritoneum of the vesical -uterine, recto -uterine recesses, ovaries, fallopian tubes, broad ligaments, uterus, distal part of the rectum, sigmoid colon;
2. Assessment of the size of the detected foci, the degree of invasion into the surrounding tissues, examination of their surface using atraumatic clamps (lifting and displacing the peritoneum surrounding the lesion); when growing into the underlying tissue, the pathological areas are displaced relative to the subperitoneal tissue;
3. creation of optimal conditions for the elimination of pathological foci (removal of intestinal loops, omentum to the upper floors of the abdominal cavity, dissection of adhesions, etc.);
4. excision or local destruction of endometriosis foci on the pelvic peritoneum (electrocoagulation)

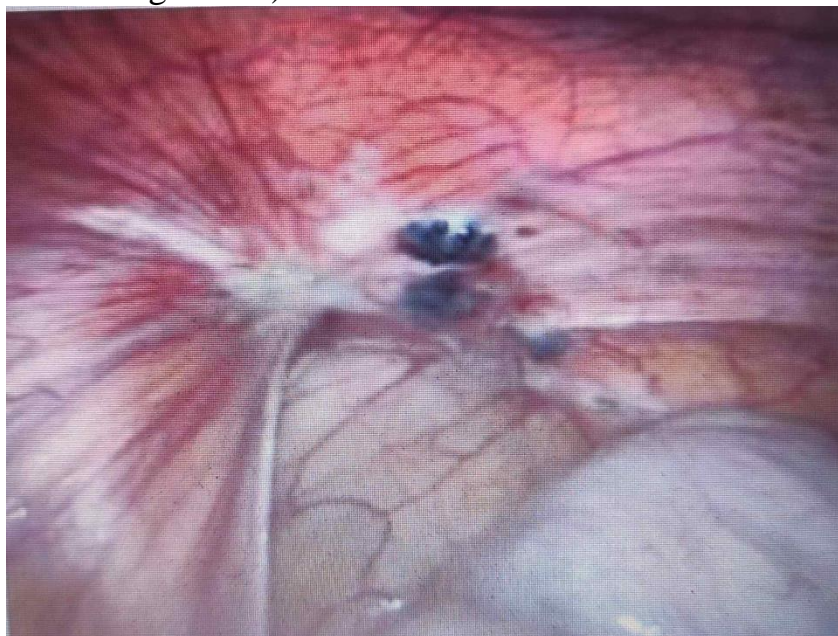


Fig. 4. Foci of endometriosis on the parietal peritoneum.

Endoscopic treatment of the adhesion process of the pelvic organs.

Scissors, aquadissection, electrosurgery, laser surgery, and an ultrasonic scalpel are used for dissection of adhesions. With a pronounced degree of the adhesion process, there is a danger of damage to internal organs (Fig. 5).

Monopolar electrodes should not be used during manipulations on the intestines, as sparks and damage to the intestines are possible.

which is out of sight. When dividing adhesions on the intestines, scissors are most often used, and if necessary, bipolar coagulation.

adhesion barriers and fluids are used to prevent the recurrence of adhesion disease.



Fig. 5. Adhesion process of pelvic organs.

— **Requirements for results work, including to registration.**

1. Oh, and you too patient with infertility.
2. To prescribe examination of patients with infertility.
3. Evaluate data clinical laboratory and instrumental examination patients with infertility.
4. Determine the stages of endometriosis during diagnostic laparoscopy.
5. Determine the volume of surgical intervention in the treatment of external genitalia endometriosis in patients with infertility.
5. Prescribe the most appropriate treatment for a patient with UTI.
6. Prescribe the most appropriate treatment for a patient with SHTB, hydrosalpinx.

— **Control materials for the final stage of the lesson: problems, tasks, tests, etc.**

Unusual situational tasks:

1. During a diagnostic laparoscopy, a 34-year-old patient who applied to the clinic for infertility was found to have: hemorrhagic effusion in the abdominal cavity, blue " eyes ", stellate -scarring lesions of the peritoneum. Fallopian tubes pass from both parties _ Ovaries visually unchanged. _ Done biopsy specified formations _ Previous diagnosis ? Volume of surgical intervention.

Answer. Frivolous genital endometriosis _ Laparoscopy. Excision of endometriosis foci followed by histological examination.

2. A 28-year-old patient was admitted to the gynecology department with complaints of infertility for 4 years, CPPSS. From the anamnesis: 1 childbirth, 1 artificial abortion, menstrual cycle without any features, basal temperature – biphasic. The man's spermogram is normal. She was repeatedly treated for pelvic inflammatory processes. 2 years ago, she underwent a right-sided tubectomy due to a broken tubal pregnancy.

What are the driving tactics?

Answer: Laparoscopy. Chromohydrotubation. Separation of adhesions

Test tasks krok-2

1. (2020) A 26-year-old patient has been married for 5 years. In the absence of contraception and the presence of regular sexual life pregnancy absent, husband examined, fertile. From the anamnesis: at the age of 19 operated on the phenomena spilled peritonitis. Which research is it necessary to find out the causes of infertility ?

- A. Hysterosalpingography or laparoscopy *
- B. Research sexual steroids, gonadotropins, folliculometry
- C. Functional tests diagnostics
- D. Hysteroscopy with assessment functional state of the endometrium
- E. Kymographic pertubation fallopian tubes.

2.(2019) A 32-year- old woman turned to the doctor with complaints about absence pregnancy during 4 years. History: first pregnancy 5 years ago ended artificial abortion. According to the data vaginal examination and ultrasound examination (ultrasound) is established diagnosis: endometrioid cyst of the right ovary. Which optimal method of treatment ?

- A. Anti-inflammatory therapy
- B. Androgen therapy
- S. Conservative therapy estrogen-progestogen drugs
- D. Sanatorium- resort treatment
- E. Operative laparoscopy *

3. (2018) 25-year- old patient complains of infertility and secondary amenorrhea. Objectively: excessive nutrition, phenomena hirsutism. Bimanual: uterus normal sizes, ovaries from both sides something enlarged, painless. The level of LH and testosterone is elevated, the ACTH test is negative. Put diagnosis:

- A. Polycystic syndrome ovaries *
- B. Adrenogenital syndrome
- S. Two-sided chronic salpingo-oophoritis
- D. _ Virilizing tumors ovaries
- E. Syndrome of resistant ovaries

4. Summary results:

Current control: oral survey, testing, evaluation implementation practical skills, solutions situational clinical tasks, assessment activity in class etc. _

The structure of the current evaluation in the practical lesson:

1. Assessment theoretical knowledge on the topic of the lesson:
 - methods: survey, solution situational clinical tasks;
 - the maximum score is 5, the minimum rating - 3, unsatisfactory rating - 2.
2. Rating practical skills and manipulations on the topic of the lesson:
 - methods: assessment correctness implementation practical skills;
 - the maximum score is 5, the minimum rating - 3, unsatisfactory rating - 2.
3. Assessment work from the patient on the subject of the lesson:
 - methods: assessment: a) communicative skills communication with the patient, b) correctness assignments and evaluations laboratory and instrumental studies, c) compliance with the algorithm of conducting differential diagnosis d) rationale clinical diagnosis, e) drawing up a treatment plan ;
 - the maximum score is 5, the minimum rating - 3, unsatisfactory rating - 2.

Current assessment criteria for practical lesson:

"5"	The student is fluent in the material, takes an active part in discussing and solving a situational clinical problem, confidently demonstrates practical skills during the examination of a patient and the interpretation of clinical, laboratory and instrumental research data, expresses his opinion on the subject of the lesson, demonstrates clinical thinking.
"4"	The student has a good command of the material, participates in the discussion and solution of the situational clinical problem, demonstrates practical skills during the examination of the patient and the interpretation of clinical, laboratory and instrumental research data with some errors, expresses his opinion on the topic of the lesson, demonstrates clinical thinking.
"3"	The student does not have sufficient knowledge of the material, is unsure of participating in the discussion and solution of the situational clinical problem, demonstrates practical skills during the examination of the patient and the interpretation of clinical, laboratory and instrumental research data with significant errors.
"2"	The student does not master the material, does not take part in the discussion and solution of the situational clinical problem, does not demonstrate practical skills during the examination of the patient and the interpretation of clinical, laboratory and instrumental research data.

5. List of recommended literature.

Basic:

1. Obstetrics and Gynecology: in 2 vol.:textbook. Volume 2. Gynecology / V.I. Gryshchenko, M.O. Shcherbina, B.M. Ventskiivskiyi et al.; edited by V.I. Gryshchenko, M.O. Shcherbina. — 3th edition. — K.: AUS Medicine Publishing, 2022 – 352 p.
2. Oats, Jeremy Fundamentals of Obstetrics and Gynaecology [Text]: Llewellyn-Jones Fundamentals of Obstetrics and Gynaecology / J. Oats, S. Abraham. – 10th ed. – Edinburgh [etc.]: Elsevier, 2017. – VII, 375 p.
3. Llewellyn-Jones Fundamentals of Obstetrics and Gynaecology (10th Ed). Jeremy Oats, Suzanne Abraham. Elsevier. 2016. – 384 pp.
4. Dutta, Durlav Chandra. D. C. Dutta's Textbook of Gynecology including Contraception / D.C. Dutta; ed/ Hiralal Konar. – 7th.ed. – New Delhi: Jaypee Brothers Medical Publishers, 2016. – XX, 574 p.

Additionally:

1. 2011 IFCPC Colposcopic Terminology. Clarification on practical use.- K.. - "Polygraph Plus", 2018.- 62 p.
2. Modern technical teaching aids (see appendix to the work program of the 4th year) Prevention of purulent-septic complications during laparoscopic surgeries on pelvic organs with the risk of vaginal microbiota contamination / Zaporozhan VN, Gladchuk IZ, Rozhkovska NM, Volyanska AG, Shevchenko OI //World of Medicine and Biology.-2020- #1(71). - P.49- 53. (Web of science)

Electronic information resources

1. <https://www.cochrane.org/>- Cochrane / Cochrane Library
2. <https://www.acog.org/>- The American College of Obstetricians and Gynecologists
3. <https://www.uptodate.com>– UpToDate
4. <https://online.lexi.com/>- Wolters Kluwer Health
5. <https://www.ncbi.nlm.nih.gov/>- National Center for Biotechnology Information / National Center for Biotechnology Information
6. <https://pubmed.ncbi.nlm.nih.gov/>- International Medical Library / National Library of Medicine
7. <https://www.thelancet.com/>- The Lancet
8. <https://www.rcog.org.uk/>- Royal College of Obstetricians & Gynecologists
9. <https://www.npwh.org/>- Nurse practitioners in women's health
10. <http://moz.gov.ua>- Ministry of Health of Ukraine
11. www.ama-assn.org– American Medical Association / [American Medical](#)

Association

12. www.who.int- World Health Organization
13. www.dec.gov.ua/mtd/home/- State Expert Center of the Ministry of Health of Ukraine
14. <http://bma.org.uk>– British Medical Association
15. www.gmc-uk.org- General Medical Council (GMC)
16. www.bundesaerztekammer.de– German Medical Association
17. www.euro.who.int- European Regional Office of the World Health Organization