MINISTRY OF HEALTH OF UKRAINE

ODESA NATIONAL MEDICAL UNIVERSITY

Department of Obstetrics and Gynecology

APPROVED

Vice-rector for scientific and pedagogical work

_____ Eduard BURIACHKIVSKYI

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METHODOLOGICAL RECOMMENDATIONS FOR LECTURES ON THE ACADEMIC DISCIPLINE "OBSTETRICS AND GYNECOLOGY"

for 4th year students

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Head of the Department, Doctor of Medicine, Professor _____ Ihor GLADCHUK

Developers:

Ph.D., assistant professor of obstetrics and gynecology department V. KOZHAKOV

Ph.D., assistant professor of obstetrics and gynecology department O. NADVORNA

Ph.D., assistant professor of obstetrics and gynecology department L. BERLINSKA

Ph.D., assistant professor of obstetrics and gynecology department

Y. ONYSHCHENKO

Reviewers:

Head of the Department of Histology, Cytology, Embryology and Pathological Morphology with a Course of Forensic Medicine Doctor of Medical Sciences, Professor Varvara SYTNIKOVA

Ph.D., assistant professor of the Department of Surgery

with postgraduate education Sergey POLYAK

LECTURE №1. TOPIC: Physiology of female genital organs. Methods of examination of gynecologic patients. General Symptomology in Gynecology.

1. Relevance of the topic:
Recognition of gynecologic diseases is based on data from the anamnesis, subjective and objective examinations. A total of subjective and objective methods of examination promotes cognition of the processes which really occur in the patient's organism.
Exact diagnostics, as a result, and rational treatment of gynecologic diseases can be conducted only under conditions of correct examination of the gynecologic patients, conducted on a certain system, which helps to take into account all the details and find the main facts, promoting correct recognition of the disease.

2. Goals:
To introduce students to current topics, normal menstrual cycle, regulation of menstrual cycle, the volume of the survey of it.

3. Basic concepts:
1. Clinical anatomy and physiology of female genitalia.
2. Special gynecological anamnesis.
3. General and special methods of examination of gynecological patients.
4. Main special examination methods in gynecology: visual examination of genitals, speculum examination, bimanual examination.
5. Additional specific examination methods.
6. Methods of functional diagnostics of ovaries.
7. Laboratory methods of examination in gynecology: microscopy of urogenital discharge, oncocytology, bacteriological study, PCR, ELISA, pathomorphological study.
8. Instrumental examination methods in gynecology: uterine probing, curettage of uterine cavity and cervical canal, biopsy, puncture of abdominal cavity through posterial fornix.
9. Endoscopic methods of examination in gynecology: colposcopy, hysteroscopy, laparoscopy.
10. Radiological examination methods in gynecology: MRI, CT, MSG.
11. Ultrasonic examination methods in gynecology: transvaginal and transabdominal USD.
12. General symptomatics of gynecological pathology.

4. Content of the lecture material:
Clinical anatomy of female genitals
The female genital tract is divided into external and internal genitalia.
The external genitalia (genitalia externa) include the vulva (vulva), which contains all the anatomical structures from the pubis to the perineum: pubis, large pudendal and small pudendal lips, clitoris, hymen, inlet to the vagina and its glands, female urethra, and also glands and vessels (codogram).

Pubis (mons pubis, mons Veneris) is the lowest part of the anterior abdominal wall, the spherical fat pad above the pubic symphysis (symphisis pubica) covered by skin and hair. Hair ap-pearance and fat sediment on the pubis takes place at the beginning of puberty. The upper edge of the hair forms a horizontal line in women (female type) and in men the hairy integument is located along the white line as a stripe or in the form of a narrow triangle with its apex near the umbilicus (male type). In women hair grows down along the external surface of the large pudental lips (triangle with its apex downwards). The appearance of the pubic hair changes during the phases of a woman's life. It does not exist in girls before puberty; during the reproductive age it varies in thickness, length and coloration, during menopause the hairy integument becomes thinner. The skin of the pubis contains sudoriferous and sebaceous glands. Quantity of subcutaneous fat depends on heredity, age, diet and, possibly, on the influence of steroid hormones. On the right and left side of the pubic surface, there are pubic tubercles (tubercula pubica). They are description points for determining the external openings of the inguinal canals, where the round ligaments of the uterus come from.

Innervation of the pubis is maintained by branches of the ilioinguinal and genitofemoral nerves.

Blood supply comes from the external genital arteries and veins. The inguinal lymph nodes ac-cumulate lymph from the genital area and surface of the abdomen. Cross lymphatic circulation has an important clinical meaning, because the spread of cancer of the vulva through the inguinal lymph nodes both with the direction of lesion and in a reverse one occurs.

Clinical meaning. Dermatitis, pediculosis (phthyrius pubis) may evolve in the area of the mons pubis. Edema of the mons pubis may appear secondary as a result of infection, trauma, cancerous infiltration of the lymph nodes. Cancer of the vulva may spread to the mons pubis.

The large pudendal lips (labia majora pudendi) - two folds of skin with connective and adipose tela, numerous vascular plexi descending from the mons pubis to the perineum on either side of the pudendal slit (rima pudendi) and forming anterior and posterior commisura of the lips. The large pudendal lips as a rule join in nulliparae but after each labour the distance between them increases and in aged women atrophy occurs. The skin on the lateral (external) surface of the large pudendal lips is covered by hair and pigmented, on the medial (internal) surface - smooth, very thin, and looks like mucous membrane. It contains a lot of sudoriferous and sebaceous glands, their secretion gives off a specific smell to the area of genitalia. The secretion of the sudoriferous glands which are innervated by the sympathetic nervous system (SNS) moistens the pudendal lips and protects them from irritation by vaginal discharge. The secretion of the glands is regulated by hormonal and psychogenic stimuli, its discharge decreases in aged women. In the middle of the large pudendal lips on the border between their medial part and lower one third on either side are the greater vestibular glands (the Bartholin's glands) 10-15 mm in length and 7-10 mm width. Their duct opens on the inner surface of the labia minora at the entrance to the vagina. The viscous grayish secret with alkaline reaction of these glands corresponding with the Cowper glands of the husband, is discharged due to pressing

or sexual excitation, which allows normal moisture of the mucous membrane at the entrance to the vagina. The frenulum is a thin bridge, skin fold between the commisurra of the labia minora and the large pudendal lips which as a rule ruptures during first labour. To the middle from the frenulum behind the hymen there is a small recess, the fossa of the vestibule of the vagina (fossa vestibuli vaginae).
Clinically between the frenulum of the pudental lips and the anus, the gynaecologic (anterior) perineum is located; between the anus and superior coccyx – posterior perineum.
Innervation. The large pudendal lips are innervated by ilioinguinal and genital nerve anteriorly, and laterally and posteriorly by a branch of femoral cutaneous nerve.
Blood supply of the large pudendal lips comes from the internal (from the internal iliac artery) and external genital (from the femoral artery) arteries. Venous blood outflows by the internal and external genital veins.
Clinical meaning. The large pudendal lips have no special functions. Cyst of the inguinal canal may occur; sometimes it is diagnosed as an indirect inguinal hernia. The large pudendal lips may stick together at vulvites in girls. As a consequence of external force (trauma) or complicated labour a hematomae may form. The tumour of the apocrine sudoriferous glands - hydpoadenoma, malignase very rarely. Cysts of the sudoriferous glands are benign, but often they become infected.
The small pudental lips (labia minora pudendi) are two small, narrow and thin (there is no adipose layer) folds of skin between the labia majora and the vaginal opening. As a rule, they are covered by labia majora. The labia minora have sudoriferous glands, smooth muscular and elastic fibres and a lot of veins. They are extremely sensitive due to the presence of a number of nervous endings. On the outside the labium minora are lined with stratified squamous epithelium, pink in color, they have no sudoriferous glands and hair follicles. During puberty the sebaceous glands form, they may infect at this period and atrophy during menopause. At the upper part each labium minora is divided into two less folds which encompass the clitoris from aloft form the prepuce (praeputuim clitoridis) and on the underside the frenulum of the clitoris (frenulum clitoridias). In the low part the labia minora become thinner, coalescing with the inner surface of the labia majora and forming a small cross partition, the frenulum of the labia-minora (frenulum labiorum pudendi).
Innervation of the labia minora is provided by the ilioinguinal, genital and rectal nerves.
Blood supply of the labia minora is provided by the internal and external genital arteries.
Clinical meaning. The labia minora close the vaginal entrance. They increase as the response to the stimulation by ovarian hormones and without oestrogen stimulation the atrophic changes take place in it. Squamous cell carcinoma of vulva often starts from the labia minora, exactly from the sebaceous glands. A sticking together of the labia minor in girls is an evidence of their inflammation (vulvitis), their adhesion may be an evidence of sexual differentiation disorders.
The clitoris is homologous to the penis cylindrical erectile body 2-3 cm in length, located in the anterior coner of the genital rima, between the labia minor. The head of the clitoris is nearly 0.5 cm in diameter, covered by squamous epithelium with

numerous nervous endings and sebaceous glands. The clitoris is attached to the lower part of the pubic symphysis by lig. suspensoium clitoridis and consists of two corpi cavernosum. During sexual excitement they observe their erection and as a consequence of it the vaginal entrance narrows. The corpi cavernosum comes from the low edge of the descending branches of the pubic bones, unite in the middle and form the body of the clitoris. The end of the clitoris is surrounded by the edges of the labia minora, their anterior edge forms the prepuce of the clitoris and both posterior edges form its frenulum (frenulum clitoridis). Because of numerous vessels and nerves clitoris is extremely sensitive, its friction causes orgasm. The clitoris is the main erogenic zone in women.
Innervation of the clitoris is provided by the ilioinguinal and genital nerves.
Blood supply of the clitoris is provided by its arteries, branches of the inner genital artery (a. pudenda interna).
Clinical meaning. Cancer of the clitoris is seen very seldom, early metastatic spreading is inherent in it and it involves wide excision. Inguinal and femoral lymph nodes are damaged first, as a rule.
The vestibule of the vagina (vestibulum vaginae) is a triangle-shaped cavity, formed from the urogenital sinus and limited at the top by the clitoris, laterally by the labia minora, and inferiorly and posteriorly by the posterior commissure of the pudental lips and the vaginal vestibule. Its bottom is the hymen. The vestibule vagina is lined with thin squamous epithelium. Six orifices open into it, they are: the urethra, the vagina, two ducts of the greater vestibular glands and two ducts of the smaller vestibular glands.
In the vaginal vestibule under the clitoris the outer orifice of the urethra (urethra feminina) is located. It may be of different forms (round, compressed, with two lateral lips) while usually it looks like a turned over letter "V". It, like the whole urethra, is lined with transitional epithelium and as a consequence has more intensive pink color than the mucous of the vaginal vestibule covered with squamous epithelium. Low two thirds of the urethra are located directly over the anterior vaginal wall. The urethral diaphragm supports the urethra position.
Innervation of the urethra is provided by the genital nerve.
Blood supply to the urethra is provided but the internal genital artery and vein.
Clinical meaning. One may observe vegetation of the urethra mucosa, planocellular and transition-cellular carcinoma, developing from urovestibular zone may occur.
Just below the orifice of the urethra there are two small openings of the smaller vestibular (paraurethral, the Skene's) glands (glandulae vestibularis minors), which are rudiments of the Wolffian duct (Fig). These glands are homologous to the prostate (prostata). Their ducts are lined with transitional epithelium. They have common with the urethra innervation and blood supply.
Clinical meaning. The Skene’s glands, which produce a small amount mucous, are especially prone to gonococcus infections, which can be revealed for the first time in them. After successful anti-gonococcus therapies, non-specific infection can be recurring, that demands electro-cauterization or laser destruction of the glands’ ducts.
The greater vestibular glands (the Bartholin s glands, glandulae vestibulares majores) are homologous to the Cowper's glands (bulbourethral glands) in men. They lie on

the posterio-lateral surface of the vaginal opening. Their ducts open on either side of the hymen in the vaginal vestibular (Fig. 4, b). Each gland has a narrow duct approximately 2 cm long and partially covered with cavernous tissue, bulbs of the vestibular (bulbi vestibuli, Fig. 5) located from the both sides of the vagina between skin and m. bulbospongiosus. They are homologous to the bulbs of the penis. Viscous greyish mucoid secretion of these glands has alkaline reaction; it excretes at press, sexual excitement and supports normal moistness of the mucosa of the vaginal orifice.

The hymen is a thin elastic duplicate of mucosa covered with squamous epithelium which as a rule partially closes the vaginal orifice. It has one (rarely several) excentric opening for the outflow of the menstrual blood. Rarely the hymen has no an orifice. During first sexual contacts the hymen usually tears slightly, mainly inferiorly and laterally and after labour only its remnants may stay, papillae of hymen (carunculae hymenalis).

Innervation and blood supply of the hymen is provided by the genital and inferior rectal nerves, arteries and veins.

Clinical meaning. Bartholinitis is an often complication of sexually transmitted diseases and espe-cially honorrhea. Abscess of the greater vestibular gland (the Bartholin's) needs a surgical intervention and under relapsing the cyst's marsupialization should be performed. Rigid hymen may cause pain during sexual contacts which requires its dissection (surgical defloration).

The female internal genitalia (organa genitalia feminina interna) consist of the vagina, the uterus, the Fallopian tube and the ovaries.

The vagina is a tubular muscular-connective structure joining genital area with the uterus located between the urethra and the urinary bladder anteriorly and the rectum posteriorly. Its length along the anterior wall is 7-8 cm and 9-10 cm along the posterior wall. The vagina is narrowed near the hiatus; upwards it widens and ends with the vaults of the vagina. The vagina is a polyfunctional organ; it is an excretory organ of the uterus, the female organ of copulation and part of labour canal. Its upper part is formed from the Miiller's ducts, and the low one from urogenital sinus.

Anteriorly the vagina is separated from the bladder and the urethra orifice by the vesicovaginal septum; posteriorly it is limited from the rectum by the recto-vaginal septum. The superior one fourth of the vagina is separated from the rectum by the dome-shaped pocket of the peritonium, the rectouterine (Douglas') pouch.

The superior part of the vagina encompasses the uterus' cervix and forms the anterior, posterior and two lateral vaults (fornix). The vaginal walls, anterior and posterior, consist of muscular fascicles, connective tissue and mucous membrane. The muscular fascicles of the vaginal anterior wall spread on the muscular layer of the urethra and the muscular fascicles of its posterior wall — on the inferior part of the rectum. The thickness of the vaginal wall is approximately 3 mm. The vaginal wall consists of the three layers. The mucous membrane of an adult woman vagina is lined with stratified squamous epithelium; it is comparatively smooth on the lateral walls and forms anterior and posterior transversal folds (columnae rugarum) which allows it to stretch well in labour. The vaginal connective tissue is rich in blood vessels and contains lymph nodes. The vaginal mucous membrane is pale pink and during pregnancy it is

cyanotic, it is glands-free. The vaginal discharges contain alkaline secretion of the cervix, desquamous epithelial cells and bacteria. Epithelium of the vagina is rich in glycogen which transforms into lactic acid under the influence of normal vaginal flora (Doder-lein's bacilli). That is why pH of the vagina is acid (approximately 4.5) what is a protective barrier against infections.
Innervation of the vagina comes from the genital and rectal nerves and pelvic sympathetic plexus.
Blood supply of the vagina is provided by the vaginal branches of the uterine artery which supply blood to its upper one third. The middle one third of the vagina is supplied by blood from the inferior vesical arteries; its low one third is supplied from the middle rectal and inner genital arteries. The venous plexis is located around the vagina, the veins pass along arteries to the inner iliac vein; the veins of the low one third of the vagina go to the femoral arteries. Lymphatic drain of the low one third of the vagina as well as the genital area is provided in the direction of the vaginal lymph nodes and the middle and upper one third of the organ in the direction of the iliac lymph nodes.
Clinical meaning. The vaginal discharge (leukorrhea) is a frequent complication, symptom of local or systemic diseases. The most frequent reason of] the vaginal discharge is an infection of the low parts of the reproductive tract. Other reasons may be either oestrogenic or psychogenic stimulation or deficiency of oestrogens as a result of senile atrophic vaginitis. Metastatic cancer of the vagina is met morel often than primary one.
The uterus (s. metra, hystera) is an unpaired cavitary muscle organ located in the pelvic, cavity between the urinary bladder anteriorly and the rectum posteriorly.
The uterus consists of two parts: the upper, the body of the uterus (corpus uteri) and the low, the neck of the uterus (cervix). The upper part of the corpus is called the fundus of the uterus (fundus uteri) and in the cervix has 2 parts supravaginal and vaginal parts. There is the isthmus of the uterine (isthmus uteri) between its corpus and cervix, the clinical title is orificium internum uteri (some authors distinguish the anatomic and hystologic internum uteri). The uterine wall consists of three layers, the internal mucous membrane, (endometrium), the middle, muscular layer (myometrium), the external serous membrane (perimetrium). The uterine mucous membrane has two layers, the basal layer and the functional layer.
The cervix of the uterus is conic-shaped in a nullipara and 2-4 cm long with an average caliber of 2.5 cm. The canal of the neck of the uterus (canalis cervicalis uteri) has a rounded orifice (ostium of the uterus) which has anterior and posterior lips. Approximately half of the length of the cervix is its supravaginal portion; to the front the urinary bladder lies. The vaginal portion of the cervix up to the uterine orifice is lined with squamous epithelium, the cervical canal – cylindrical secretory epithelium, its glands, produce cervical mucous. Apart from the epithelial layer of the canal, the cervix 85% consists of connective tissue and 15% consists of circular muscular fibers which merge with myometrium superiorly. The corpus uterus, vice versa, consists of 85% muscular fibers and only 15% —connective tissue. The anatomic structure of the cervix changes during pregnancy and labour. Traumatic damage during labour cause changes connected with its location and form. The uterine orifice becomes slot-

like. The cervix is held in its position due to the pubocervical, sacrouterine and transversal (cardial) ligaments.
Innervation of the cervix is from the second, third and fourth pair of sacral nerves and pelvic sympathetic plexus.
Blood supply is provided by the uterine, ovarian and internal genital arteries and veins.
Clinical meaning. Ectopia of the cylindrical epithelium of the cervical canal can lead to postcoital (contact) bleedings and infections. Squamous cell carcinoma of the cervix (second most frequent disease in women) in 90% of cases occurs at the junction of the cylindrical and flat epithelium. Cervicitis, especially with specific etiology, is often accompanied by leucoria and can cause infertility.
In reference to the pelvic axis the uterus is curved forward (anteflexio) in most cases or (rarely) backward (retroflexio). The body of the uterus is bent forward (anterversio) in reference to the cervix too. The peritoneum covers the posterior surface of the urinary bladder, turns at the level of the uterine isthmus and forms the vesicouterine pouch (excavatio vesicouterine). Encompassing the uterus from behind, the peritoneum comes down the cervix, covers the posterior vaginal fornix and turns on the rectum, forming the rectouterine pouch (excavatio retrouterinae, Douglas pouch). Laterally the rectouterine pouch is limited by the rectouterine folds (plical rectouterinae) of the peritoneum which stretch to the lateral surface of the rectum and are the uterine fixating apparatus. The fascicles of the smooth muscles (mm. rectouterini) pass in these folds. From the both sides of the uterus the peritoneum forms the folds, the right and left broad ligaments of the uterus located in the frontal plane. This ligament forms the mesosalpinx relating to the Fallopian tube, and relating to the ovary it forms the mesovarium and relating to the uterus — mesometrium. Part of the broad ligament of the uterus fixating its cervix is called the transversal (cardial) ligament of the uterus. The anterior layer of the large ligament of the uterus covers the round ligament of the uterus (lig. teres uteri) which stretches from the corner of the uterus, passes via the deep inguinal ring, comes up to the pubic symphysis and fixates on the mons pubis to the tub. pubicum.
The blood supply to the uterus includes the uterine, ovarian arteries and the arteries of the round ligament of the uterus. The uterine arteries run from internal iliac artery (a. iliaca interna s. a. hypogastrica) the ovarian — from the aorta, and they enter the broad ligament of the uterus via the ligament which supports the ovary. The uterine artery stretches along the uterine rib; on the level of the orificium internum uteri it divides into two branches - the ascending and descending branch, which in turn give off branches to the broad and round ligament, Fallopian tubes, ovary and superior portion of the vagina. At about 1-2 cm from the uterus the uterine artery crosses with the ureter and branches off again (ramus uretericum).
The ureters cross with the ovarian vessels, located above them on the level lin. innominata. They go retroperitoneally to the broad ligament of the uterus attaching to its posterior layer then discending entering into the parametrium behind the uterine arteries crossing it transversally. Then the ureters almost close adjoins the anterior vaginal fornix and comes to the cervix in front of the the urinary bladder (from the right - 102 cm; from the left - 2-3 cm).

Lymph outflow from the uterus into the superficial inguinal nodes, external iliac, lateral sacral, paraaortal and paracaval lymph nodes.
The uterine innervation is provided mainly by sympathetic nervous system. Parasympathetic nervous system is represented by the branches of the middle inferior pelvic plexus and by the second, third and fourth pairs of the sacral nerves.
Clinical meaning. The uterus is one of the organs of the female reproductive function. The development or acquired defects (for example, Ashermann's syndrome) may be the reason for reproductive dysfunction. The endometrium is the most frequent localization of cancer in women. Benign tumoral processes, leiomyomae and adenomyosis, develop often in the myometrium.
The uterine appendages include the Fallopian tubes and ovaries.
The Fallopian tube (tuba uterina, s. tubae Fallopii) is a pair organ stretching from the uterus to the ovaries; it performs transportation of the ovocytes into the cavity of the uterus. It is approximately 10 cm long; its caliber differs from 0.5-10 mm to 5-8 mm in different portions. They differentiate the uterine portion of the tube - the narrowest portion, isthmus, ampule and infundibulum (the broadest portion.
The wall of the tube consists of three membranes, external (serous), middle (muscular) and internal (mucous). The serous membrane of the uterine ligament which forms the mesosalpinx. There is the subserous layer of connective tissue under serous membrane. It contains vessels and nerves. The muscles of the Fallopian tube consists of the internal circular and external longitudinal layers which supply its peristaltic contractions. The mucous membrane of the uterus forms longitudinal tubular folds and it is laid with monostratal columbar ciliated epithelium with goblet glands.
The infundibulum of the Fallopian tube is the broadest portion of the tube. There is an orifice opening into the peritonium with a caliber from 5 to 10 mm in it. There are a great number of the fimbriae of the tube around the opening. The largest fimbria is called the ovarian fimbria. These structures may form small fimbrial cysts, hydatids, which are mesonephral by origin. Such rudimentary formations as epoophoron and its longitudial duct (ductus Gartneri) and paraophoron start from mesonephros. Distention intraligamental and nearovarian cysts and malignant tumors can form these formations.
Innervation of the Fallopian tubes is provided by the branches of the pelvic and ovarian parasympathetic and sympathetic ligaments.
Clinical meaning. Tubal pregnancy, salpingitis (mainly of gonococcal and chlamydial etiology), perisalpingitis (often of streptococcal etiology) are the most often pathological process in the Fallopian tubes. Tubal deformity with formation of commissures because of infection may be the reason of unfertility. Primary tubal cancer is met very rarely.
Ovary (ovarium, oophoron) is the female sexual gland, a pair oval organ. Its sizes vary during reproductive period; it is 2.5 cm to 5 cm long; 1.5 to 3 cm broad and 0.6-1.5 cm thick. After menopause the ovarian sizes decrease significantly. The ovary is attached to the broad ligament of the uterus with the mesovarium. During the uterine corner it is connected by the proper ovarian ligament (lig. ovarii pro-prium), with the pelvic lateral wall by the suspensory ligament of the ovary (lig. suspensorium ovarii).

They distinguish two surfaces in the ovary, the internal surface facing to the abdominal cavity and the external surface facing to the pelvic wall; two ends, the uterine and pelvic; two margins, the convex free (margo liber) and mesovarian (margo mesovaricus). In the area of the mesoovarian margin the ovarian hili are located (hilium ovarii), the vessels and nerves enter the ovary via them.
On the ovarian section one can see the external layer, a cortical substance of the ovary and the internal layer, a medullar substance of the organ.
The external layer, laid with the germinal epithelium is called the tunica albuginea. The ovarian stroma is located under it (stroma ovarii), it is the area of follicles, of different stages of development. The free surface of the ovary is laid with monostratal cubical epithelium.
The follicles increase as they maturate. Tertiary (dominant, Graafian) follicle reaches the ovarian surface, ruptures, pushes out the ovum via stigma and then it luteinizes throught the retention of the follicular liquid and forms the corpus luteum, the function of which is the progestins secretion and the organism preparation for the impregnated ovum implantation. The hormones secretion (mainly progestins, oestrogens and androgens) is effected by endocrinocytes (luteinocytes and tecal endocrinocytes) of the corpus luteum. In the course of time the corpus luteum hyalizes and forms the white body (corpus albicans).
A newborn girl has 100,000 of primary (primordial) follicles, but only 400 of them can maturate. But in every cycle during the reproductive period several follicles can start to develop and produce hormones; later they will be subject to atresia and absorbed.
Clinical meaning. The function of the ovaries is the production of hormones and development of the ovum for fertilization and pregnancy. This function is depended upon many factors. Benign and malignant tumors often develop in the ovary. The ovarian torsion may result in its necrosis. Infectious damages of the ovary may develop in climacterium.
Physiologic position of the female internal genitalia is kept by fixating, supporting and suspending apparatuses. Supporting the uterus and uterine appendages in physiologic position, they afford their mobility in considerable limits, what is important for normal development of pregnancy and course of labour.
The suspending apparatus of the uterus and uterine appendages consists of the following pair ligaments connecting these organs with one another and with the pelvic walls:
1) the broad ligament of the uterus (lig. latum uteri), which leads to the lateral walls of the pelvis and there turns into parietal peritoneum, form the mesometrium, mesosalpinx, and mesovarium;
2) the suspensory ligament of the ovary (lig. suspensorium ovari) is an external portion of the large ligament of the uterus which runs from the ovary to the lateral pelvic wall. The ovarian vessels pass in it (a. et v. ovarica);
3) the proper ovarian ligament (lig. ovarii proprium) runs in the depth of the posterior layer of the large lig. of the uterus and goes from the uterine margin of the ovary to the uterus. The ligament contains smooth muscular fibers, it is crossed with the ovarian branches of the uterine arteries and veins;

4) the round ligament of the uterus (lig. teres uteri).
Subperitoneally there is the layer of the fatty tissue, parametrium, between the layers of the broad ligament of the uterus as well as around the cervix and the vagina.
The fixating apparatus of the uterus contains the following ligaments formed from smooth muscular and connective tissue:
1) the mesometrium (mesometrium, the transversal, main lig. of the uterus) encompasses the cervix from the isthmus; the fibers turn into the pelvic fascia which fixates the uterus to the pelvic fundus;
2) the pubovesical muscle (m. pubovesicalis) runs in the depth of the rectouterine folds (plica rectoute-rina) which go posterior surface of the cervix to the lateral surface of the rectum.
3) the sacrouterine ligament which runs from the posterior surface of the cervix below the internal orifice, to the side by the rectum and comes together with the pelvic fascia at the internal surface of the sacrum.
During pregnancy the suspending and fixating folds stretch and give the uterus mobility, necessary for it to grow.
The supporting apparatus of the female internal genitaliais formed by a group of muscles and fascia which constitute the perineum or the pelvic fundus. The muscles of the pelvic fundus are divided into three layers – external, middle, internal.
The internal layer consists of these muscles:
1) two m. ishiocavernosus – paired muscles which run from the sciatic tuberculum to the clitoris;
2) two m. bulbospongiosus, which run along both sides of the entrance to the vagina;
3) external muscle, the sphincter of the anus, which makes a ring around the anus;
4) Superficial transversal muscles which run from the internal surface of the ishiac tuberculum to the fascia center of the perineum where it joins the same muscle on the other side.
The middle layer of the perineum (urogenital diaphragm) is formed by two layers of the perineum 1) m. sphincter urethrae, 2) m. transverses perinea profundus.
The internal layer (the pelvic diaphragm) is formed by m. levator ani. It in turn, is formed by three pairs: pubococcygeal muscles, puborectal muscle, iliococcygeal muscle.
As a result of trauma to the perineum during labor, the pelvic diaphragm is damaged. During reconstructive operations on the perineum, the muscles should be reconstructed carefully because it is these muscles that keep the female internal genitalia in the physiological position.

Physiological changes of female genitals in different age periods.
Neuroendocrine regulation of reproductive system function.
The Female Reproductive Cycle
Towards the end of puberty, girls begin to release eggs as part of a monthly period called the female reproductive cycle, or menstrual cycle (menstrual referring to "monthly"). Approximately every 28 days, during ovulation, an ovary sends a tiny egg into one of the fallopian tubes. Unless the egg is fertilized by a sperm while in the fallopian in the two to three days following ovulation, the egg dries up and leaves

the body about two weeks later through the vagina. This process is called menstruation. Blood and tissues from the inner lining of the uterus (the endometrium) combine to form the menstrual flow, which generally lasts from four to seven days. The first period is called menarche. During menstruation arteries that supply the lining of the uterus constrict and capillaries weaken. Blood spilling from the damaged vessels detaches layers of the lining, not all at once but in random patches. Endometrium mucus and blood descending from the uterus, through the liquid creates the menstruation flow.

Menstrual cycle

The reproductive cycle can be divided into an ovarian cycle and a uterine cycle (compare ovarian histology and uterine histology in the diagram on the right). During the uterine cycle, the endometrial lining of the uterus builds up under the influence of increasing levels of estrogen (labeled as estradiol in the image). Follicles develop, and within a few days one matures into an ovum, or egg. The ovary then releases this egg, at the time of ovulation. After ovulation the uterine lining enters a secretory phase, or the ovarian cycle, in preparation for implantation, under the influence of progesterone. Progesterone is produced by the corpus luteum (the follicle after ovulation) and enriches the uterus with a thick lining of blood vessels and capillaries so that it can sustain the growing fetus. If fertilization and implantation occur, the embryo produces Human Chorionic Gonadotropin (HCG), which maintains the corpus luteum and causes it to continue producing progesterone until the placenta can take over production of progesterone. Hence, progesterone is "pro gestational" and maintains the uterine lining during all of pregnancy. If fertilization and implantation do not occur the corpus luteum degenerates into a corpus albicans, and progesterone levels fall. This fall in progesterone levels cause the endometrium lining to break down and sluff off through the vagina. This is called menstruation, which marks the low point for estrogen activity and is the starting point of a new cycle.

Common usage refers to menstruation and menses as a period. This bleeding serves as a sign that a woman has not become pregnant. However, this cannot be taken as certainty, as sometimes there is some bleeding in early pregnancy. During the reproductive years, failure to menstruate may provide the first indication to a woman that she may have become pregnant.

Menstruation forms a normal part of a natural cyclic process occurring in healthy women between puberty and the end of the reproductive years. The onset of menstruation, known as menarche, occurs at an average age of 12, but is normal anywhere between 8 and 16. Factors such as heredity, diet, and overall health can accelerate or delay the onset of menarche.

Signs of ovulation. The female body produces outward signs that can be easily recognized at the time of ovulation. The two main signs are thinning of the cervical mucus and a slight change in body temperature. Thinning of the Cervical Mucus After menstruation and right before ovulation, a woman will experience an increase of cervical mucus. At first, it will be thick and yellowish in color and will not be very plentiful. Leading up to ovulation, it will become thinner and clearer. On or around the day of ovulation, the cervical mucus will be very thin, clear and stretchy. It can be

compared to the consistency of egg whites. This appearance is known as ‘spinnbarkeit'.

Temperature Change

A woman can also tell the time of ovulation by taking her basal body temperature daily. This is a temperature taken with a very sensitive thermometer first thing in the morning before the woman gets out of bed. The temperature is then tracked to show changes. In the uterine cycle, a normal temperature will be around 97.0 – 98.0. The day of ovulation the temperature spikes down, usually into the 96.0 – 97.0 range and then the next morning it will spike up to normal of around 98.6 and stay in that range until menstruation begins.

Both of these methods are used for conception and contraception. They are more efficient in conception due to the fact that sperm can live for two to three days inside of the fallopian tubes. A woman could be off by a couple of days in her calculations and still become pregnant.

Menopause is the physiological cessation of menstrual cycles associated with advancing age. Menopause is sometimes referred to as "the change of life" or climacteric. Menopause occurs as the ovaries stop producing estrogen, causing the reproductive system to gradually shut down. As the body adapts to the changing levels of natural hormones, vasomotor symptoms such as hot flashes and palpitations, psychological symptoms such as increased depression, anxiety, irritability, mood swings and lack of concentration, and atrophic symptoms such as vaginal dryness and urgency of urination appear. Together with these symptoms, the woman may also have increasingly scanty and erratic menstrual periods.

Technically, menopause refers to the cessation of menses; the gradual process through which this occurs, which typically takes a year but may last as little as six months or more than five years, is known as climacteric. A natural or physiological menopause is that which occurs as a part of a woman's normal aging process. However, menopause can be surgically induced by such procedures as hysterectomy. The average onset of menopause is 50.5 years, but some women enter menopause at a younger age, especially if they have suffered from cancer or another serious illness and undergone chemotherapy. Premature menopause is defined as menopause occurring before the age of 40, and occurs in 1% of women. Other causes of premature menopause include autoimmune disorders, thyroid disease, and diabetes mellitus.

Premature menopause is diagnosed by measuring the levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH). The levels of these hormones will be higher if menopause has occurred. Rates of premature menopause have been found to be significantly higher in both fraternal and identical twins; approximately 5% of twins reach menopause before the age of 40. The reasons for this are not completely understood. Post-menopausal women are at increased risk of osteoporosis.

Perimenopause refers to the time preceding menopause, during which the production of hormones such as estrogen and progesterone diminish and become more irregular. During this period fertility diminishes. Menopause is arbitrarily defined as a minimum of twelve months without menstruation. Perimenopause can begin as early

as age 35, although it usually begins much later. It can last for a few months or for several years. The duration of perimenopause cannot be predicted in advance.
The neuroendocrine system is composed of the hypothalamus and pituitary gland and is under the influence of neurotransmitters and neuropeptides that regulate hypothalamic releasing and hypothalamic release inhibiting hormones secreted into the blood vessels that connect the hypothalamus and pituitary gland. The release of these hypothalamic hormones influences the secretion of anterior pituitary hormones that subsequently regulate tissue function. The hypothalamus and pituitary gland have the capacity to detect humoral secretions (hormones secreted) from target tissues and adjust hormone production to maintain an optimal internal "milieu" appropriate for normal function. It is well-established that the neuroendocrine system has a critical role in integrating biological responses and influencing: (1) cellular protein synthesis and general metabolism through the release of growth hormone and thyroid-stimulating hormone (TSH), respectively, (2) reproductive function through the release of luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, and oxytocin, and (3) plasma electrolytes and responses to stress through regulation of the hormones vasopressin (antidiuretic hormone, or ADH) and adrenocorticotropin (ACTH). In addition, the hypothalamus also has an important role in the integration of parasympathetic and sympathetic nervous system activity, and can thereby influence a wide variety of functions, including heart rate, blood pressure, vascular responses, and glucose metabolism. The hypothalamus has been implicated in the regulation of biological rhythms by its interactions with hypothalamic nuclei. More recently, the regulation of fat metabolism and food intake has been shown to be regulated through the hypothalamus by its response to the protein, leptin, and its synthesis of neuropeptide Y. It should be noted that the classification of hormones and their primary function presented here is an overly simplistic view of the neuroendocrine system, since critical interactions occur among these hormones that contribute to the coordinated regulation of cellular and tissue function.
Three classic examples of age-associated changes in neuroendocrine regulation, and the resulting consequences for tissue function, help emphasize the importance of this system in the development of the aging phenotype. First, with increasing age there is a decline in growth-hormone secretion that results in a decrease in insulin-like growth factor-1 (IGF-1) production in the liver and other tissues. The loss of these anabolic hormones contributes to the general decline in cellular protein synthesis, skeletal muscle mass, immune function, and cognitive ability in rodents, nonhuman primates, and humans. The decrease in growth-hormone release from the pituitary gland results from impaired release of growth-hormone-releasing hormone and increased release of somatostatin (an inhibitor of growth hormone) from hypothalamic neurons. Second, decreased secretion of gonadotropin-releasing hormone (GnRH) from hypothalamic neurons results in a decline in luteinizing hormone. This is the primary factor in the loss of reproductive cycles in the female rodent, and, in conjunction with the loss of ovarian follicles, contributes to the decline in estrogen levels in women. These latter changes result in atrophy of secondary reproductive tissues and have been implicated in the post-menopausal loss of bone and cognitive function.

Decreased GnRH secretion in the male also contributes to a decrease in LH and androgen levels and to the corresponding loss of skeletal muscle mass and reproductive function. Finally, increased secretion of ACTH and the adrenal hormone, cortisol, in response to stress have been reported to contribute to atrophy and/or loss of neurons, as well as age-related decline in cognitive function. These latter findings have contributed to the hypothesis that increased levels of glucocorticoids contribute to brain aging

Although other mechanisms are possible, the alterations in the secretion of hypothalamic hormones with age have been traced to deficiencies in the secretion of brain neurotransmitters. For example, the activity of dopamine and norepinephrine decreases with age, and both acute and chronic procedures used to increase levels of these neurotransmitters in aged animals have been shown to restore some aspects of neuroendocrine function. Studies have shown an increase in growth hormone release and a restoration of some aspects of reproductive function in older animals in response to the L-Dopa, dopamine and norepinephrine precursor. These findings have led investigators to conclude that a decline in neurotransmitter activity is a contributing factor in the neuroendocrine decline that accompanies aging. Nevertheless, the possibility that interactions with other hypothalamic peptides, the loss of neurons, or intracellular changes within hypothalamic neurons contribute to the loss of function cannot be excluded. In fact, the inability of hypothalamic neurons to compensate for the age-related alterations in circulating levels of hormones supports the concept that the normal feedback mechanisms that occur within the hypothalamus are impaired in aged animals. Whether these altered feedback mechanisms are related to the deficiencies in neurotransmitters or result from other aberrations within the aging neuroendocrine system remain to be established. Nevertheless, deficits in the regulation of these critical hormonal systems contribute to deterioration of tissue function and undoubtedly are an important factor in age-related disease and disability.

Menstrual function regulation.

The activity of reproductive system is to reproduct, preservation of the species, that causes its ultimate reliability. Reproductive system as well as other systems of the organism is functional and is based on hierarchical principle consisting of 5 central and peripheral levels of regulation interacting by the direct and retroaction connections model.

I level of regulation – suprahypotalamic cerebral structures. The classical example of the cyclic process in female organism in the maturity period is ovario-menstrual cycle.

II level of reproductive system regulation - hypophysiothropic zone of mediodorsal pituitary gland. A pulsing secretion of hypotalamic releasing-hormones(HRH) in the neurons of arcuate nucleus in cirochal regimen occurs. The neurosecretion.(HRH) is transmitted to the portal system through the axons of nervous cells and is transported to the frontal part of pituitary gland with blood

III level of regulation – adenohypophysis (the frontal part of the pituitary gland). The secretion of honadotropic hormones is performed in adenohypophysis; lutenizing

one(LH), folliclestimulating(FSH), prolactine(Pl), thyreotrophic hormon or thyreotropin(TH or TTH), somatotophic hormon or somatotropin(STH), adenocorticotrophic hormon or cortycotropin(ACTH), melanocytstimulating hormon of melanotropin(MSH).
IV level of reproductive system regulation is ovarian. Cyclic changes in ovaries are called ovarian cycle. In the first phase primordial follicle develops, at the second one Luteal follocle developes from the cells of Graafian follicle(the follicle where the process of ovulation occured) endocrine gland – yellow body is formed.
Organs and target organs (geitals, mammary glands, hair follicles, skin, fat tissues) belong to to the V level of regulation. The cells of these organs have receptors to sex hormones (estradiol, progesterone, testosterone). The ammount of steroid hormones in blood changes depending on the phase of menstrual cycle. The molecule of hormon is taken by the cytoplasmic receptor and compex hormon-receptor is trasported to the cell nucleus. In the nucleus the complex is attached to the chromatin, which regulates the processes of transcription. Cyclic adenosinamonophosphat (cAMP) and prostogladines also belong to the V level of reproductive system which act as intracellular regulators. On the V level of regulation cyclic the changes are mostly marked in endometrium (uterine cycle), the process of its preparation to menstruation or implantation is on.
The menstrual cycle regulation starts in pituitary gland. The neurons of hypothalamus integrate exogenous and endogenous information that comes from different departments of central nervous system (CNS). Such factors as starvation, stress may influence menstrual cycle through hypothalamus. Hypothalamus takes part in the regulation of sexual behavior, body temperature, consumption of food and water. Honadotrophin-releasing hormon is a mediator for hypophysis , it is secreted in pulsating rhythm and is transported to the adenohypophysis through hypothalamo-hypophysial portal vessels. Slight amplitudal and pulsatile drift during the discharge of HT-RH show changes in hypothalamic and hypophysial functions, causing new menstrual cycle. Pulsatile secretion of honadotrophin-releasing hormone by hypothalamus not inhibited by a considerable amount of estrogen and progsterone, contributes to increase of honapotrophine discharge by hypothalamus(PSH and LH in a lesser degree). PSH stimulates folliculogenesis in ovaries. Developing follicles discharge estrogen. By the 5-7th day of menstrual cycle one follicle starts to dominateand intensively to discharge estradiol, other follicles are involuted (athresia). Thos is a follicular phase, it responds to the proliferative phase of menstrual cycle.
The secretion of GH-PH is under the influence of neuromediators: dopamine and norepinephrine, B-endorphine, the amount of which depends on the action of estrogen and progesterone. That is why the drugs which affect the metabolism of neurotransmitters can influence the secretion of HT-RH and prolactine(Prl) by hypothalamus (methyldopa, reserpine, antidepressants).
Menstrual dysfunction may result from intense production of estrogen and progesterone by the functional cyst of ovaries (for example in yellow bode persistanse etc.).

The age of menarche (the first menstruation in life) normally ranges from 10 to 16 years old and on average is 12-13. Stabilization of ovulatory menstrual cycle is characterized by regular, cyclic prognosed menstruations with 24-35 day intervals, the bleeding duration is 3-8 days and general loss of blood about 30-8-ml.

Main methods of examination in gynecology: visual examination of external genitals, speculum examination, bimanual examination.

Main methods of examination in gynecology includes:
1) Examination of the external genitalia;
2) The study with the help of a speculum;
3) Vaginal examination;
4) two-handed (bimanual) study;
5) rectal and vaginal-rectal research;

1.1. On examination of the external genitalia take into account the degree and nature of hair (on the female or male pattern), the development of small and large labia, the state of the perineum, the presence of pathological processes (varices, ulceration, discharge, warts), the state of the external opening of the urethra, excretory ducts Bartholin glands, the hymen.
1.2. When vaginal study determined the state of the pelvic floor, palpate the area location Bartholin glands, urethra overtures. Determine the condition of the vagina, the vaginal part of the cervix, cervical mobility, identifying features of vaginal vault.
1.3. When vaginal study determined the state of the pelvic floor, palpate the area location Bartholin glands, urethra overtures. Determine the condition of the vagina, the vaginal part of the cervix, cervical mobility, identifying features of vaginal vault.
1.4. Handed vagina to bryushnostenochnoe isledovanie is the primary method of detection of diseases of the uterus, appendages, uterine ligament apparatus, pelvic peritoneum and fiber. First, examine the uterus (the position, size, shape, consistency, mobility, tenderness), on each side of the uterus - the appendages (if physiology can not be palpated), ligaments, pathological processes in the pelvic peritoneum.
1.5. Rectal and rectal vlagalischno- study produced for girls in the case of atresia or stenosis of the vagina, in addition to the two-handed at the genitals tumors (cancer w / uterus), with vospolitelnyh diseases, presence of secretions from the rectum. During the study, determine the presence of pathological processes in the rectum to feel w / the uterus, pelvic fat, sacro-uterine ligaments. When recto-bryushnostenochnom method of investigating body of the uterus and appendages. In the case of patoprotsesov in the walls of the vagina, intestine and surrounding tissue produce rectovaginal study to determine the tumor infiltrates and others.

Instrumental examination methods: probing of uterus, curettage of uterine cavity, biopsy, puncture of abdominal cavity through posterior vaginal fornix.

1. Probing the uterus produce under aseptic and antiseptic. It allows you to specify the length of the uterus, cervical canal patency, stenosis and atresia, partitions, fibroids. Probing is used not only for diagnostic purposes, but before endometrial curettage, abortion. Sounding the uterus is contraindicated in acute and subacute

vospolitelnyh diseases vagina, w / uterus and appendages, when establishing or suspected pregnancy.
2. Fractional diagnostic curettage of the mucous membrane of the cervix and uterine body channel produce to determine the state of the mucous membrane in benign and malignant processes (hyperplasia, precancerous lesions, cancer). First, scrape the mucous membrane of the cervical canal, then the body of the uterus. Scrapings are collected separately in receptacles with formalin, labeled and sent for histological examination.
3. Biopsy produced in pathological processes, suspected malignancy localized in the area of the cervix, vagina, external genitals and the uterus. Material taken by excision with a scalpel on the border of healthy tissue and the altered area.
4. Aspiration biopsy is performed by Brown syringe in inpatient and outpatient. Get the endometrium of the uterus different departments (bottom corners). From the resulting material make smears on a slide.
5. Aspiration curettage performed a special hollow curette, connected to a vacuum pump. Aspiration preparation method has advantages over the endometrial mucosa of the uterus due to scraping traumatization of tissue at the possibility of re-use and during the menstrual cycle.
6. Puncture of the abdominal cavity through the posterior vaginal fornix is carried out in order to generate content for the differential diagnosis of ectopic pregnancy and inflammation of the uterus, at break cystic abscess formation or breakout. If you suspect an ovarian cancer - to detect in the ascites fluid of atypical cells. A puncture is made in the center of the posterior fornix of the vagina to a depth of 2 cm. Thick needle.

Endoscopic examination methods: colposcopy, hysteroscopy, laparoscopy.
1. Colposcopy - method of diagnosis of pathological states vlagalichnoy of the cervix, cervix, vagina and external genitalia. With the help of a colposcope inspect the mucous membranes of the vagina and the cervix, vulva, produce biopsy. To evaluate the pathological focus in the dynamics method is used repeatedly, it is harmless. It uses simple (Review), enhanced, color (hromokolposkopiya) and fluorescent colposcopy. Simple colposcopy estimated, determine the shape and size of the vaginal w / uterus, the external os, color and relief of the mucosa, the transition zone of a flat columnar epithelium, vascular pattern. Extended colposcopy based on the use of pharmacological agents to detect changes in the tissue level of the cell and its components. 3% solution of acetic acid, 0.5% solution of salicylic acid causes swelling of the epithelium of the cervix treatment reduced blood flow, thereby detecting patoizmeneny clear. Lugol solution (Sheeler test) reveals tumor and premalignant sites consisting of depleted glycogen cells: cells containing a sufficient amount of glycogen (normal), painted in a dark brown color, with a deficit of glycogen cells (pathological) remain pale. The sample allows purposefully to explore certain areas and carry out biopsy. Colposcopy can detect background processes w / uterus (ectopic, conversion zone, erosion, polyps), precancerous lesions (dysplasia), malignant diseases, to produce differential. diagnosis. When colposcopy fluorescent

histochemical study used. Kolpomikroskopiya - vivo study of morphological study of the vaginal part of the cervix.
2. Hysteroscopy - the uterine cavity examination method using an optical instrument (hysteroscope) inserted into the uterus through the cervical canal. Highly informative method for the diagnosis of intrauterine pathology (as compared to MSG, US), allowing to make surgery. Environment for distention is 30-70% solution of dextran, 5-10% solution of dextrose and carbon dioxide. According to its purpose diagnostic hysteroscopy is divided into (establishment of intrauterine pathology), surgical (operational) and control (evaluation of the effectiveness of therapy).
Indications for hysteroscopy: DMK, infertility, developmental abnormalities, intrauterine adhesions, submucous uterine fibroids, uterine cavity examination and cervical canal after the abortion and haemorrhage after caesarean section, plastic surgery on the uterus, endometrial hyperplasia, polyps, foreign bodies in the uterus (IUD), aiming biopsy, monitoring the effectiveness of therapy, endometriosis, uterine tuberculosis.
Contraindications: acute infectious processes, pregnancy, heavy uterine bleeding, suspected cancer of the cervix and uterine body, severe somatic diseases.
hysteroscopy technique involves the preparation and examination of the patient for surgery, the choice of anesthesia method (intravenous anesthesia), carrying out the procedure. Complications: exacerbation of chronic inflammatory disease, uterine perforation, uterine rupture, bleeding, air embolism, vascular overload, thermal lesions of the pelvic organs, anaphylactic shock.
3. Laparoscopy -osmotr abdominal organs and pelvis using the laparoscope through the anterior abdominal wall, in the background pneumoperitoneum used oxygen, nitrous oxide or carbon dioxide. Laparoscopy involves the steps of: abdominal wall puncture needle, the introduction of gas through it to create a pneumoperitoneum, trocar laparoscope, viewing pelvic and abdominal surgery, removal of the endoscope and gas removal. Laparoscopy is done for diagnostic and surgical purposes is carried out in a planned or emergency basis. Indications for routine diagnostic laparoscopy, infertility, dif. diagnosis of tumors of internal genital malformations of internal genital organs, sklerokistoz ovarian ectopic, pregnancy. The indications for emergency laparoscopy: a suspicion of uterine perforation, cyst capsule rupture, piosalpinks, ovarian torsion leg tumor, ovarian rupture, pipe miscarriage, dif. Diagnosis of acute adnexitis, ectopic pregnancy and appendicitis.
Contraindications: decompensation of somatic diseases, extensive adhesions, acute infectious diseases. Complications: emphysema, damage of the abdominal cavity needle or trocar, vascular injury, complications of anesthesia.

Ultrasonic examination methods in gynecology.
US - the leading method of research in gynecology: screening, non-invasive, harmless, highly informative, relatively simple, affordable. With this method it is possible to visualize and evaluate the condition of the pelvic organs: the bladder, uterus, ovaries, vagina proximal department rektosigmoidalny thick intestine, muscle, and blood vessels of a small basin. Ultrasound does not require special preparation of the patient, only filling bladder bubble.

Contraindications method does not. The main indication for ultrasound examination in gynecology is a refinement of data on the size of the uterus and ovaries. Ultrasound reveals diseases of the uterus, ovaries, fallopian tubes, abnormal development of the internal reproductive organs, tubo-ovarian formation, ectopic pregnancy, the IUD, and their complications. For the detection of endometrial pathology, dynamic assessment of maturing follicles preferred transvaginal sonography. This method is highly informative studies (assessment of the pelvic organs in severe adhesions, accurate topical diagnosis of education, the use in women with metabolic disorders, flatulence, abdominal pain), there is no need for filling the bladder. Preferred is in urgent gynecology. Ultrasound is now complemented by Doppler studies for blood flow in the arteries and veins of the internal reproductive organs to diagnose tumors, genesis of infertility, other endocrine diseases.

Radiological examination methods: MRI, CT, MSG.

With the development of ultrasound and endoscopic methods of X-ray diagnostics was used less frequently.

The following types of x-ray studies are used in gynecology: hysterosalpingography, pnevmopelviografiya, contrast peritoneografiya, vaginografiya, phlebography, arteriography and lymphography pelvis and retroperitoneal space, X-rays of the skull, the adrenal glands.

1. Hysterosalpingography (MSG) - a radiological method isledovanija, allowing to determine the status of the uterus and fallopian tubes. MSG is carried out on 8-12 day of the menstrual cycle, for the diagnosis of CIN MSG - 23-24 days. A study carried out with X-ray contrasting solutions: liposoluble (lipildol), water-soluble (urografin) and vodnoviskoznymi (polyvidone, medopak). Preparation of the patient includes: a survey to assess the general condition and exclusion of inflammation, intestinal cleansing and emptying of the bladder, the introduction of antispasmodics for 30 minutes. prior to the study. Perform 2 shots: 1 after the uterine cavity filling contrast agent, 2- after the new administration of contrast.

Indications: uterine infertility options, suspected tuberculosis, internal genitalia anomalies, monitor the effectiveness of plastic surgery on the uterus and tubes, tumors and uterine polyps, endometrial hyperplasia, suspected malignancy. Contra-indications: feverish conditions of different etiology, acute and subacute inflammatory processes, pregnancy, DMK, decompensated somatic diseases. Complications: 1) early (reflux vascular, lymphatic reflux pipe rupture, perforation of the uterus, and allergic reactions); 2) recent (acute inflammation).

2. Pnevmopelviografiya - the second most common method of x-ray studies in gynecology, it is the introduction of air into the abdominal cavity and allows to define the contours of the uterus and ovaries. As contrast medium is used, nitrous oxide, carbon dioxide and oxygen. Indications: the need to obtain information about the external contours of the internal genitalia in individuals not sexually active, if pronounced scar or atrophic vaginal changes, adhesive process in the pelvis; ovarian tumors, and primary amenorrhea psevdogermofroditizm, dif.diagnostika uterus and appendages, genital tumors, uterine podbryushinnye nodes. Contraindications: acute and subacute vospolitelnye disease decompensation somatic pathology women.

Complications: gas embolism, subcutaneous tissue emphysema, pneumothorax, intra-abdominal bleeding and a hematoma of the anterior abdominal wall.
3. X-ray examination of the skull is used for the diagnosis of neuroendocrine diseases. X-ray study of the shape, size, sella circuits are used for the diagnosis of pituitary tumors.
4. Computed tomography (CT) is based on the change in the intensity of x-ray radiation as it passes through different densities of tissue. Computed tomography provides a complete picture of the organ or the pathological focus, which explores quantitative information on the layer thickness and the nature of the lesion. With the help of computer tomography can obtain reflected longitudinal study area, rekonstruktirovat slice and get it in any plane. Currently, imaging region sella reveals small tumors located intrasellyarno and non-deformable wall of the sella. Radiation exposure during CT is lower than with other methods of x-ray studies.

Methods of functional diagnostics of ovarian condition.
To evaluate the functional state of the ovaries using cytological examination of vaginal smears, cervical mucus study of channel, measurement of basal body temperature.
1. Cytology vaginal smears based on the definition in these specific kinds of vaginal epithelium. Surface flat layered neorogovevayuschii vaginal epithelium - gormonozavisim is the target organ. When 2-phase ovulatory menstrual cycles in vaginal smear are found in different proportions superficial and ediate epithelial cells. In the assessment of the proportion of the surface stratum and the total number of superficial cells based calculation kariopiknoticheskogo index (CPI). In the follicular phase of the normal menstrual cycle is 25-30% of the CPI, during ovulation - 60-70%, in the phase of development of the corpus luteum - 25-30%. With this! the method can determine the woman's hormonal background (estrogen deficiency, hyperandrogenism), hormone treatment to control, diagnose, and to justify hormone miscarriage in early pregnancy, to make selection OK DMK treatment, the premenstrual syndrome.
2. "Pupil Symptom" - the amount of mucous secretion in the cervical canal, reflects the production of estrogen by the ovaries. Based on the expansion of the external opening of c / channel and it appears in a transparent glassy mucus. Determined during the inspection w / uterus in the mirror, the external os resembles a zrachek. Symptom "pupil" depending on its degree is estimated at points (1.3): negative (-), weak positive (+), positive (++), rezkopolozhitelny (+++). The greatest amount of mucus is observed at the time of ovulation, the smallest - before menstruation. No symptoms of the pupil indicates a weak estrogenic effects, long rezkovyrazhenny symptom - of hyperestrogenism. The test gives an indication of the form of the MQM, premenstrual syndrome and other endocrine disorders. The test is not characteristic pathological changes of the cervix.
3. Symptom "fern leaf" is based on the crystallization of cervical mucus deposited on a glass slide. The crystallization of the mucus occurs in the presence of mucin by the action of estrogen, a symptom can be set between 7-20 day of a normal menstrual cycle, reaching its highest development at the time of ovulation, there is no before

menstruation. Estimated in points (1-3): negative (-), weak positive (+), positive (++), zerkopolozhitelny (+++).
4. Symptom tension of cervical mucus - a simple and informative method of determining the body's estrogen saturation. Kortsangom take cervical mucus and by diluting the jaws define its elasticity (stretchability). Pulling mucus more than 6-8 cm. Evidence of sufficient estrogen saturation.
5. The basal temperature test is based on hyperthermal effects of progesterone on the thermoregulatory center. Change the basal body temperature (rectal morning) allows you to establish the presence, severity and duration of the progesterone phase. In the normal menstrual cycle, the basal temperature rises by 0.4-0.8 in the progesterone phase. Measuring basal body temperature is made within 2-3 months. With this test it is possible to judge about ovulation and anovulation, the shortening of the luteal phase, nedortatochnosti corpus luteum function.

Laboratory diagnostics: oncocytology, bacterioscopy, bacteriology, ELISA, PCR, pathomorphological examination.

Along with common laboratory tests: general blood and urine tests, blood chemistry, blood test group and Rh factor, coagulation (determination of blood clotting), there are specific tests in gynecology, which include: analysis on TORCH-complex (identification of woman's blood antibodies to rubella, herpes, toxoplasma, cytomegalovirus and chlamydia), a hormonal screening, microbiological diagnostic methods, enzyme-linked immunosorbent blood analysis, polymerase chain reaction, a pregnancy test, a blood test for the presence of tumor markers.

Identification hormone concentration in the blood (hormonal screening)

This diagnostic method allows to identify endocrine pathology. Hormonal screening can reliably assess the nature of the basal secretion of steroid and tropic hormones in a woman's blood. In this study the level of hormone activity in the different phases of the menstrual cycle (study performed prolactin, gonadotropins (LH, FSH), testosterone, estradiol, cortisol, thyroid hormones (T3, T4), and many others).

Microbiological diagnostic methods

Microbiological examination reveals bacteria in the genital tract of women and thus set the etiological cause of the disease or condition. This method allows the diagnosis of infectious and inflammatory diseases of the female reproductive organs.
Microbiological method bacteriological diagnosis has been rendered crops: a smear of vagina, uterine cervix, urine or blood are plated on a nutrient medium and grown colonies of microorganisms which are then examined under a microscope. This method also allows to identify the sensitivity of a pathogen to antibiotics and correctly, given the sensitivity of a microorganism to pick antimicrobial agent to treat the disease. Microbiological testing is the cheapest method of diagnosis, however, does not always provide accurate, objective results.

ELISA, or enzyme-linked immunosorbent blood test

Immunoassay blood is more accurate (compared with a microbiological method) research method. This method of diagnosis other than to identify the etiology of the pathogen can also identify the stage of pathological process (acute, subacute, chronic, reinfection, subsidence of the pathological process, the traumas of the inflammation process).

Polymerase chain reaction - PCR (or method of DNA-diagnostics)
PCR is the most accurate method of reliable diagnosis of infectious and inflammatory diseases (but also the most expensive). In carrying out this reaction from biological material (vaginal swab, urine, blood) being withdrawn microorganism DNA fragment. PCR has a high degree of diagnostic accuracy and detect a wide range of pathogens (protozoa, bacteria, fungi, viruses).

Pregnancy test
It is used for the diagnosis of pregnancy. It is based on the identification in the urine of pregnant women chorionic gonadotropin, which is produced by the embryo in the first weeks of pregnancy.

A blood test for the presence of tumor markers
This assay is non-specific, is appointed in cases of suspicion of the presence of ovarian cysts, malignant neoplasms of the female reproductive organs, therefore, it requires repeated repetition and additional diagnostic techniques.

Additional examination methods in gynecology.
Morphological (histologic) methods.
Biopsies obtained from the cervix, uterus, ovaries necessarily subject to histological examination. Material prepared by various gynecological operations.
1. Biopsy - vivo excision of a small piece of tissue for microscopic examination. Produce in pathological processes, suspected malignancy with in the area of the cervix, vagina, external genitals and take material by excision with a scalpel on the border of healthy tissue and the altered portion is collected in containers filled with formalin, labeled and sent for histological examination.
2. Split (fractional) diagnostic curettage of the mucous membrane of the cervix and uterine body channel produce to ascertain the condition of the mucous membrane in benign and malignant processes (cyclic changes, hyperplasia, precancerous changes, endometrial cancer, cervix). The operation is performed in a hospital under obezbolivaniem.Vnachale scrape mucous membrane of the cervical canal, then the body of the uterus. Scrapings are collected separately in receptacles with formalin, labeled and sent for histological examination.
3. Aspiration Biopsy is performed by Brown syringe in inpatient and outpatient. Get the endometrium of the uterus different departments (bottom corners). From the resulting material make smears on a slide. This method allows us to determine the state of the mucous membrane in benign and malignant processes (cyclic changes, hyperplasia, precancerous changes, endometrial cancer), to monitor the effectiveness of hormonal treatment.

4. Aspiration curettage performed a special hollow curette, connected to a vacuum pump. Aspiration method for the preparation of the endometrium has advantages over the uterine curettage due to less traumatization of the tissues and the ability to re-use during the menstrual tsikla.Danny method allows us to determine the state of the mucous membrane in benign and malignant processes (cyclic changes, hyperplasia, precancerous changes, endometrial cancer) monitor the effectiveness of hormonal treatment.
5. Puncture the abdominal cavity through the posterior vaginal fornix is carried out in order to generate content for the differential diagnosis of ectopic pregnancy and inflammation of the uterus, at break cystic abscess formation or breakout. If you suspect an ovarian cancer -for detection of atypical kletok.Prokol ascites produced in the center of the posterior fornix of the vagina to a depth of 2 cm. Thick needle.
6. Mandatory histological examination of organs and tissues removed during surgery (uterus, appendages, fibroids, part of the resected ovarian ovarian cyst shell, oil seal, etc.) In order to verify the diagnosis, determine the extent of surgical treatment, the appointment of pathogenetic therapy.

5. Materials of student activization during lecture:

Questions:

1. Specifics of anamnesis gathering in gynecological patients?
2. What special examination methods in gynecology do you know?
3. What is colposcopy and how is it performed?
4. What laboratory methods in gynecology do you know?
5. What endoscopic methods in gynecology do you know?
6. What concerns the external genital organs of a woman?
7. What internal genital organs of a woman do you know?

6. Self-control questions on the topic:

1. Clinical anatomy and physiology of female reproductive organs.
2. Special gynaecological anamnesis.
3. General and special methods of examination of gynaecological patients.
4. Basic special methods of examination in Gynaecology: examination of external genital organs, speculum examination, bimanual examination.
5. Methods for evaluation of ovarian function.
6. Laboratory tests in Gynaecology: bacterioscopic/bacteriological test of the female genital tract microflora, PAP smear, PCR, ELISA.
7. Instrumental methods of examination in Gynaecology: uterine sounding, dilation and uterine curettage, biopsy, culdocentesis.
8. Endoscopic methods in Gynaecology: colposcopy, hysteroscopy, laparoscopy.
9. Ultrasound methods in Gynaecology: transvaginal and transabdominal ultrasound examination. Radiation methods in gynaecology: MRI, CT, MSG.

LECTURE №2. TOPIC: Benign tumors of female genital organs. Precancerous diseases of female genital organs

1. Relevance of the topic:

Importance and background of the topic. The problem of benign and precancerous diseases of female genital organs is significant all over the world. Mainly it is due to the high frequency of these diseases, their potential to malignization, disabling of reproductive function and invalidization of patients. Majority of gynecological operations including hysterectomy have indications of benign and precancerous process of female genitals. It creates not only social but also economical burden of these diseases.

2. Goals:

- educational: to introduce students to main benign and precancerous diseases of female genital organs, to teach methods of diagnostics and differential diagnostics, prevention and treatment of these pathologies.
- formative: formation of contemporary professional thinking in students; stressing of the role of different and local scientific schools in research of this problem; learning of deontological and ethical aspects. Learn to make plan of examination, including necessary invasive methods. Carry out modern methods of examination which allow to find and include all specifics that enable correct diagnostics and determination of further management.

3. Basic concepts:

1. The concept of ovarian cysts and tumours.
2. Benign ovarian tumours: epithelial tumours, sex cord-stromal tumours, lipid cell tumors, germ cell tumors.
3. Ovarian tumour-like formations.
4. Benign tumours of the uterus.
5. Clinical features, diagnosis and management of complications, prevention.
6. Precancerous conditions of the cervix: classification.
7. Endometrial hyperplasia: aetiology, pathogenesis, classification, modern diagnostic methods, modern management.
8. Prevention of precancerous diseases of the female reproductive organs.

4. Content of the lecture material:

Ovarian tumors

Summary

The ovaries consist of different kinds of tissue (epithelial, germ cells, and sex cord tissue), which may give rise to benign or malignant tumors. Symptoms depend on the type of tissue affected and range from local abdominal discomfort to endocrinological phenomena caused by hormone-producing tumors.

Ovarian cysts

Ovarian cysts are fluid-filled sacs within the ovary. The most common types are functional follicular cysts, corpus luteum cysts, and theca lutein cysts, which all develop as part of the menstrual cycle and are usually harmless and resolve on their own. Nonfunctional cysts include chocolate cysts, which are related to endometriosis, dermoid cysts, cystadenomas, and malignant cysts (a type of ovarian cancer). All types can be diagnosed via pelvic ultrasound. While ovarian cysts are usually asymptomatic, complications due to rupture of a cyst can occur and may require treatment. Moreover, individuals with ovarian cysts are at increased risk of ovarian torsion, which requires surgical correction.

Definition

Ovarian cysts are fluid-filled sacs within the ovary.

Types

- Functional cysts: result from a disruption in the development of follicles or the corpus luteum; often resolve on their own
- Follicular cyst of the ovary (most common ovarian mass in young women)
- Develops when a Graafian follicle does not rupture and release the egg (ovulation) but continues to grow; eventually becomes a large cyst (7 cm) lined with granulosa cells
- Associated with hyperestrogenism and endometrial hyperplasia
- Corpus luteum cyst
- Enlargement and buildup of fluid in the corpus luteum after failed regression following the release of an ovum
- Produces progesterone, which may delay menses
- Associated with progesterone-only contraceptive pills and ovulation-inducing medication
- Theca lutein cysts
- Multiple cysts that typically develop bilaterally
- Result from exaggerated stimulation of the theca interna cells of the ovarian follicles due to excessive amounts of circulating gonadotropins such as β-hCG
- Strongly associated with gestational trophoblastic disease and multiple gestations
- Usually resolve once ß-hCG levels have normalized
- Nonfunctional cysts
- Chocolate cysts: related to endometriosis
- Dermoid cysts
- Cystadenoma (serous or mucinous)

- Malignant cysts (form of ovarian cancer): higher risk in postmenopausal women

Clinical features

- Most often asymptomatic unless complications occur
- In some cases, there may be signs of the underlying cause (e.g., menorrhagia in endometriosis or hirsutism, acne, and infertility in PCOS).

Diagnosis

- Pelvic ultrasound
- Smooth lining on all sides
- Single (e.g., follicular cyst of the ovary, corpus luteum cyst) or multiple (e.g., polycystic ovary syndrome, multilocular theca lutein cysts)
- Hypoechoic to anechoic
- Fluid level

Complications

- Ovarian torsion
- Ruptured ovarian cyst

Treatment

- In most patients with functional cysts, watchful waiting is recommended, as cysts often regress spontaneously.
- NSAIDs in the case of painful cysts
- Surgery in the case of complications, large cysts, or persistent cysts that are painful
- Treatment of underlying conditions such as PCOS, endometriosis, or ovarian cancer

Ruptured ovarian cyst

- Etiology: physical activity
- Clinical features
- Sudden-onset unilateral lower abdominal pain
- In the case of a very large cyst: Fluid and blood loss may cause acute abdomen and shock.
- Diagnosis: Pelvic ultrasound shows free fluid, most commonly in the pouch of Douglas (rectouterine pouch).
- Treatment
- Hemodynamically stable patients can be observed and given analgesics.

- Hemodynamically unstable patients require laparoscopy to control hemorrhaging.

Ovarian torsion

- Etiology
- Physical activity
- The primary risk factor is ovarian enlargement (e.g., due to cysts, ovarian stimulation, pregnancy, tumors).
- Clinical features
- Sudden-onset unilateral lower abdominal pain
- Nausea and vomiting
- Diagnosis: Pelvic ultrasound with Doppler velocimetry shows enlarged, edematous ovaries with decreased blood flow.
- Treatment: Detorsion via laparoscopic surgery is recommended as soon as possible to restore blood flow.

Ovarian tumors

Epidemiology

- Lifetime prevalence of malignant ovarian cancer: 1–2%
- Peak incidence: 60–70 years
- Genetic predisposition may play a role in familial incidence and in younger patients (< 30 years) developing tumors.
- Epithelial ovarian carcinomas account for 70% of all ovarian malignancies.

Etiology

Risk factors

- Genetic predisposition
- BRCA1/BRCA2 mutation
- HNPCC syndrome
- Peutz-Jeghers syndrome
- Hormonal imbalance and menstrual cycle
- Elevated number of lifetime ovulations (the contraceptive pill appears to have a protective effect)
- Infertility/low number of pregnancies
- Early menarche and late menopause
- PCOS

Overview of ovarian tumors

Epithelial Tumors

- 65–75% of all ovarian tumors; ~ 70% of all malignant ovarian tumors
- Cystadenoma/cystadenocarcinoma
- Serous
- Most common ovarian tumor
- Serous cystadenocarcinoma is the most aggressive ovarian cancer
- Frequently bilateral (65% of cases)
- Histology:
- Tumor cells with papillary structures and small cytoplasm
- Psammoma bodies are a typical feature.
- Mucinous
- Second most common ovarian tumor
- Up to 75% of cases are benign.
- Endometrioid carcinoma
- Frequently associated with endometrial cancer and endometriosis
- Commonly malignant
- Clear cell carcinoma

Epithelial ovarian tumors may be benign, malignant, or borderline!

Germ cell tumors

- 15–25% of all ovarian tumors
- Teratoma
- Mature
- Dermoid cysts: most common of all germ cell tumors (90% of cases)
- Malignant transformation in 2% of cases
- Can theoretically contain any type of tissue, e.g., hair, teeth, and sebaceous glands, but mostly include parts of ectodermal origin
- Differentiated, mostly benign tumor
- Struma ovarii: teratoma with endodermal differentiation into thyroid tissue
- Very rare: malignant transformation into a thyroid carcinoma
- May produce thyroxine and cause hyperthyroidism symptoms
- Differentiated, mostly benign tumor
- Immature:
- Rare, undifferentiated
- May contain tissue of embryonic/fetal period
- High risk of malignancy

- Dysgerminoma: most common malignant ovarian tumor in young women (20–30 years); female histological equivalent to the male seminoma
- Yolk sac tumor of the ovary: often malignant; occurs mainly in childhood and adolescence
- Non-gestational choriocarcinoma: rare and extremely malignant; normally accompanied by beta hCG production

Sex cord-stromal tumors of the ovary

- 5–10% of all ovarian tumors
- Estrogen producing: granulosa cell tumor and theca cell tumor
- ~ 75% of cases affect postmenopausal women.
- Androgen producing: Sertoli-Leydig cell tumor
- Occurs very rarely; ~ 20% malignant transformation
- Production of androgens → virilization
- Primarily affects women aged 30–40 years
- Ovarian fibroma
- Benign, although may cause Meigs' syndrome

Metastasis

- 10–15% of all ovarian tumors
- Primary tumors are most often found in the gastrointestinal tract, breast, or endometrial cancer
- Krukenberg tumor: bilateral ovarian metastases from an undifferentiated gastric carcinoma (mucin-secreting, signet ring cell carcinoma)

Clinical features

General symptoms

- In most cases, there are no early symptoms.
- In advanced stages, the size and growth of the tumor can lead to:
- Abdominal pain and ascites
- Cancer cachexia
- Possible disruption of menstrual cycle
- Dyspnea due to malignant pleural effusion
- Abdominal or pelvic mass
- Complication: tumor can cause ovarian torsion→ tissue infarction → surgical emergency

The first symptom is often increasing abdominal girth (clothes no longer fit at the waist)!

Specific symptoms

- Granulosa cell tumor: Granulosa cells express aromatase (estrogen synthesis occurs in 25% of tumors).
- Menstrual irregularities such as postmenopausal bleeding and metrorrhagia
- Increased risk of endometrial cancer
- Precocious puberty
- Sertoli-Leydig cell tumor: can produce either estrogen or testosterone
- Virilization due to tumor-induced testosterone production:
- Symptoms in females: Amenorrhea, hirsutism, decreased fertility, and acne
- Symptoms in males: Precocious puberty in boys and gynecomastia in men, feminization in males if estrogen is produced
- Yolk sac tumor, dysgerminoma: rapid growth, acute onset of symptoms (pelvic mass and pain)
- Struma ovarii: symptoms of hyperthyroidism
- Pseudomyxoma peritonei
- Bursting of a mucinous cystadenoma/carcinoma may spread tumor cells throughout the peritoneum.
- Mucinous cells cause gelatinous ascites and intra-abdominal adhesions.
- May require several surgical treatments and, in the long term, usually leads to cachexia and death.
- Meigs syndrome
- Ascites and pleural effusion in association with an ovarian tumor (e.g., ovarian fibroma)
- In 90% of cases, the ovarian tumor is unilateral.
- The cause is unknown.
- Surgical removal of the tumor leads to a complete resolution of symptoms.

Diagnostics

- Hypercalcemia due to paraneoplastic synthesis of PTHrP
- Tumor markers
- Epithelial ovarian tumor: CA-125
- Yolk sack tumor: alpha-fetoprotein
- Non-gestational choriocarcinoma: beta hCG
- Granulosa cell tumor: inhibin B

- Imaging: Transvaginal ultrasound is the gold standard, but abdominal or rectal ultrasound may also be conducted.
- Histology:
- Granulosa cell tumor: Call-Exner bodies (granulosa cells arranged in clusters surrounding a central cavity with eosinophilic secretions, resembling primordial follicles)
- Sertoli-Leydig cell tumor: contain Reinke crystals
- Ovarian fibroma: clusters of spindle-shaped cells (fibroblasts)

Fine needle aspiration cytology is absolutely contraindicated in ovarian tumors because it increases the risk of spreading tumor cells to the peritoneum!
Differential diagnoses

- Ovarian cysts
- Endometriosis
- Tubo-ovarian abscess
- Ectopic pregnancy
- Pelvic inflammatory disease

Ultrasound workup of ovarian masses		
	Benign	Malignant
Internal structure	Uniform, thin walls	Irregularly thickened septa
Margins	Smooth	Indistinct borders; papillary projections
Echogenicity	Anechoic	Hypoechoic, anechoic, and hyperechoic components
Content	Cystic	Cystic or solid components
Vascularization	Unremarkable	Possible central vascularization
Pouch of Douglas	Unremarkable	Possible free fluid (ascites)

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Treatment

- Surgery
- Frozen section and histology positive for carcinoma: radical surgical staging
- Removal of the greater omentum
- Lymphadenectomy
- Hysterectomy with bilateral salpingo-oophorectomy
- Appendectomy if involvement is suspected during surgery

- Biopsy from all noticeable locations/adhesions
- Frozen section negative for carcinoma: tumor resection, but no surgical staging
- Chemotherapy
- Indicated for all patients as adjuvant therapy
- First-line therapy: carboplatin polychemotherapy and antimitotics (e.g., paclitaxel)
- Radiation therapy: rarely used due to the intraperitoneal location and low radiosensitivity of the tumor

Malignant germ cell tumors respond particularly well to polychemotherapy because they are highly aggressive!

Benign tumors of uterus

Fibroid is a commonest benign tumor of the uterus and also the commonest benign solid tumor in female. Histologically this tumor is composed of smooth muscle and fibrous connective tissue, so named as uterine leiomyoma, myoma or fibromyoma. Incidence – at least 20 per cent of women at the age of 30 have got fibroid in their wombs. The incidence of symptomatic fibroid in hospital outpatient is about 3 per cent.

Etiology still remains unclear. The prevailing hypothesis is that, it arises from the neoplastic single smooth muscle cell of myometrium. The possible causes are: chromosomal abnormality (rearrangements, deletions), role of polypeptide growth factors, a positive family history is often present. The growth is predominantly oestrogen-dependent tumour.

Increased risk factors include nuliparity, obesity, hyperoestogenic state, black woman, reduced risk multiparity, smoking.

Uterine fibroids are the most common pelvic tumor, occurring in about 70% of women by age 45. However, many fibroids are small and asymptomatic. About 25% of white and 50% of black women eventually develop symptomatic fibroids. Fibroids are more common among women who have a high body mass index. Potentially protective factors include parturition and cigarette smoking.

Most fibroids in the uterus are

- Subserosal
- Intramural
- Submucosal

Occasionally, fibroids occur in the broad ligaments (intraligamentous), fallopian tubes, or cervix.

Some fibroids are pedunculated. Most fibroids are multiple, and each develops from a single smooth muscle cell, making them monoclonal in origin. Because they respond to estrogen, fibroids tend to enlarge during the reproductive years and decrease in size after menopause.
Fibroids may outgrow their blood supply and degenerate. Degeneration is described as hyaline, myxomatous, calcific, cystic, fatty, red (usually only during pregnancy), or necrotic. Although patients are often concerned about cancer in fibroids, sarcomatous change occurs in < 1% of patients.

Symptoms and Signs

Fibroids can cause abnormal uterine bleeding (eg, menorrhagia, menometrorrhagia).

If fibroids grow and degenerate or if pedunculated fibroids twist, severe acute or chronic pressure or pain can result. Urinary symptoms (eg, urinary frequency or urgency) can result from bladder compression, and intestinal symptoms (eg, constipation) can result from intestinal compression.

Fibroids may increase risk of infertility. During pregnancy, they may cause recurrent spontaneous abortion, premature contractions, or abnormal fetal presentation or make cesarean delivery necessary. Fibroids may also cause postpartum hemorrhage.

Diagnosis

- Imaging (ultrasonography, saline infusion sonography, or MRI)

The diagnosis of uterine fibroids is likely if bimanual pelvic examination detects an enlarged, mobile, irregular uterus that is palpable. Confirmation requires imaging, which is usually indicated if

- Fibroids are a new finding.
- They have increased in size.
- They are causing symptoms.
- They need to be differentiated from other abnormalities (eg, ovarian masses).

When imaging is indicated, ultrasonography (usually transvaginal) or saline infusion sonography (sonohysterography) is typically done. In saline infusion sonography, saline is instilled into the uterus, enabling the sonographer to more specifically locate the fibroid in the uterus.

If ultrasonography, including saline infusion sonography (if done), is inconclusive, MRI, the most accurate imaging test, is usually done.

Treatment

- Sometimes gonadotropin-releasing hormone (GnRH) agonists (analogs) or other drugs for temporary relief of minor symptoms

- Myomectomy (to preserve fertility) or hysterectomy for symptomatic fibroids

Asymptomatic fibroids do not require treatment. Patients should be reevaluated periodically (eg, every 6 to 12 months).

For symptomatic fibroids, medical options, including suppression of ovarian hormones to stop the bleeding, are suboptimal and limited. However, clinicians should consider first trying medical treatment before doing surgery. GnRH agonists can be given before surgery to shrink fibroid tissues; these drugs often stop menses and allow blood counts to increase. In perimenopausal women, expectant management can usually be tried because symptoms may resolve as fibroids decrease in size after menopause.

Drugs for fibroids

Several drugs are used to relieve symptoms, reduce fibroid growth, or both:

- GnRH agonists

- Exogenous progestins

- Antiprogestins

- Selective estrogen receptor modulators (SERMs)
- Danazol

- Nonsteroidal anti-inflammatory drugs (NSAIDs)

- Tranexamic acid

GnRH agonists are often the drugs of choice. They can reduce fibroid size and bleeding. They may be given as follows:

- IM or subcutaneously (eg, leuprolide 3.75 mg IM every month, goserelin 3.6 mg subcutaneously every 28 days)

- As a subdermal pellet

- As nasal spray (eg, nafarelin)

GnRH agonists can decrease estrogen production. They are most helpful when given preoperatively to reduce fibroid and uterine volume, making surgery technically more feasible and reducing blood loss during surgery. In general, these drugs should not be used in the long term because rebound growth to pretreatment size within 6 months is common and bone demineralization may occur. To prevent bone demineralization when these drugs are used long term, clinicians should give patients supplemental estrogen (add-back therapy), such as a low-dose estrogen-progestin combination.

Exogenous progestins can partially suppress estrogen stimulation of uterine fibroid growth. Progestins can decrease uterine bleeding but may not shrink fibroids as much as GnRH agonists. Medroxyprogesterone acetate 5 to 10 mg orally once a day or megestrol acetate 40 mg orally once a day taken for 10 to 14 days each menstrual cycle can limit heavy bleeding, beginning after 1 or 2 treatment cycles. Alternatively, these drugs may be taken every day of the month (continuous therapy); this therapy often reduces bleeding and provides contraception.

Depot medroxyprogesterone acetate 150 mg IM every 3 months has effects similar to those of continuous oral therapy. Before IM therapy, oral progestins should be tried to determine whether patients can tolerate the adverse effects (eg, weight gain, depression, irregular bleeding). Progestin therapy causes fibroids to grow in some women. Alternatively, a levonorgestrel-releasing intrauterine device (IUD) may be used to reduce uterine bleeding.

For antiprogestins (eg, mifepristone), the dosage is 5 to 50 mg once a day for 3 to 6 months. This dose is lower than the 200-mg dose used for termination of pregnancy; thus, this dose must be mixed specially by a pharmacist and may not always be available.

SERMS (eg, raloxifene) may help reduce fibroid growth, but whether they can relieve symptoms as well as other drugs is unclear.

Danazol, an androgenic agonist, can suppress fibroid growth but has a high rate of adverse effects (eg, weight gain, acne, hirsutism, edema, hair loss, deepening of the voice, flushing, sweating, vaginal dryness) and is thus often less acceptable to patients.

NSAIDs can be used to treat pain but probably do not decrease bleeding.

Tranexamic acid (an antifibrinolytic drug) can reduce uterine bleeding by up to 40%. The dosage is 1300 mg every 8 hours for up to 5 days. Its role is evolving.

Surgery for fibroids

Surgery is usually reserved for women with any of the following:

- A rapidly enlarging pelvic mass
- Recurrent uterine bleeding refractory to drug therapy
- Severe or persistent pain or pressure (eg, that requires opioids for control or that is intolerable to the patient)
- A large uterus that has a mass effect in the abdomen, causing urinary or intestinal symptoms or compressing other organs and causing dysfunction (eg, hydronephrosis, urinary frequency, dyspareunia)
- Infertility (if pregnancy is desired)
- Recurrent spontaneous abortions (if pregnancy is desired)

Other factors favoring surgery are completion of childbearing and the patient's desire for definitive treatment.

Myomectomy is usually done laparoscopically or hysteroscopically (using an instrument with a wide-angle telescope and electrical wire loop for excision), with or without robotic techniques.
Hysterectomy can also be done laparoscopically, vaginally, or by laparotomy.
Most indications for myomectomy and hysterectomy are similar. Patient choice is important, but patients must be fully informed about anticipated difficulties and sequelae of myomectomy vs hysterectomy.

Morcellation is often done during myomectomy or hysterectomy. Morcellation involves cutting fibroids or endometrial tissue into small pieces so that the pieces can be removed through a smaller incision (eg, laparoscopically). Very rarely, women who have surgery for uterine fibroids have an unsuspected, undiagnosed sarcoma or other uterine cancer. If morcellation is done, malignant cells may be disseminated into the peritoneum. Patients should be informed that if morcellation is used, there is a very small risk of disseminating cancerous cells.
If women desire pregnancy or want to keep their uterus, myomectomy is used. In about 55% of women with infertility due to fibroids alone, myomectomy can restore fertility, resulting in pregnancy after about 15 months. However, hysterectomy is often necessary or preferred by the patient.

Factors that favor hysterectomy include

- It is more definitive treatment. After myomectomy, new fibroids may begin to grow again, and about 25% of women who have a myomectomy have a hysterectomy about 4 to 8 years later.
- Multiple myomectomy can be much more difficult to do than hysterectomy.
- Other, less invasive treatments have been ineffective.
- Patients have other abnormalities that make surgery more complicated (eg, extensive adhesions, endometriosis).
- Hysterectomy would decrease the risk of another disorder (eg, cervical intraepithelial neoplasia, endometrial hyperplasia, endometriosis, ovarian cancer in women with a BRCA mutation).

Newer procedures may relieve symptoms, but duration of symptom relief and efficacy of the procedures in restoring fertility have not been evaluated. Such procedures include

- High-intensity focused sonography
- Cryotherapy
- Radiofrequency ablation
- Magnetic resonance-guided focused ultrasound surgery

- Uterine artery embolization

Uterine artery embolization aims to cause infarction of fibroids throughout the uterus while preserving normal uterine tissue. After this procedure, women recover more quickly than after hysterectomy or myomectomy, but rates of complications and return visits tend to be higher. Treatment failure rates are 20 to 23%; in such cases, definitive treatment with hysterectomy is required.

Choice of treatment

Treatment of uterine fibroids should be individualized, but some factors can help with the decision:

- Asymptomatic fibroids: No treatment
- Postmenopausal women: Trial of expectant management (because symptoms tend to remit as fibroids decrease in size after menopause)
- Symptomatic fibroids, particularly if pregnancy is desired: Uterine artery embolization, another new technique (eg, high-intensity focused sonography), or myomectomy
- Severe symptoms when other treatments were ineffective, particularly if pregnancy is not desired: Hysterectomy, possibly preceded by drug therapy (eg, with GnRH agonists)

Medical treatment for fibroids and menorrhagia can be achieved by the use of mefenamic acid, tranexamic acid, non-steroidal antiinflammatory drugs (NSAIDs) or antifibrinolytic agents. All are useful medical treatment for menorrhagia, but are not effective in every patient. Commonly in fibroid menorrhagia, one or another of these agents may control bleeding but not the pain. If the pain persists, the patient becomes reluctant to persevere with medical treatment. The luteinizing hormone releasing hormone (LHRH) analogue (goserelin) is used to shrink fibroids and control bleeding by suppressing ovarian function, generally as pretreatment for myomectomy or prehysterectomy for very large fibroids. Decapeptyl 3mg injection on a monthly basis for 6 months or goserelin 3.6mg monthly by injection for the same duration are both acceptable. Patients administered either of these medications should be warned about the side-effect of premature chemical menopause and might need some adback treatment such as tibolone or low-dose estrogens to reduce the disturbing effect of estrogen withdrawal.

The introduction of interventional radiology (embolization) has presented a new option for the management of fibroids. In 2004 the National Institute of Clinical Excellence (NICE) provided guidance for clinicians to consider uterine artery embolization for the treatment of fibroids, although it is important to note that currently no concrete data exist pertaining to the effectiveness or outcome of embolization procedures for treatment of fibroid tumors, including the preservation of fertility potential, or the reduction of potential fecundity in patients who wish to conceive. The NICE document comments on indications, means of performance of

the procedure, ethics, safety and reduction in mean fibroid volume and blood loss. Counseling and consenting of such women is essential for those who consider this alternative procedure in the management of fibroid uterus. Uterine artery embolization should not be recommended without careful consideration in the treatment of symptomatic uterine fibroids, endometrial polyp or submucosal fibroid.

Women who have had the uterine cavity open during a prior myomectomy should be offered cesarean section when they become pregnant to minimize or avoid the risk of uterine rupture.

Endometrial polyps

Definition

Endometrial polyps are localized tumors within the mucosa of the uterine cavity. Endometrial polyps may be pediculate or sessile, and the size may vary from a few millimeters to 3-4 centimeters.

Occurrence

Endometrial polyps are common findings, both in women with and without gynaecological symptoms. The prevalence of endometrial polyps is reported to be 7.8 % - 34.9 % depending on the population studied.

Symptoms

Most endometrial polyps are asymptomatic. Symptomatic premenopausal women with endometrial polyps most commonly suffer from abnormal uterine bleeding (inter-menstrual bleedings/spotting and/or menorrhagia). Previous studies have reported that the prevalence of endometrial polyps is increased in infertile women, and the results of a randomized controlled trial indicates that removal of endometrial polyps may improve fertility in infertile women. Postmenopausal bleeding is the most common symptom of endometrial polyps in postmenopausal women.

Aetiology/pathogenesis

The aetiology and pathogenesis of endometrial polyps is unknown. Endometrial polyps are commonly benign. The occurrence of malignant endometrial polyp varies with the population studied, and are reported to be up to 13 %. Postmenopausal women with symptomatic polyps (postmenopausal bleeding) carry the highest risk of malignant endometrial polyp.

Risk factors

• Increasing age (the prevalence increases with age in the reproductive age, it is not known whether the prevalence increases with age in postmenopausal women).

• Obesity

• Use of Tamoxifen

• Hypertension

• A possible association between endometrial polyps and other benign gynaecological conditions such as fibroids, cervical polyps and endometriosis has been reported.

Examinations

Endometrial polyps are diagnosed by transvaginal ultrasound examination, by hysteroscopy or by histological examination. Installation of saline in the uterine cavity increase the sensibility of the examination and is recommended when the occurrence of endometrial polyp is suspected based on ultrasonic findings in women with abnormal uterine bleeding, infertile women and in postmenopausal women. Women with postmenopausal bleeding should be examined within 4 weeks because of a relatively high risk of endometrial cancer (5-10 %). (Please see the guideline entitled ”Postmenopausal bleeding”).

Differential diagnosis

Submucous fibroids.

Treatment

Indications of treatment of women with endometrial polyps are:

• Symptomatic endometrial polyp (most commonly abnormal uterine bleeding)

• Obesity

• Infertility

• In order to exclude malignancy

About 25 % of all endometrial polyps regress spontaneously. Small polyps (< 10 mm) are more likely to regress spontaneously compared to larger polyps. Consequently, small polyps in asymptomatic women without increased risk of malignancy may be left untreated. The risk of malignant endometrial polyp is highest in women with postmenopausal bleeding and in asymptomatic postmenopausal women with larger polyps and other known risk factors for endometrial cancer.

Endometrial polyps should be removed by transcervical resection (hysteroscopy). Treatment of endometrial polyps by curettage is not recommended as the risk of leaving the polyp behind is relatively large.

Transcervical resection of endometrial polyps is effective in women suffering from spotting/inter-menstrual bleedings and postmenopausal bleeding. In women with endometrial polyps and menorrhagia, a concomitant resection of the endometrium in perimenopausal women should be considered in order to reduce periodic blood loss and the risk of recurrent menorrhagia.

When atypical hyperplasia or malignancy is diagnosen by histopathological examination within an endometrial polyp, the woman should be treated in accordance with the guidelines for treatment of atypical endometrial hyperplasia or endometrial cancer, respectively.

Complications

Complications during transcervical resection of endometrial polyps is most frequently related to the dilatation of the cervix in nulliparous and postmenopausal women. Preoperative treatment with local oestradiol is recommended in order to reduce the risk of such complications in postmenopausal women.

Recommendations

• Instillation of saline into the uterine cavity (hydrosonography) is recommended when intrauterine pathology such as endometrial polys are suspected during transvaginal ultrasound examination in women with abnormal vaginal bleeding, infertile women and postmenopausal women.

• Endometrial polyps should be removed in symptomatic women, infertile women and women who have an increased risk of endometrial malignancy.

• Endometrial polyps should be removed by transcervical resection (hysteroscopy). Curettage is not recommended for removal of endometrial polyps.

• Preoperative treatment using local estradiol reduces the risk of complications during transcervical resection of endometrial polyps in postmenopausal women

Endometrial Hyperplasia and Neoplasia

Introduction

By definition, adenocarcinoma of the endometrium is an invasive disease, invading either the endometrial stroma or the underlying myometrium of extrauterine tissues. Most endometrial carcinomas maintain endometrioid differentiation; these also can contain areas of mucinous or squamous differentiation. Other nonendometrioid subtypes seen in routine practice include clear cell carcinoma, papillary serous carcinoma, and other rare variants. According to the US Gynecologic Oncology Group histologic grading system, grade 1, well-differentiated carcinoma, consists of a neoplasm with less than 5% of solid cancer; grade 2, moderately differentiated carcinoma, contains 6–50% solid cancer; and grade 3, poorly differentiated carcinoma, contains more than 50% of solid tumor.

Tumor grading is of greater independent prognostic value for endometrioid endometrial adenocarcinoma and its related types (i.e., endometrial, secretory, mucinous, squamous) than for papillary serous and clear cell adenocarcinomas. Papillary serous and clear cell cancers do not show the grade-dependent changes in aggressiveness seen with the endometrioid tumors; instead, as a group they are consistently aggressive. Division of endometrial adenocarcinomas into the clinicopathologic classes of endometrioid and nonendometrioid types is paralleled further by differences in epidemiologic risk factors and precursor lesions. Type I, or endometrioid, endometrial adenocarcinomas are more frequent in women taking exogenous estrogen and often are preceded by precursor lesions, which is the subject of this discussion.

It has traditionally been suggested that endometrioid endometrial adenocarcinoma is preceded by endometrial hyperplasia (EH). EH previously was considered a continuum of morphologic changes often beginning with simple glandular/stromal overgrowth (simple hyperplasia) and ending with complex, highly atypical histologic and cytologic proliferations, variously referred to as atypical adenomatous hyperplasia, dysplasia, or carcinoma in situ. The figure most often cited in the literature for progression of atypical adenomatous hyperplasia to carcinomas was 30% at 10 years.

This hyperplasia model, as defined by the World Health Organization (WHO), was developed primarily by pathologists as a morphologic classification into four classes of hyperplasia, composed of complex or simple architecture combined variously with presence or absence of cytologic atypia. These do not cleanly correspond to four distinctive biologic categories, nor are there comparable numbers of clinical interventions individually matched to each hyperplasia subtype. A contraction of the number of categories to three was suggested by merging all atypical hyperplasia (AH) groups into one diagnostic category (atypical endometrial hyperplasia) which contained the highest endometrial cancer risk. Pathologist scoring of presence or absence of cytologic atypia is notoriously unreliable, and has become a major limitation of this approach. In a Gynecologic Oncology Group study only 38% of community diagnosed atypical endometrial hyperplasia were confirmed as atypical hyperplasia upon central review by a panel of gynecologic pathologists. A further complication of this contraction of diagnostic groups by cytologic atypia alone is the de-emphasis on architectural features which remain of value in stratifying high from low risk subgroups.

New data that have emerged in the last decade have changed the underlying assumptions upon which endometrial precancer diagnosis is constructed. The assumption of gradual evolution of endometrial histologic patterns across hyperplastic groups is incorrect. Endocrine induced endometrial changes, such as those conferred by unopposed estrogens, do produce a field-wide effect that gradually changes the histologic pattern as a function of time and dose. This can be described as a dynamically changing histotype, which early on has the appearance of a disordered proliferative endometrium, and with subsequent remodeling assumes a variable gland density that we prefer to designate as the benign endometrial hyperplasia sequence. Bona fide premalignant lesions, however, are of an entirely different character. Precancerous lesions of the endometrium originate focally as a result of clonal outgrowth of genetically mutated glands which have a differing cytologic and architectural pattern relative to the background. Their morphology is discontinuous from that of the background endometrium itself, and can only be recognized through a combination of newly defined histologic features which define the entity of endometrial intraepithelial neoplasia (EIN). This is more completely described in the next section.

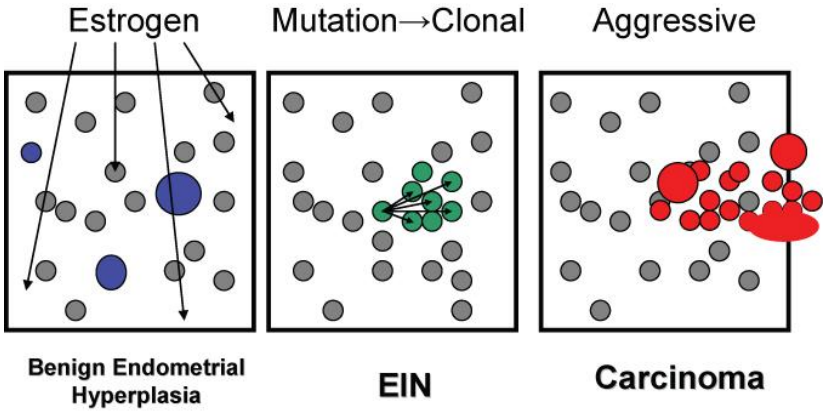
EIN is not synonymous with carcinoma but indicates a lesion that may regress, persist, or progress to invasion. Approximately one third of women diagnosed with

EIN will have a concurrent carcinoma diagnosed within the first year, and the long term cancer risk is 45 times increased beyond benign endometrial hyperplasia.

Morphologically, an altered relationship between glands and stroma distinguishes carcinoma from EIN. Even when present in the patient, myoinvasion is rarely evident in an endometrial curettage or biopsy, which rarely succeeds in sampling the underlying myometrium. For this reason, distinction between EIN and adenocarcinoma must commonly be performed in isolated endometrial samples devoid of myometrium. Within the endometrial compartment itself, examination of stromal quality and character in the region of a glandular lesion is not a reliable indicator of whether the stroma has been invaded. EIN lesions are made up of aggregates of individual glands which may have some branch points, but lack the complex folded sheets that produce a maze of interconnected lumens or villoglandular architecture in some carcinomas. The architectural pattern of the glands is an indicator of an altered interaction between glands and stroma. Functional changes which correspond to malignant behavior in vivo include loss of anchorage dependent growth. The histologic equivalent of this feature is growth of epithelial cells without a requirement for contact with a basement membrane. This is evident histologically by areas of solid epithelial growth without lumen formation or a cribriform pattern of multiple gland lumens within a single gland. The presence of myoinvasion, or any one of the above described patterns (solid, cribriform, villoglandular, maze-like), is diagnostic of adenocarcinoma.

Benign endometrial hyperplasia and endometrial intraepithelial lesion

A primary objective of endometrial diagnosis and therapy is distinction between primary hormonal abnormalities having a secondary endometrial effect (the benign endometrial hyperplasia sequence) and intrinsically abnormal neoplastic endometrial glands prone to malignant transformation (EIN). Unopposed estrogen creates field-wide changes in the endometrium, including cyst formation, randomly scattered tubal metaplasia, and remodeling of glands. In contrast, EIN is a clonal proliferation of abnormal endometrial glands which arises at a point in space and spreads peripherally, eventually involving the entire endometrial compartment in approximately a quarter of women at the time of initial EIN diagnosis. The diagnostic, nomenclature, and therapeutic distinctions between these processes are projected into the EIN diagnosis schema which is described below. This is intended to replace, rather than supplement, older classification using the 1994 WHO hyperplasia standards. The application of new diagnostic criteria which were not part of the 1994 WHO descriptions prevents an absolute concordance between the old and new systems. Below we review the expanded evidence base for revised criteria, and summarize diagnostic implemetation strategies.



Topography of hormonal and neoplastic endometrial disease. The diffuse field-wide endometrial effects of unopposed estrogens in benign endometrial hyperplasia are randomly scattered throughout the endometrial compartment and include cysts, and locally variable gland density. EIN lesions arise through local proliferation of genetically mutated glands which are characterized by an altered cytology and gland area exceeding stromal area. Adenocarcinoma has a similar clonal origin (often within a pre-existing EIN lesion) but with solid, cribriform, or maze-like architecture. With time, EIN and adenocarcinoma lesions can expand to occupy the entire endometrial compartment and thus no longer retain their earlier localizing character.

Endometrial precancers first were identified as premalignant lesions by virtue of their temporal and spatial association with cancer in large patient series. Of all women with atypical EH, 25% have an adenocarcinoma at hysterectomy. Although these strategies generally have been successful in defining broad classes of morphologic lesions most likely to be associated with cancer, clinical outcomes are highly insensitive in detection of precancers. A low precancer-to-cancer progression efficiency predicts that most premalignant lesions will never display a malignant end point. Further difficulty in standardizing diagnosis of endometrial precancers comes from poor reproducibility by pathologists of histopathologic criteria used for lesion classification. This situation has spurred development of novel diagnostic strategies applicable to lesional tissues of individual patients that are capable of accurately discriminating between biologic precancers and non-precancers. Even if such a laboratory approach were impractical for everyday use, it would constitute a powerful tool for critical evaluation and refinement of current histologic diagnostic practices.

Monoclonal growth and mutation of tumor-suppressor genes are measurable features of the premalignant phase of endometrial tumorigenesis that can be directly ascertained in paraffin-embedded tissues and correlated with histology on a case-by-case basis. The idea that endometrial precancers are monoclonal proliferative products of a single transformed cell is based on a multistep model of tumorigenesis in which progression is driven by sequentially acquired mutations manifest as altered morphology and increasing aggressiveness. Although initial stages may not show an invasive phenotype, it is anticipated that premalignant lesions have sufficient growth advantage relative to their source tissues that they expand monoclonally. This expansion has now been shown to be the case for putative

endometrial precancers using a variety of polymerase chain reaction-based molecular genetic methodologies applied to DNA isolated from targeted regions of paraffin sections: nonrandom X chromosome inactivation, clonal propagation of altered microsatellites in microsatellite-unstable tissues, and clonal propagation of acquired mutations of tumor-suppressor genes such as K-ras and PTEN. Monoclonal growth seems to be one of the seminal qualities of premalignant tissues at a variety of sites, including the oral mucosa, cervix, skin, stomach, and vulva.

Early stages of carcinogenesis are characterized by incremental growth advantages, which are necessarily small in relation to normal tissues and exquisitely sensitive to environmental modification. Hormonally mediated selection of latent transformed clones is one mechanism that might link genetic and endocrine events in genesis of this disease. This selection may occur through changes in precancer clone proliferation rates or remodeling of adjacent normal tissues. In the case of precancers confined to the functionalis, persistence is enhanced by absence of regular shedding (anovulation). Shedding is also a key part of progestin therapy for precancers because patients who have biopsies before a withdrawal bleed often have persistent lesions, albeit with an altered cytology. For this reason, repeat biopsy for confirmation of postprogestin precancer ablation is best accomplished after a withdrawal bleed to realize the full benefit of shedding and to avoid the confounding effects of progestins on histopathology interpretation.

Multiple marker systems (X inactivation, novel microsatellites) used together are approximately 80% sensitive in detection of monoclonal precancers from paraffin sections, a significant improvement over the 25% sensitivity of precancer detection realized when using a clinical standard of progression to carcinoma. In cases that do have an associated carcinoma, conservation of acquired genetic changes between matched premalignant and malignant tissues has provided a highly specific basis to conclude evolution from the former to the latter. Detailed lineage reconstruction, including hierarchical ordering of steps from precancer to cancer, has been accomplished in cases in which the repertoire of informative genetic markers is sufficiently rich. High cost and technical complexity place a molecular genetic laboratory standard of precancer diagnosis beyond the reach of a routine diagnostic setting.

areful histopathologic study of genotypically ascertained endometrial precancers explains prior problems in diagnosis and provides specific directions for improvement. Close correlations between histopathology and genotype are possible by isolating DNA from delineated regions of a paraffin section, which is also available as a serially sectioned stained slide. Epithelial differentiation of monoclonal precancers is usually endometrioid, but foci of squamous, mucinous, and tubal differentiation may be present. Changes in the hormonal environment, such as progesterone administration, may reduce the degree of cytologic atypia. Although most genetic precancers are diagnosed as atypical EH, poor reproducibility of this diagnosis compromises consistent management and raises the possibility that existing diagnostic criteria are inadequate. A particular void in precancer diagnosis has been

absence of informative architectural criteria. Computerized morphometric analysis of monoclonal endometrial precancers, using algorithms that previously were shown to predict relevant clinical outcomes of concurrent or future endometrial adenocarcinoma, has broken this stalemate. When cytologically altered endometrial glands become so crowded that they comprise more than half of the sectioned surface, they predict monoclonality with a sensitivity and specificity at least equal to the clinical judgment of experienced subspeciality gynecologic pathologists. The absolute appearance of EIN cytology varies greatly between individual examples, and not all have the appearance of rounded nuclei with prominent nucleoli that is the classic definition of atypia in this tissue. What is consistent, however, is that the crowded glands of an EIN lesion always have an altered cytology relative to the background endometrium in the same patient. A relative internal, rather than absolute fixed, standard for recognition of altered cytology is the common feature of premalignant endometrial disease and EIN. Size is an important consideration in evaluation of a localizing lesion, such as an emergent EIN. A threshold of clinical relevance is when the crowded focus (areas with gland area exceeding stromal area) of cytologicially altered glands reaches a maximum dimension greater than 1 mm within a single fragment. Smaller lesions are not necessarily associated with heightened cancer risk, and should not be diagnosed as EIN.

The term endometrial intraepithelial neoplasia accurately describes endometrial precancers because monoclonal origin from a single transformed cell is the pathognomonic feature of all neoplasms. The superb performance of computerized morphometric analysis in classifying all genetically and clinically defined precancers into one group reaffirms the feasibility of using routine hematoxylin and eosin–stained tissue sections to define a singular category of precancers.

Classification of endometrial disease based on lesion biology aspires to place all precancers into a single group (EIN) and in contrast with mutually exclusive entities corresponding to different management options. Introduction of refined precancer diagnostic criteria, such as volume percentage stroma (VPS) (that function of the sectioned tissue occupied by stroma), may improve histopathologic resolution between benign anovulatory (BEH) and premalignant (EIN) disease.

There are now several large clinical outcome studies outlining the clinical outcomes of patients diagnosed with EIN. There is a high rate of concurrent occult carcinoma in women diagnosed with EIN by biopsy. In a large GOG trial in which 153 women with EIN underwent hysterectomy, 36% (56) were found to have carcinoma. This is concordant with a retrospective pathology review study in which 39% of women diagnosed with EIN developed adenocarcinoma within the first year. In addition to this high rate of concurrent adenocarcinoma which is not evident from the initial EIN-containing biopsy, there is a 45-fold increased risk of developing carcinoma after the first year.

The relatively low risk of benign endometrial hyperplasia compared to EIN is evident in a study of over 600 women with various "endometrial hyperplasias" which were

stratified as EIN vs. benign (usually estrogen effect, or benign endometrial hyperplasia sequence). The results shown in the figure indicate a very high negative predictive value for absence of cancer outcomes in women with benign endometrial hyperplasia.

Clinical management of EIN is similar to that previously applied to a diagnosis of atypical endometrial hyperplasia. In the US this is usually hysterectomy. There is a clinical need for nonsurgical alternative therapies in women who wish to retain fertility, or are poor surgical candidates, but there is a paucity of clinical trail data on the subject. High dose progestin therapy can succeed in ablating some EIN lesions, but, because of the high concurrent cancer rate and unpredictable response, must be accompanied by careful clinical surveillance.

Risk indicators for endometrial cancer and precursors

Age ≥60 years
Obesity (with upper body fat pattern)*
Estrogen-only replacement therapy
Previous breast cancer
Tamoxifen therapy for breast cancer
Chronic liver disease
Infertility
Low parity
Chronic anovulation (polycystic ovarian disease, estrogen secreting ovarian stroma or tumors)

*With or without diabetes and hypertension.

Screening and diagnostics

In the case of endometrial carcinoma, the current consensus among experts in the field of periodic health examinations is not to recommend screening for endometrial cancer and its precursors because there is no scientific evidence to support such examinations in menopausal and postmenopausal women. The arguments against screening for endometrial carcinoma are as follows:

1. Although endometrial carcinoma is common, morbidity rates are low, comparatively less important in number than breast carcinoma, colon carcinoma, lung carcinoma, leukemia, lymphoma, brain carcinoma, pancreas carcinoma, and ovary carcinoma.

2. Based on the incidence of endometrial carcinoma in asymptomatic women, it would take about 1000 procedures to detect a single case of either a carcinoma or its precursor, atypical hyperplasia (AH).

3. The techniques available for diagnosing endometrial disease in asymptomatic women suffer from pitfalls in interpretation or instrumentation. One is the difficulty in interpreting relatively inexpensive cytologic material; the other is that

office biopsy aspiration techniques are relatively expensive and uncomfortable to painful, and tissue insufficient for diagnosis rates may be 25%.

4. No controlled randomized trials have been done to evaluate the effectiveness of screening in endometrial carcinoma. Even in high-risk menopausal women, screening would detect only 50% of all cases of endometrial carcinoma.

5. Most patients with disease eventually become symptomatic (i.e., presenting with abnormal uterine bleeding, yet have early clinical stage disease at the time of surgical diagnosis and treatment). This contention is supported by the excellent 5-year survival rates of patients with stage I endometrial carcinoma (i.e., 80–91%). The clinicopathologic and epidemiologic data suggest that about 80% of endometrial carcinomas are slow growing with a favorable course, and earlier treatment of asymptomatic carcinomas would be no more effective than treatment given when symptoms appear.

6. Elderly people are difficult to enroll into screening programs, and the dropout rate is relatively high. This is particularly true if painful techniques are used for endometrial evaluation.

7. The incidence of endometrial carcinoma and its precursors is low in women aged younger than 50 years and in women receiving combination-type HRT (estrogen/progestins).

Screening for endometrial carcinoma or its precursor, EIN, in asymptomatic, postmenopausal women is presently not recommended because of the low incidence of endometrial carcinoma in this group of women, estimated to be 1.7 cases per 1000 women per year, and the low prevalence, in the order of 1 per 1000 women.[36] In the Postmenopausal Estrogen/Progestin Intervention (PEPI) trial, no patients developed endometrial carcinoma while on daily estrogen-only replacement therapy, 0.625 mg, during a follow-up of 36 months versus 1% of women who developed endometrial carcinoma on placebo. The average age of women with EIN is 52 years, which is about 8 years earlier than the average age of 60 for endometrioid endometrial adenocarcinoma in the same patient population. The interval for progression from EIN to adenocarcinoma can be more directly estimated in individual patients who undergo protracted surveillance following an EIN diagnosis. Once patients with concurrent adenocarcinoma are excluded (defined as cancer found within the first year of follow-up), the average interval to diagnosis of adenocarcinoma is 4 years.

Who should be screened?

Women receiving unopposed estrogens need endometrial sampling once every 2 years (relative risk increases only after 2 years of estrogen use), particularly if endometrial hyperstimulation has been documented previously and has not been treated by short-term administration of progestins. Also, if the informed, high-risk individual requests an endometrial evaluation before or during HRT or at any time during her periodic health examinations, she should not be deprived of an office-

based investigative procedure to rule out endometrial pathology. An endometrial evaluation also should be performed in women at high risk for endometrial carcinoma, such as women with history of Lynch II syndrome.

The term diagnosis, as opposed to screening, refers to the application of a test to women presenting with symptoms (most commonly abnormal uterine spotting or bleeding) that presumably are related to endometrial carcinoma or its precursors. A study addressed the optimal evaluation strategy for patients with a first period of postmenopausal bleeding at various risks for endometrial carcinoma and AH. Among four options—office endometrial biopsy, dilation and curettage (D&C), hysterectomy, and observation alone (unless bleeding recurred)—office biopsy with the Vabra technique was the most cost-effective initial means, costing less than $41,000 US per year of life saved for patients with a 10% risk of having endometrial carcinoma or AH. For patients at 5% risk, the cost of endometrial biopsy increased, however, to $66,000 US per year of additional life saved for 60-year-old patients. Neither D&C nor hysterectomy was as cost-effective as office biopsy as an initial diagnostic evaluation procedure in patients with any risk for carcinoma/AH and abnormal uterine bleeding. Based on this decision-analytic model, the patient's age and the risk for endometrial carcinoma/AH seem to be important determinants for the use of a given endometrial evaluation technique.

Screening and diagnostic techniques

At present, seven methods exist for assessing the endometrium: cervical/vaginal cytology, endometrial cytology, endometrial biopsy, transvaginal ultrasonography (TVUS), magnetic resonance imaging, hysteroscopy, and D&C.

CERVICAL/VAGINAL CYTOLOGY

The main drawbacks of this method are that it detects mainly advanced endometrial carcinoma and has a high false-negative rate (80%) in postmenopausal, asymptomatic endometrial carcinoma patients. In one study, the odds ratio of endometrial carcinoma in symptomatic postmenopausal women was three times greater in the presence of histiocytes with phagocytosis of acute inflammatory and red blood cells compared with controls.[45] Histiocytes alone failed to predict either endometrial carcinoma or hyperplasia. Endometrial cells on cervical smears carried a fourfold odds ratio for EH. Vaginal cytology may detect recurrent cancer in women treated for endometrial carcinoma. Because the risk of recurrence of endometrial carcinoma (11–17%) and adjunct radiotherapy complications (70%) are greatest during the first 3 postoperative years and because most patients with recurrence are symptomatic and only few survive their recurrent disease, annual follow-up examination that includes vaginal cytology is sufficient.

It is generally accepted that the best yield is obtained with tests that directly sample the endometrial lining.[38] Numerous endometrial cell samplers are available commercially. Most of them obtain cellular samples either by brushing or by aspirating the superficial endometrial mucosa. All endometrial cell samplers have

been used under experimental conditions; the results in detection rates do not represent detection rates at large. Nevertheless, if cytologic atypia is the only feature to look for, endometrial cytology may be highly accurate in distinguishing carcinoma from normal or hyperplasia without cytologic atypia. In one study, endometrial cytology using plastic brushes yielded 79% sensitivity, 95.4% specificity, and 80.5% negative predictive value. If the smear contains normal endometrial cells, the patient may have either a normal or a hyperplastic uterine lining. Often, hyperplasia without cytologic atypia is indistinguishable from normal proliferative endometrium. Because this form of hyperplasia is not a carcinoma precursor, however, the patients with symptoms such as uterine bleeding can be treated conservatively. Most cytologic laboratories lack expertise for distinguishing cytologic atypia related to neoplasia from atypia associated with degeneration or repair. As a result, false-positive rates may be too high to justify the routine use of cytology for endometrial disease. Also, the screening of an endometrial smear is time-consuming, and interpretation is difficult because of the complexity of endometrial gland cell morphology. Many carcinoma mimics lead to false-positive results.

At present, histologic sampling is the best means to diagnose either asymptomatic or symptomatic (abnormal uterine bleeding) endometrial neoplasia. Plastic disposable or metal reusable devices using brushing, aspiration biopsy, suction curettage, or stroke biopsy have been used with similarly high diagnostic accuracy. The pitfalls of histologic methods lie in their relatively high cost and degree of discomfort. The latter leads to low compliance rates for repeat testing. Conventional curettage is much too costly yet not 100% foolproof as far as diagnostic accuracy is concerned. According to current experience including our own, the endometrial devices that seem to be the most cost-effective and are associated with the least discomfort for patients are the endometrial aspirators. In cases in which tissue is not obtained with one of the low-vacuum, suction-type aspirators, particularly in an elderly postmenopausal woman whose endometrium is more often than not atrophic, aspirators with a powerful vacuum suction force (e.g., Vabra aspirator; Tis-u-Trap; or sharp-bladed, four-stroke biopsy curette) provide diagnostic tissues.

Although some physicians had success in using endometrial brushes such as the Gynecyte (Looper Surgical, Inc; European version of Endocyte) for cytologic sampling of the endometrium, most prefer to sample the endometrium for histology. The instrument used most frequently is the endometrial Pipelle (Sepal, Boston, MA) and, when appropriate, the Kevorkian curette (EuroMed, Redmond, WA) for histologic sampling in asymptomatic and symptomatic women at risk for endometrial carcinoma and its precursors. In about 10% of postmenopausal women, the endometrial cavity is difficult or impossible to penetrate because of severe stenosis of the external/internal os or because of internal os spasm. In these cases, placing the patient on sequential cyclic therapy with conjugated estrogens (Premarin) (0.625 mg for 25 days) and medroxyprogesterone (Provera) (5 mg for 11–12 days) for 3 consecutive months often results in adequate dilation of the external/internal os to allow penetration of the endometrial cavity. Another alternative is to perform TVUS

and assess the thickness of the endometrium (see Transvaginal Ultrasonography below). Finally, traction of the uterus with the endocervical Emmett's tenaculum or a skin (Iris) hook is of considerable help for entering the endometrial cavity in the office. If an endometrial aspirator of the Pipelle type is used, it is important to move and rotate the cannula under negative action suction force within the endometrial cavity at least six times to sample the greatest surface area of the endometrium. In a comparison of the Pipelle versus the Vabra aspirator, the percentage of endometrial surface mucosa sampled with the Pipelle was 4.2% versus 42% with the Vabra aspirator and 60% with D&C under general anesthesia. The difference in percentages of area sampled is likely due to the comparatively greater suction force of the Vabra than the Pipelle device.

Sampling for histology: a step-by-step guide

1. Bimanually examine the uterus to determine its position.
2. Clean the cervix and vagina with acetic acid or other aseptic solution.
3. Insert an Emmett's tenaculum or iris hook into the outer one third of the endocervical canal and pull gently to obtain traction of the uterus.
4. Insert an endometrial aspirator into the endocervical canal. When the aspirator is at the lower uterine segment level, push and rotate it to facilitate entering the endometrial cavity.
5. When it is at the fundus, pull the plunger back rapidly and completely in the cannula to create a high negative pressure gradient.
6. Move the cannula back and forth 6–12 times in the endometrial cavity and rotate it at the same time.
7. Remove the cannula with the plunger pulled back (retain suction) from the endometrial cavity. Empty the material on a lens paper by pushing the plunger forward and place it in 10% buffered formalin tissue fixative.

If little or no tissue is obtained, the procedure can be repeated once. If still no tissue has been obtained, endometrial sampling can be performed using either the Vabra or other powerful aspirators or a metal curette. If still no tissue is obtained and the uterus is small, one can assume endometrial atrophy or fibrous pedunculated polyps are present. Transvaginal sonography or hysteroscopy, if the patient is symptomatic, may be performed.

In current practice, staging of endometrial carcinoma is surgical (hysterectomy, bilateral salpingo-oophorectomy, and pelvic node biopsy) and includes the histologic assessment of invasion of the endocervical mucosa (International Federation of Gynecology and Obstetrics [FIGO] stage IIA) versus the stroma (FIGO stage IIB) in the hysterectomy specimen. As a result, the preoperative evaluation of the endocervical canal is no longer necessary. The exception to the rule is a younger,

premenopausal woman in whom a fractional sampling of the uterus can determine whether the patient has an endocervical or an endometrial primary tumor.

TRANSVAGINAL ULTRASONOGRAPHY

TVUS can visualize the endometrium on a monitor when a 5-MHz probe is placed against the vaginal fornix. The thickness of the endometrium can be measured with precision because the endometriomyometrial junction has a distinct halo-like appearance. TVUS is highly sensitive but also has high false-positive rates (low specificity) for identifying endometrial carcinoma. Studies suggested that specificity may be improved without jeopardizing sensitivity rates if the cutoff values were based on length of time since menopause. When the endometrial thickness is 4 mm for women less than 5 years since menopause and 3 mm for women more than 5 years since menopause, TVUS had a 97.4% sensitivity, 75.7% specificity, and 99.7% negative predictive value. With respect to TVUS, the cutoff points for a minimum thickness have varied from one country to another. However, there is consensus that the mean double endometrial thickness in cases of endometrial hyperplasia/carcinoma is significantly greater than that in patients without such lesions. In the USA, the recommended lower limit of finding endometrial cancer is 4 or 5 mm, and at 3 mm, it is not necessary to perform endometrial biopsy.

MAGNETIC RESONANCE IMAGING

At present, magnetic resonance imaging and computed tomography have been proved to be useful for obtaining preoperative data on the extent and depth of myometrial invasion by endometrial carcinoma rather than in the primary diagnosis of endometrial carcinoma and its precursors. Its role in the primary diagnosis of endometrial cancer and its precursors remain to be determined.

HYSTEROSCOPY

The value of hysteroscopy in the diagnosis and directed biopsy of a variety of intracavitary or endometrial lesions in women with postmenopausal bleeding has been extensively documented. If insufficient tissue is obtained on suction curettage, or if a patient continues to have abnormal bleeding, a formal D&C is often recommended, despite the fact that its superiority over office procedures in the diagnosis of cancer has not been established.

Absolute indications for hysteroscopy have not been established. When available, however, hysteroscopy is indicated in any woman with abnormal uterine bleeding in whom an intrauterine abnormality is suspected. Other indications include recurrent miscarriages, infertility caused by endometrial pathology, removal of an impacted intrauterine device, and suspected submucous leiomyomas before abdominal myomectomy. Hysteroscopy is contraindicated in the presence of active infection and intrauterine pregnancy. Active bleeding is a relative contraindication to office hysteroscopy only because blood interferes with vision if carbon dioxide is used as a distending medium. In patients who have severe medical problems, it is prudent to

perform hysteroscopy in an outpatient setting where full monitoring and resuscitation facilities are available.

DILATION AND CURETTAGE

D&C essentially has been replaced by office-based endometrial biopsy using flexible aspiration devices. The latter is more cost-effective than D&C, and the diagnostic yield in symptomatic and asymptomatic women is similar to D&C with sensitivity and specificity rates of 90% and 95%. Cervical stenosis prevents successful endometrial sampling in about 10% of cases.

FALSE-NEGATIVE HISTOLOGY

Even direct sampling of the endometrium for histology may fail to detect adenocarcinoma. In several studies, D&C under general anesthesia missed 10% of endometrial carcinomas. This is not surprising for, as was stated earlier, only 60% of mean surface area is sampled with D&C versus 40% for Vabra curettage and 4% for endometrial biopsy with the Pipelle endometrial aspirator. Others found four of 86 (4.6%) women with postmenopausal bleeding with endometrial carcinoma who had either a negative endometrial biopsy result or D&C within 2 years before cancer diagnosis. In another study from Australia, the false-negative rate of endometrial biopsy of focal adenocarcinomas of the endometrium was 47%.

Treatment

Management depends on whether the underlying disease is primarily hormonal (benign endometrial hyperplasia) or intrinsic premalignant disease (EIN). The choice of surgical or hormonal therapy depends on the histopathologic diagnosis, the reproductive status of the woman, whether the patient is on estrogen-only replacement therapy, and her general health. In general, EIN is managed using algorithms that have been previously developed for treatment of atypical endometrial hyperplasia, and benign endometrial hyperplasia using those previously employed for non-atypical hyperplasias. The high cancer risk conferred by an EIN diagnosis, including a 36% incidence of occult carcinoma of which one third are myoinvasive, must be carefully considered in deciding upon appropriate therapy. Although some cases of EIN/early intramucosal adenocarcinoma respond to exogenous progestogens, ovulation inducers, or both, in most cases the lesions tend to recur within a few months to a few years after delivery of the newborn. Medical hormone therapy is also given to women whose general health is unsuitable to withstand surgery.

Benign endometrial hyperplasia responds well to medroxyprogesterone acetate (MPA), 10 mg orally, or micronized progesterone, 300 mg orally, once a day for 14 days per month for 3 months. Such cyclic regimens lead to withdrawal bleeding; a biopsy specimen is obtained at the end of the progestin therapy at 3–4 months. Complete responders should be maintained on cyclic progesterone therapy or, if appropriate, combined cyclic or continuous HRT. If a partial response is obtained, another 3-month trial with MPA, 10 mg orally four times per day, or megestrol

acetate, 80 mg, for 3 months may be carried out. Nonresponders and patients with intractable breakthrough bleeding may have transabdominal hysterectomy. Progestin therapy for premenopausal women with EIN calls for larger doses of MPA, 100 mg orally daily; megestrol acetate, 160 mg; or 1 g/week of MPA intramuscularly for 12 weeks. In recent years, another means to treat endometrial hyperplasia with or without atypia has been the medicated intrauterine device (IUD) such as the LNG-(levonorgestrel) releasing intrauterine system (Mirena®, Bayer Healthcare Pharmaceuticals, Inc. Wayne, NJ, USA). Several studies have shown complete response (reversal of endometrial hyperplasia to progestational-type endometrium) ranging from 25 to over 90%. In general, EH responds better (90–100%) than EIN (67–88%) to intrauterine LNG. In addition to the powerful progestational effect of Mirena on the endometrium, adverse events (side effects) that are commonly experienced by patients with oral progestational therapy are considerably reduced. This is because the systemic absorption of LNG is considerably reduced compared to oral progestational therapy. The biopsy specimen should show progestational-type endometrium with marked stromal decidualization. Careful follow up surveillence, including repeated biopsy at approximately 6 month intervals until several are free of disease is advised to ensure complete ablation. Induction of ovulation should follow the progestational therapy.

Surgery (i.e., transabdominal hysterectomy) with or without bilateral salpingo-oophorectomy is recommended for women who have persistent benign endometrial hyperplasia but are symptomatic (abnormal uterine bleeding) and women in the postreproductive age group with EIN. Surgery is justified in this group in the face of 25–35% progression rates to invasion and an 80% failure rate to respond to progestational therapy.[60] Women who develop benign endometrial hyperplasia during estrogen-alone replacement therapy may benefit from the addition of progestins into their replacement regimen. The rare patient (1%) who develops benign endometrial hyperplasia while on combined cyclic or continuous HRT may benefit from either higher doses of combined HRT or simply switching to a progestin-only replacement therapy for 3 months to attempt reverting the hyperplastic endometrium to normal.

It has been shown that duration of progestin administration is crucial for inhibiting endometrial mitotic activity; this is important because control of endometrial growth is primarily related to control of epithelial mitotic activity. Inhibition of endometrial mitotic activity is noted after 11 days of progestin treatment. The most frequent hormone preparations used for medical treatment of evaluated hyperplasia with or without atypia are presented below.

Treatment regimens by type of hormone, dosage, and duration*

	Endometrial Histology	
Hormone Preparations	**Benign Endometrial Hyperplasia**	**EIN**
Medroxyprogesterone acetate	10 mg PO × 14 days/month	100 mg PO or 1000 mg/week IM
Micronized progesterone	300 mg PO × 14 days/month	300 mg/day PO
Megestrol acetate	80 mg PO × 14 days/month	160 mg/day PO
LNG-IUD	20 μg/day x 6 months to 2 years	

IM, intramuscularly; PO, orally; LNG, levonorgestrel.
*All regimens are given for 3 months.

Conclusions

Invasive carcinoma of the endometrium is preceded by EIN, which by genetic markers is monoclonal and morphologically is identified by significant cytologic change relative to the same patient's background endometrium within a region of glands in which gland area exceeds stromal area. Benign endometrial hyperplasia is not a carcinoma precursor lesion, but rather it is an endometrial response to an abnormal hormonal environment of unopposed estrogens.

Although endometrial carcinoma and its precursors are significant because of their morbidity, mortality resulting from carcinoma is low. As a result, mass screening for asymptomatic endometrial carcinoma and its precursors is not cost-effective and is not recommended. Nevertheless, if screening for endometrial carcinoma is desired in a private practice, it should focus on women aged 55 years old and older and women with high carcinoma risk indicators.

Cytologic sampling of the endometrium directly is limited to communities in which cytologic expertise is available. The most often used method to evaluate the endometrium is histology; to reduce cost, it should be carried out in the office, and the device used should employ vacuum suction force, be disposable, and be of low cost. TVUS seems to be a potentially useful alternative to histology for screening and diagnosing endometrial carcinoma and hyperplasia. Hysteroscopy is the diagnostic method of choice for patients in whom office biopsy and TVUS failed to provide a definite diagnosis. Patients with EH without cytologic atypia and patients with atypia who desire to conceive should have progestational therapy. Patients with atypia or intractable uterine bleeding without atypia benefit from hysteroscopy.

CIN

Introduction

Cervical intraepithelial neoplasia (CIN) is a premalignant cervical disease that is also called cervical dysplasia or cervical interstitial neoplasia or cervical squamous intraepithelial lesions (CSIL).

The nomenclature in use in the past was mild, moderate, and severe dysplasia, these were the terms used to describe premalignant squamous cervical cellular changes. Although still in use by some, it has generally been replaced by the term Cervical Intraepithelia Neoplasia(CIN), which is used to describe histologic changes on the uterine cervix. The trend is now tending towards the use of Squamous Intraepithelia Lesions(SIL).

Cervical intraepithelial neoplasia (CIN) is a premalignant lesion that is diagnosed by histology as CIN1, CIN2, or CIN3. If left untreated, CIN2 or CIN3 (collectively referred to as CIN2+) can progress to cervical cancer. It is estimated that approximately 1–2% of women have CIN2+ each year, with higher rates reported for women of HIV-positive status, at 10% (2–6). A diagnosis of CIN2+ is an histological diagnosis obtained from biopsies of the suspect lesions, either with or without colposcopy, for which treatment is recommended. Adenocarcinoma in situ (AIS) is a precursor lesion for cervical cancer that is diagnosed by cytology and can be treated. The majority of AIS are found in the transformation zone. AIS may be associated with CIN. There are three principal treatments available in low- and middle-income countries to treat CIN: cryotherapy, large loop excision of the transformation zone (LLETZ, or LEEP), and cold knife conization (CKC).

Definition

It is a potentially premalignant transformation and abnormal growth (dysplasia) of squamous cells on the surface of the cervix. CIN is not cancer, and is usually curable. Most cases of CIN remain stable, or are eliminated by the host's immune system without intervention. However a small percentage of cases progress to become cervical cancer, usually cervical squamous cell carcinoma (SCC), if left untreated.

It can actually be defined as a spectrum of intraepithelial changes (dysplasia) with indistinct boundaries that begins with mild atypia and progresses through stages of more marked intraepithelial abnormalities to carcinoma in situ if untreated or managed.

Dysplasia is a potentially reversible change characterized by an increase in mitotic
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Dysplasia is a potentially reversible change characterized by an increase in mitotic
rate, atypical cytologic features (size, shape, nuclear features) and abnormal organization (cellularity, differentiation, polarity) that fall short of invasive carcinoma (premalignant change). Dysplasia may progress to cancer and dysplastic changes may be found adjacent to foci of cancer.

Epidemiology

Population distribution of cervical intraepithelial neoplasia/dysplasia resembles the epidemiology of an infectious disease that is sexually transmitted. Multiple male sexual partners, early age at first sexual intercourse and male partner with multiple previous/current female sexual partners are very important risk factors.

Incidence

The estimated annual incidence in the United States of CIN among women who undergo cervical cancer screening is 4 percent for CIN 1 and 5 percent for CIN 2,3. High grade lesions are typically diagnosed in women 25 to 35 years of age, while invasive cancer is more commonly diagnosed after the age of 40, typically 8 to 13 years after a diagnosis of a high grade lesion. Between 250,000 and 1 million American women are diagnosed with CIN annually. Women can develop CIN at any age, however, women generally develop it between the ages of 25 to 35.

In developing Nations like Nigeria the mean age for cervical intraepithelial neoplasia (CIN) was 37.6 years. CIN I accounted for 3.6%, CIN II 0.8% and CIN III was only 0.4%.The combined prevalence was 48 per 1000.The peculiarity of the developing nations result is the poor uptake or use of screening methods.

In view of the fact that CIN is a premalignant or precursor of cervical cancer it is pertinent to briefly see the incidence and prevalence of this disease condition. Cervical cancer is second only to breast cancer in its incidence world wide. Cancer registry data shows that that there are approximately 400,000 new cases of cervical cancer and 200,000 deaths from this disease every year.

The incidence rate varies from country to country with eighty percent (80%) of the cases occurring in less developed countries. The reasons for this may lie in the socio economic conditions that prevail in these countries where facilities for family planning, obstetric and gynaecological health care are scarce and cervical screening programmes are virtually non existent.

Cervix-normal histology

Most of the cervix is composed of fibromuscular tissue. The Epithelium is either squamous or columnar.

The endocervix is lined by columnar epithelium that secretes mucus this epithelium has complex infoldings that resemble glands or clefts on cross section and the mucosa rests on inconspicuous layer of reserve cells.

The ectocervix (exocervix) is covered by nonkeratinizing, stratified squamous epithelium, either native or metaplastic; has basal, midzone and superficial layers. After menopause and in prepubertal girls the superficial layer becomes atrophic with mainly basal and parabasal cells with high nucleo-cytoplasmic ratio that resembles dysplasia.

Squamocolumnar junction: where squamous and glandular (columnar) epithelium

Squamocolumnar junction: where squamous and glandular (columnar) epithelium meets this a major land mark in cervical dyplasia,it is usually in exocervix.The nearby reserve cells are involved in squamous metaplasia, dysplasia and carcinoma.

Transformation zone: also called ectropion, between original squamocolumnar junction and border of metaplastic squamous epithelium; epidermalization and squamous differentiation of reserve cells transform this area to squamous epithelium; site of squamous cell carcinomas and dysplasia.

In the cervix a lot of metaplasia takes place which was what encouraged a lot of study to be conducted.

- Metaplasia is the name given to the process by which one fully differentiated type of epithelium changes into another.
- It is usually an adaptive change which occurs in reaction to longstanding (chronic) irritation of any kind, or in response to hormonal stimuli.
- Metaplastic change is reversible and theoretically transformed epithelium should revert to its original form after the stimulus is removed but this does not always happen.
- Metaplasia occurs at many body sites eg gastric mucosa, bladder,bronchi etc. The

metaplastic process has been extensively studied in the cervix.
The Clinical significance of squamous metaplasia in the cervix is that, this area of the cervical epithelium has under gone metaplasia(Transformation zone) and all the immature metaplastic are susceptible to carcinogens. In view of the afore mentioned it is not surprising that most cervical cancers arise here.
Histology:
Basal cells (reserve cells): cuboidal to low columnar with scant cytoplasm and round/oval nuclei; acquire eosinophilic cytoplasm as they mature; positive for low molecular weight keratin and estrogen receptor; negative for high molecular weight keratin and involucrin.
Suprabasal cells: have variable amount of glycogen, detectable with Lugol/Schiller's test (application of iodine).
Glandular epithelium: positive for estrogen receptor.

Etiology
Human papillomaviruses (HPV) are members of a family of viruses known as the Papovaviruses. They are epitheliotropic viruses which promote cell proliferation which results in the development of benign papillomatous lesions of the genital tract upper respiratory tract, digestive tracts and cutaneous lesions of the skin. More than 70 distinct HPV types have been identified as a result of molecular hybridisation of DNA extracted from condylomata or warty lesions from a variety of sites. Each virus type has a very restricted site of infection and viruses which occupy similar niches appear to be genetically related. Molecular hybridisation of anogenital warts and cervical biopsies have shown that about 30 of the 70 distinct types of HPV are confined to the female genital tract.

DNA analysis of anogenital warts, CIN and cervical cancerous tissue has shown that two groups of HPV can be identified in the female genital tract. One group of HPV is almost always associated with low grade CIN lesions and exophytic anogenital warts which have a low risk of progressing to cervical cancer (HPV type

6, 11, 42, 44, 53, 54, 62, 66). A second group of viruses is found most commonly in CIN2 and CIN3 which have a high risk of developing into invasive cancer (HPV type 16,18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68).

The major cause of CIN is chronic infection of the cervix with the sexually transmitted human papillomavirus (HPV), especially the high-risk HPV types 16 or 18 (viruses from the high risk group (HPV16 and HPV 18) have the ability to immortalise primary human keratinocytes ie extend their lifespan) In comparison viruses from the low risk group (HPV-6 and HPV -11) do not extend the life span of transfected human cells which mature and die at the same rate as non infected cells. Similarly the low risk viruses perform poorly in experiments concerned with the malignant transformation of rodent cells in comparison to the high risk HPV types. Moreover, HPV-16 and HPV -18 infected human keratinocytes in raft culture (an organotypic culture medium) exhibit a differentiation pattern very similar to that seen in vivo in CIN. Over 100 types of HPV have been identified. About a dozen of these types appear to cause cervical dysplasia and may lead to the development of cervical cancer. Other types cause warts.

The viral DNA Integration is a consistent finding in all cancers harbouring the high risk virus types HPV16 and HPV18 and provides the strongest evidence that HPV16 and HPV18 play an important role in the development of cervical cancer. HPV DNA is present in 90% of all cervical invasive cancer.
It is not sufficient to say that simple infection with high risk HPV or even integration of HPV 16 /18 into the host cell nucleus is enough for malignant transformation of the cervical epithelium. Obviously Infection of the genital tract with HPV 16 is relatively common whereas invasive cancer is rare; and integration has been detected in some cases of genital warts and CIN lesions. A number of associated-factors have been proposed such as impaired immune response, persistence of virus, smoking and administration of steroid hormones (as oral contraceptives). Other genetic events such as loss of tumour suppressor genes and the activation of oncogenes may also play a role. Mutations in ras ,fos and other oncogenes have been detected in cervical cancer cell lines but their role in vivo is still to be determined. The knowledge of HPV infection has made a remarkable improvement in the screening, diagnosis, treatment, prevention and prognosis of cancer of the cervix.
The host immunity plays a significant role in the control of this disease entity. The fact that HPV remains localised to cervix and vagina further indicates that local immune responses are sufficient in controlling and resolving HPV infection. Both cell mediated immunity and humoral immunity. Also immunosuppression has been implicated as an associated factor. The majority of infections are transient and not clinically evident with 70-90% of infections clearing within 12-30 months. This suggests that host immunity is generally able to clear HPV infection.

Histopathological features
Abnormal cellular proliferation, maturation and atypia characterize cervical intraepithelial neoplasia(CIN). Nuclear abnormality is the hallmark of CIN and includes hyperchromasia, pleomorphism, irregular borders, and abnormal chromatin

distribution. These nuclear abnormalities persist throughout the epithelium irrespective of cytoplasmic maturation towards the surface. Mitotic rate is increased and abnormal mitotic figures may be seen.
Histologic grading of CIN is based on the proportion of the epithelium occupied by dysplastic cells. The epithelium is divided into thirds.

Grading

CIN 1 is considered a low grade lesion. It refers to mildly atypical cellular changes in the lower third (basal 1/3) of the epithelium (formerly called mild dysplasia/Abnormal cell growth). HPV viral cytopathic effect (koilocytotic atypia) is often present. This corresponds to infection with HPV, and typically will be cleared by immune response in a year or so, though can take several years to clear.
CIN 2 is considered a high grade lesion. It refers to moderately atypical cellular changes confined to the basal two-thirds of the epithelium (formerly called moderate dysplasia) with preservation of epithelial maturation.
CIN 3 is also considered a high grade lesion/Severe dysplasia. It refers to severely atypical cellular changes encompassing greater than two-thirds of the epithelial thickness, and includes full-thickness lesions (formerly called severe dysplasia or carcinoma in situ).
Cytologic grading of CIN also uses a three-tier system. However, the new Bethesda System for cytological diagnosis divides precursors of cervical squamous cell carcinoma into low-grade squamous intraepithelial lesion and high-grade intra-epithelial lesion.

Clinical presentation

CIN is asymptomatic.
CIN lesions are characterized by the appearance of white patches on the cervix following application of acetic acid. Distinct vascular patterns can be seen on colposcopic examination of the cervix in high grade CIN. Lesions occur on the anterior lip twice as commonly as the posterior lip. They are found in the transformation zone and areas of squamous metaplasia in the endocervix and stop abruptly at the junction with the native portio squamous epithelium but can extend along the entire endocervical canal. In general, the portion of CIN on the portio surface is low grade (CIN 1) whereas the portion that extends into the endocervical canal is high grade (CIN 2 and 3).
CIN may regress (spontaneously, especially CIN1), persist or progress. If untreated, up to 16% of CIN1 will progress to CIN3 and up to 70% of CIN3 will progress to invasive squamous cell carcinoma in 1 to 20 years. It is not presently possible to predict which lesions will progress. However, the risk of progression to invasive cancer increases and the time required is shorter with increasing severity of the lesion.

Screening

The aim of screening is to prevent the development of cancer. For screening to be effective, a disease should satisfy the following criteria:

- Be common, serious and an important public health concern for the individual and the community.
- The disease condition must have a long, latent interval in which pre-malignant change or occult cancer can be detected for the case of cancer of the cervix it is 10-15years.
- The natural history of the disease, especially, its evolution from latency to disease should be adequately documented.
- There should be effective treatment for pre-malignant change or condition.

Cervical cancer screening satisfies the above criteria, especially with regards to developing countries where it really is a public health problem. Cervical screening has been shown to be effective in several countries. Cervical cancer prevention efforts worldwide have focused on screening women at risk of the disease using Pap smears. Treating precancerous lesions has also prevents cervical cancer in many of the developed countries. In view of the afore mentioned cancer of the cervix is

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almost extinct in the developed nations, making it the 11 cancer in women and 2 commonest in developing nations.

Pap smear

The Pap test was developed by Dr George Papanicolaou an American anatomist in 1944. Pap test is used primarily as a tool for screening healthy women for preinvasive cervical cancer (CIN) and early invasive cancer.In as much as pap test is a screening tool,it could also be use to identify women at risk of cervical cancer. Women with early invasive cancer (FIGO Stage 1) are often unaware that they are harbouring the tumour as they are usually symptom free. Diagnosis and treatment of invasive cancer while it is still in the early stages of development signficantly improves the prognosis (chances of long term survival) of the patient.

It has been proven over time that the cervical smear may be negative even in the presence of an advanced invasive cervical cancer. This is because blood, inflammatory cells and necrotic debris from the cancer site frequently obscure the abnormal cells in the smear.

The sample for pap smear can be collected in two ways:

a) liquid-based cytology (LBC) - using a cervix-brush a device which samples both endo and ectocervix. These can be used for preparing conventional smear. Some devices have been modified for the preparation of liquid based cytology (LBC) specimens

b) Papanicolaou (Pap) smear test uses a brush or the Ayres spatula to sample the ectocervix. Scraping the ectocervix is performed with a modified spatula (the Ayre spatula or a variation of it), a cyto-brush is used to sample the endocervix. This is the most widely used method in developing countries and some part of Europe for obtaining material for preparing conventional cervical smears.

Pap-smear report may be delivered according to WHO classification, or Bethesda classification, which includes:

Atypical Squamous Cells of undetermined significance (ASC-US)
Low grade Squamous intraepithelia neoplasia(LSIL)
High grade Squamous intraepithelial neoplasia(HSIL)

HPV	Mild dysplasia	Moderate dysplasia	Severe dysplasia	Carcinoma in situ	Invasive cancer
HPV	CIN I	CIN II	CIN III		Invasive cancer
Low grade SIL LGSIL		High grade SIL HGSIL			Invasive cancer

Management
Management of borderline nuclear change
The smear should be repeated at 6 months, interval for 1year and 12 months later. – If all are negative, normal recall can be resumed. If in the course of the follow up, there are a maximum of 3 reports of borderline nuclear change in the follow-up period, referral for colposcopy is advised. At any point in time One report of borderline glandular cells requires immediate referral for further evaluation. In difficult cases, where there is concern that high grade disease may be present, immediate referral can be recommended.
CIN I/Low sil management
CIN I/Low SIL correlates to Nucleus occupying up to 1/2 of the area of the cell (Nucleocytoplasmic ratio of half).
It is advisable that she should have a colposcopy done, in centres where this facilities are not available, “it remains acceptable to recommend a repeat test”. If the repeat smear is the same diagnosis (mild dyskaryosis) then a referral must be advised.
CINII/High SIL
CIN II/High SIL correlates to Nucleus occupying up to ½ to 2/3 of the area of the cell(Nucleocytoplasmic ratio of ½ to 2/3).
All patients with moderate dyskaryosis should be referred for colposcopy.
CIN III/ High SIL
CIN III/High SIL correlates to Nucleus occupying more than 2/3 of the area of the cell (Nucleocytoplasmic ratio greater than 2/3). The nucleus may have a bizarre shape.
Referral for colposcopy is the standard approach of management.This will include tissue biopsy for histology.
Invasive squamous carcinoma
The histological features are essentially that of Bizarre nuclear changes and keratinisation.
In this case an URGENT referral for colposcopy and tissue diagnosis is advised.

Treatment
Low grade lesions
In the treatment of this disease entity a colposcopy, with or without a repeat smear, and or tissue biopsy is an essential requirement as stated above. The uses of

additional investigative tools are very essential in the treatment of this condition. The time interval between diagnosis and treatment can be very crucial.
The option of treatment range between Cryotherapy, cold coagulation, Laser agglutination therapy and Electrocautery. A lot of caution must be applied to avert over treatment especially in young women who are still desirous of conception (over treatment can cause fertility problems).
The follow up schedule as stated above and the patient should be encouraged to adhere to this to achieve the desired goal of screening.
High grade lesions
The additional investigations include Colposcopy, repeat smear and tissue biopsy is important toward establishing a diagnosis,because the treatment involved is usually irreversible. Such definitive treatment includes ablative procedures and amputation surgeries.
The definitive treatments include Cold coagulation, Lletz, laser agglutination therapy, electrcautery, knife cone biopsy and trachelectomy.

Follow up of patients on treatment
The Follow-up of women who have been treated for CIN is very crucial to ensure that there is no progression of the disease condition.

- CIN1 - repeat smears at 6months, 12months and 2years this is the schedule if the smear is persistently negative.
- CIN2 and above –this categories of patients require annual smears for 10 years of follow up.
- GIN (Cervical Glandular Intraepithelia Neoplasia) – are at greater risk of recurrent disease so they are recommended to have smears every 6months for 2years, then annually for 10 years

Follow-up of women with low grade smears but normal colposcopy and no biopsy – require a repeat smear at 6 months, 6 months, 12 months, then return to normal recall
Follow-up of women after hysterectomy for CIN or SCC :
Where there was complete excision and the margins were clear of dysplastic cells, vault smears should be carried out at 6 months and 18 months before recall can be cancelled as no further smears are required.
In the case of women with incomplete or uncertain excision at hysterectomy, they would require follow-up as for women with CIN2 or above.
In women who have been exposed to radiotherapy as an adjuvant therapy, Smears are not advised in this group of women.

HPV vaccination and cervical intra-epithelia neoplasia
In a randomised control study (double blinded) it was concluded that, In young women who have not been previously infected with human papillomavirus-16 (HPV16), vaccination prevents HPV16-related cervical intra-epithelial neoplasia (CIN). It should be noted that only 75% of all cervical cancers are caused the HPV viruses 16 and 18, it is therefore still possible for a woman to

develop cervical cancer even though they are immunised. This is because there are other sero types of HPV not covered by those vaccine in the market.

5. Materials of student activization during lecture:

Questions:

1. Specifics of anamnesis gathering in gynecological patients?
2. What special examination methods in gynecology do you know?
3. What is colposcopy and how is it performed?
4. What epithelium are endocervix and ectocervix covered by?
5. Can there be asymptomatic fibroids?
6. What does it mean, a functional cyst of ovary?
7. What contraindications to surgical treatment of ovarian tumors do you know?

6. Self-control questions on the topic:

1. Benign ovarian tumours (epithelial, strains of the genital strain, lipid-cellular, germinogenic tumours): clinical features, diagnostics, complications, treatment, general practitioners' strategies.
2. Benign tumours of the uterus: clinical features, diagnostics, complications, treatment, indications for surgical treatment, general practitioners' strategies.
3. Pre-cancerous diseases of the uterine cervix: aetiology, classification, clinical features, diagnosis and treatment.
4. Endometrial hyperplasia: aetiology, pathogenesis, classification, diagnosis and treatment, general practitioners' strategies.
5. Prophylaxis of precancerous diseases of female reproductive organs.

LECTURE №3. TOPIC: "Acute abdomen" in gynecology. Pelvic inflammatory diseases.

1.Relevance of the topic:

The clinical experience of medical institutions indicates that the most difficult for the doctor are clinical situations that require emergency care. Very often, while it is primarily about saving the patient's life, as incorrect or untimely actions, errors in the choice of tactics, methods and means of emergency aid rich very serious and tragic consequences. However, properly and timely provided, rationally planned and carried out by methods Lean emergency assistance can not only save the life of the patient but also to preserve reproductive function.

Exceptional value of this provision to women, families and society in general does not need supplementing arguements.In that fact that readiness to provide emergency assistance at any time and in any place, the responsibility for the life and health I

have no one who ended up in critical condition, as the main doctor of any specialty, evidence of his professional life.

The etiology and pathogenesis, methods of rational treatment of inflammatory diseases of the genitals (PID), especially in the chronic stage, for a long time is one of the major problems of gynecology, which has not only clinical but also social value. The number of patients is, according to different authors, from 60 to 82 percent of all women seeking about diseases of the genital organs. This means that out of 100 women in need prenatal doctor, 82 women suffering from STI. Should pay attention to another important feature PID: suffering by women of childbearing age. Inflammatory diseases and their complications are very adversely affect the reproductive function of women, causing the causes of infertility, miscarriage. The most adversely affected by inflammatory diseases in fruit-system mother-placenta-fetus - the risk of intrauterine infection, hypoplasia, intrauterine growth retardation, stillbirth. Children with the effects of intrauterine infections constitute a group at high risk of early childhood mortality. Inflammatory diseases are the cause of cervical cancer, menstrual tsyklu.Sotsialna and medical importance of inflammatory diseases requires very careful attention to this large group of patients, timely, complete phased treatment, prevention PID and prevention of complications.

2. Goals:

1. Get in touch with relevance of the topic, research areas developed by the department of Obstetrics and Gynecology on this issue

3. Basic concepts:

1. Determination of etiologic and pathogenetic factors of major diseases of the female reproductive system, leading to infertility.
2. Basic principles of inspection infertility when the couple married.
3. Definitions previous clinical diagnosis based on the interpretation of the special examination barren couple.
4. Modern principles and methods of treatment of female infertility (hormonal, surgical, new reproductive technologies).
5. Select from history are typical for male and female infertility information.
6. Examine patients with infertility, to evaluate the degree of importance.
7. Evaluate your clinical and laboratory examination of patients with infertility.
8. Based on history, the clinic conducted differential diagnosis to be able to make the correct diagnosis in thematic patient.
9. Assign adequate treatment of infertility.
10. Determine the extent of prevention of male and female infertility.

4. Content of the lecture material:

Ectopic pregnancy

All cases of the ovum outside the uterine cavity is called ectopic pregnancy, depending on the location of the ovum implantation of ectopic pregnancy is divided into pipe, ovarian, in rudimentary horn of the uterus and abdominal.

Etiology and pathogenesis. Ovum implants outside the uterus is due to violation of the transport function of the fallopian tubes, changing properties of the ovum.

Violation of pipes connected:

– with inflammation of any etiology;
– hormonal status of the organism;
– surgical intervention on the pipes.

Clinic and diagnostics. In urgent gynecology broken more common tubal pregnancy - pipe rupture or tubal abortion.

Pregnancy, broken by type pipe rupture, acute onset, which in some women delay preceding the next menstruation, pain below the belly spread to the anus, sub, supraclavicular area, the shoulder or the shoulder, accompanied by nausea or vomiting, dizziness until loss of consciousness, sometimes diarrhea.

Patients often inhibited, rarely shows signs of anxiety, skin and mucous pale, cold extremities, frequent superficial breath. Tachycardia, pulse weak filling, blood pressure is lowered. Tongue moist, not coated. Belly slightly swollen, tense muscles of the abdominal wall is missing. On palpation - pain below the abdomen, more on the affected side, and severe symptoms of irritation of the peritoneum. For percussion-blunting in shallow areas of the abdomen.

When viewed using mirrors, cyanosis and pallor of the mucous vagina and ekzotserviksu. Bimanual examination (very painful) reveals flattening or bulging rear or one side of the arch. The uterus is easily displaced, as it "floats" in a free fluid.

If you doubt the correctness of the diagnosis made puncture the abdominal cavity through the posterior vaginal vault.

Interruption of tubal pregnancy by type of tubal abortion presents diagnostic difficulties, as characterized by slow flow and no appreciable effect on the overall condition of the patient. It should be stressed that carefully collected history provides invaluable aid in the diagnosis of tubal abortion. The basic triad of symptoms of tubal abortion, delayed menstruation, abdominal pain, bleeding from the vagina.

Abdomen soft, painless on palpation. When viewed in the mirror, and cyanosis loosening mucous membranes and bleeding from the cervical canal. During bimanual examination: slightly enlarged uterus, increasing the unilateral appendages (often kovbasopodibnoyi or retertovydnoyi form); vaginal codes may remain high or flattened.

Additional methods:

1. Determination in serum and urine horialnoho gonadotropin (hCG).
2. Ultrasound.
3. Laparoscopy.
4. Histological examination of scraping the endometrium.

Treatment can be surgical and conservative. Surgical treatment of ectopic pregnancy in most cases -salpynhektomiya. The aim of this treatment is to preserve the woman's life. In simple cases, severe bleeding can be performed organ surgery, some of them-laparoscopy: salpinhotomiya, segmental resection and anastomosis, fimbrial

evacuation. In connection with some risk of trophoblastic disease recommend the study of hepatitis 2-3 weeks after surgery compared to the previous level. If persistent or elevated levels of hCG perform repeated conduct research or therapy with methotrexate.

Conservative treatment with methotrexate is rarely used as an independent method.

Laparotomy performed in the diagnosis of ectopic pregnancy interrupted. The delay in the operation could lead to catastrophic consequences. The first measures to be patient withdrawal from the shock, bleeding stop and support the cardiovascular system.

Algorithm for treatment of ectopic pregnancy.Principles of patients of ectopic pregnancy: 1. Suspicion of ectopic pregnancy is an indication for urgent hospitalization. 2. Early diagnosis will help reduce complications and allows you to use alternative therapies. 3. In the diagnosis of ectopic pregnancy is necessary to make urgent surgery (laparoscopy, laparotomy).
Surgical treatment of ectopic pregnancy is optimal. In modern practice may use conservative treatment of ectopic pregnancy. 4. In case of severe clinical picture excited ectopic pregnancy, presence of hemodynamic disorders, hypovolemia patient hospitalized immediately for immediate surgery as soon as possible laparotomichnym access. If the clinical picture is erased, no signs of internal bleeding and hypovolemia conduct pelvic ultrasound and / or laparoscopy. 5. prehospital when excited ectopic pregnancy emergency room volume is determined, the patient and the amount of blood loss. Infusion therapy (volume, speed of solution) depends on the stage of hemorrhagic shock (see. Protocol - "hemorrhagic shock"). 6. Severe condition of the patient, presence of severe hemodynamic disturbances (hypotension, hypovolemia, hematocrit less than 30%) -absolyutni indications for surgery laparotomy access of pregnant fallopian tube removal and holding antishock therapy. 7. Apply an integrated approach to the treatment of women with ectopic pregnancy, including: a) surgery; b) the fight bleeding, hemorrhagic shock, blood loss; c) postoperative care; d) the rehabilitation of reproductive function. 8. Surgical treatment is carried out as laparotomy and laparoscopic access. The advantages of laparoscopic techniques include: -reduction length transaction; -reduction duration of postoperative period; -reduction length of hospital stay; -zmenshennya number scarring of the anterior abdominal wall; the presence of severe hemodynamic disturbances (hypotension, hypovolemia, hematocrit less than 30%) -absolyutni indications for surgery laparotomy access of pregnant fallopian tube removal and holding antishock therapy. 7. Apply an integrated approach to the treatment of women with ectopic pregnancy, including: a) surgery; b) the fight bleeding, hemorrhagic shock, blood loss; c) postoperative care; d) the rehabilitation of reproductive function. 8. Surgical treatment is carried out as laparotomy and laparoscopic access. The advantages of laparoscopic techniques include: -reduction length transaction; -reduction duration of postoperative period; -reduction length of hospital stay; -zmenshennya number scarring of the anterior abdominal wall; the presence of severe hemodynamic disturbances (hypotension, hypovolemia, hematocrit less than 30%) -absolyutni indications for surgery laparotomy access of pregnant fallopian tube removal and

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cosmetic effect. 9. Implementation of organ operations for ectopic pregnancy provodzhuyetsya the accompanying risk of postoperative persistence of trophoblast resulting from its incomplete removal of the fallopian tubes and abdominal cavity. The most effective method of prevention of complications is closely toilet abdominal 2 to 3 liters of saline and single administration of methotrexate in doses of 75 -100 mg vnutrishnom'yazovou first, second days after surgery.

Opepatsii that apply in the case of ectopic pregnancy:

1. Salpinhostomiya (tubotomiya). Running longitudinal salpinhostomiya. After removal of the ovum salpinhostomu certainly not ushyvayut. Where no chorionic villi grow into the muscle membrane of the fallopian tube limited curettage. 2. Segmental resection of the uterine tube. Remove segment of the fallopian tube where the egg is fertilized and then perform the anastomosis at both ends of the pipe. If impossibility of performance-salpinho salpinho anastomosis can tie both ends and impose anastomosis later .. Z. Salpinhektomiya. This operation is performed in case of violations of tubal pregnancy, accompanied by massive bleeding. Surgery and blood transfusion in this case is carried out simultaneously.

Ovarian apoplexy (Rupture of the ovary). By predisposed factors vidnosyatsya-moved inflammation localized in the pelvis that led to sclerotic changes in ovarian tissue and blood vessels to congestive congestion and varicose ven.Ne exclude the role of endocrine factors. Bleeding from the ovary can promote blood diseases in violation of its collapse.

Ovarian rupture can occur in different phases of the menstrual cycle, but in most cases - in the second phase.

<u>There are three clinical forms of the disease: anemic, sickly and mixed.</u>

The clinical picture is dominated by symptoms of anemic form intraperitoneal bleeding. Getting the disease may be associated with physical injuries, physical stress, sexual intercourse, and can begin for no apparent reason. Acute intense

abdominal pain appears in the second half or in the middle of the cycle. Often the pain spreads to the anus, external genitals, sacrum; there may be symptom-frenikus.

Painful attack is accompanied by weakness, dizziness, nausea, sometimes vomiting, cold sweats, fainting. When viewed noteworthy pale skin and mucous membranes, tachycardia at normal body temperature. Depending on the amount of blood loss reduces blood pressure. The abdomen is soft, slightly swollen .. Power muscles of the abdominal wall is missing. On palpation abdominal pain appears spilled across its lower half. Symptoms of peritoneal irritation expressed in varying degrees. Percussion of the abdomen may reveal the presence of abdominal free liquid.

During bimanual (quite painful) studies define normal size uterus, sometimes - painful enlarged spherical ovary. When significant bleeding and pain are overhanging rear and / or lateral vaginal vault.

In a clinical blood test pattern prevails anemia.

Painful form of ovarian apoplexy observed in cases of bleeding into the tissue of the follicle or yellow body without bleeding or slight bleeding into the abdominal cavity.

The disease begins with acute episode of pain below the abdomen, accompanied by nausea and vomiting in the background temperature. No signs of internal bleeding. The abdomen is often mild, but some can be detected muscle tension of the abdominal wall in the iliac areas. Palpation of the abdomen is painful in the lower divisions, there are defined moderate symptoms of peritoneal irritation. Free fluid in the abdomen can not be found. Bleeding from the genital tract there.

In an internal gynecological examination determine normal size uterus, displacement of which causes pain and increased slightly painful round ovary. Vaginal vault remain high.

Clinical analysis of blood shows no significant deviations from the norm.

Treatment of ovarian apoplexy depends on the degree of intra bleeding. Anemic form of the disease requires surgery, which amounts may vary. If there was a gap corpus luteum, it should take in the T-hemostatic sutures. The most typical operation is resection of the ovary. Spay well only when all its cloth soaked with blood.

In recent years, the opportunity to conduct operations that spared using laparoscopy, during which the evacuation of blood that poured into the abdominal cavity and coagulation areas ovarian bleeding.

Painful form of ovarian apoplexy without clinical signs of growing internal bleeding can be treated conservatively. Assign calm, cold on the lower abdomen, the drugs hemostatic action vitamins. Conservative treatment is performed in a hospital under the supervision of medical staff.

Tilting legs ovarian tumor. Torsion legs can be subjected to tumors of different histological structure, not welded to adjacent organs and that have a strong leg. This usually benign and borderline neoplasms, but can meet and malignant.

Torsion stem tumor may be associated with changes in posture, physical stress, enhanced intestinal motility, bladder overflow, long movable leg cysts.

Anatomical stem tumor has stretched ties that hung ovary, ovarian ligament and own mezoovariya. In the surgical leg is part of the fallopian tubes.

Torsion legs can occur suddenly or gradually, sometimes full and partial. Pathological changes in the tumor when twisting her legs depend on the speed with which rotates on the axis of the tumor and the degree of torsion. Torsion stem tumor, accompanied perezhattyam arteries, leading to changes in necrotic tissue tumors.

The clinical picture. The disease usually begins with severe pain in nyzi .zhyvota accompanied by nausea and vomiting. Body temperature in the early hours of the disease remains normal leukocyte reaction is not expressed.

The patient takes a forced situation arisen in bed because of sharp pain. On palpation - stress the anterior abdominal wall, positive symptom SHCHetkina-Blumberg, enteroplegia, delayed stool, rarely, diarrhea. Body temperature may rise, rapid pulse, pale skin, cold sweat. When an internal gynecological examination showed the tumor in the region of the uterus, the attempt to shift causes a sharp pain. Such patients need urgent surgery.

Violation of the power unit of uterine fibroids. Violation of the blood supply to the myoma nodes is explained mainly by mechanical factors (torsion, bend, compression tumors). It is necessary to take into account the peculiarities hemodinamyky during pregnancy when there is a significant decrease in blood flow in the uterus, especially pronounced in the area mizhmyshechnoho unit, increased vascular tone in vessels of small caliber, difficulty of venous outflow, reducing blood flow velocity and venous blood. The cause of eating disorders unit may be different degenerative processes in myoma nodes (swelling, necrosis, hemorrhage, hyaline degeneration, degeneration) that develop as a result of ischemia, venous stasis, thrombosis in multiple tumor nodes mizhmyshechnyh.

There are dry and wet necrosis types of cancer. When dry necrosis is a gradual shrinkage of necrotic tissue sections, thus formed a kind of cavernous cavity with remains of dead tissue. When wet necrosis observed softening and wet tissue necrosis with subsequent formation kistepodibnyh cavities. The so-called red tumor necrosis often exposed, intramural are:

Macroscopically these tumors are painted red or brownish-red color, with soft texture, microscopic - and their veins thrombosis. Reason: toning surrounding the hub, with the subsequent development of the myometrium circulatory disorder in the capsule of the tumor and the periphery. Before joining aseptic necrosis often infection that gets the node or hematogenous lymphogenous way.

Clinical eating disorders unit depends on the degree of blood supply to the site.

Necrosis of uterine fibroids is accompanied by acute pain in the abdomen, tension anterior abdominal wall, possible fever and leukocytosis.

During bimanual examination to determine the presence of uterine myoma nodes, one of which is sharply painful on palpation.

Ultrasound facilitates detection of inaccessible sites. Clarify the diagnosis by using laparoscopy.

Treatment - operative. In some cases, conservative treatment is acceptable, the rheological active agents (reopolyglukine, trental), antispasmodics (papaverine, no-spa) in combination with antibacterial and desensitizing agents.

Pelvioperitonit and peritonitis - acute inflammation of the peritoneum.

Causes: - melting piosalpinks wall, purulent tubovarialnoho formation;

- various gynecological surgery;
- criminal abortion, including perforation of the uterus;
- ovarian tumor necrosis.

Depending on the prevalence of isolated forms of inflammation peritonitis:

1. Local (restricted and unrestricted).
2. Distributed (diffuse, diffuse and total).

Pelvioperitonit may be the result of infection to the peritoneum pelvic with serous and purulent salpingitis always accompanies development piosalpinks, piovaru and tubovarialnoho abscess.

Views: serous, fibrinous, purulent.

Clinic acute stage pelvioperitonit: abdominal pain, fever, nausea and sometimes - vomiting. An objective study, rapid pulse, advancing reaction temperature. The tongue is moist, sometimes coated with white bloom. The abdomen is inflated in the lower divisions, and muscle tension of the abdominal wall, positive symptoms of peritoneal irritation. Sluggish peristalsis, abdominal wall involved in the act of breathing. Bimanual examination zatrudnene through sharp pain and lower abdominal strain. Severe pain occurs already at the slightest shift of the cervix. Sometimes flattening or vaginal overhanging arches that indicates the presence of fluid in the pelvis.

Clinical analysis of blood at pelvioperitonit should be done repeatedly during the day. For pelvioperitonit typical moderate leukocytosis, blurred Rally leukocyte formula to the left, a small reduction in the number of lymphocytes and increased ESR.

In unclear cases, laparoscopy is performed.

Pelvioperitonit Treatment is usually conservative.

Calm, complete diet, gentle. On the lower abdomen - periodic ice pack application. Antibiotic therapy. Detoxification (infusion-transfusion therapy). Desensitizing, nonspecific anti-inflammatory drugs znebolyuyut vitamins. It is advisable sessions ultraviolet blood irradiation.

Surgical treatment requires pelvioperitonit occurring against the backdrop piosalpinks, piovaru and tubovarialnoho abscess.

Characterized by widespread peritonitis early stemming endogenous intoxication.

<u>Classification of peritonitis in K.S.Symonyanu:</u>

I phase - reactive; Phase II - toxic; Phase III - terminal.

Clinic: pain, muscle tension defending abdominal symptoms of peritoneal irritation positive, persistent paresis of the intestine.

High fever, shallow hekannya, vomiting, restless behavior and euphoria, tachycardia, cold sweat. Marked leukocytosis with a shift to the left leukocyte and toxic granularity of neutrophils, increased alkaline phosphatase, a sharp decline in the number of platelets

Treatment in 3 stages: preoperative preparation, surgery, intensive therapy in the postoperative period

Preoperative preparation: decompression of the stomach, catheterization subclavian vein (held infusion therapy aimed at eliminating hypovolemia and metabolic acidosis, correction of water, electrolyte and protein balance, detoxification of the body), the introduction of cardiac drugs, adequate oxygenation, in / in the introduction of antibiotics in the highest possible dose .

Volume surgery purely individual, special requirements - complete removal of the source of infection, followed by drainage of the abdominal cavity.

The duration of infusion therapy in the postoperative period should pursue the following objectives:

- elimination of hypovolemia by introducing colloidal solutions and protein products;
- filling losses and potassium chloride;
- correction of acidosis;
- the energy needs of the body;
- antyfermentna and anticoagulation;
- ensuring forced diuresis;
- fight against infection by the use of broad-spectrum antibiotics;
- Treatment of functional failure of the cardiovascular system;
- prevention and elimination of vitamin deficiencies.

It is important to restore motor-evacuation function of the stomach and intestines. Sessions UFOAK. Hyperbarichna oxygenation. Extracorporeal hemosorbtion.

Classification of inflammatory diseases of genitals

I. For the clinical course:

1. Acute processes;

2. Chronic processes;

a) In remission;

b) In the acute stage,

• With the advantage of infectious and toxic effects of characteristics inherent in acute inflammation (temperature, changes in blood picture) - rare (5%);

• With the advantage of changes in the nervous system in the form of "trace" the former reaction of inflammation - chronic adnexitis with pelvic hanhlionevrytom.

II. For localization:

1. Inflammation of the vulva:

• Vulva - vulvitis,

• Genital warts (warty skin formation viral etiology)

• Bartolynova gland - Bartolini;

2. Inflammation of organs:

• Vagina - vaginitis, vaginitis;

• Cervix - endocervicitis (inflammation of the vaginal cervix coated multilayered squamous epithelium);

• Endotservitsitah (inflammation of the lining facing into the cervical canal and covered with columnar epithelium);

• Tservikoz (defeat all layers of the cervix);

• Erosion (pseudo - cylindrical epithelium ectopia in multilayer, real erosion - multilayered epithelium defect, erosion being supported by insufficient ovarian hormonal function);

• The body of the uterus - endometritis (inflammation of the lining of the uterus body);

• Metroendometritis (inflammation of mucous and uterine muscle layer);

• Panmetryt (inflammation of all layers of the uterine wall);

• Perimetrity (inflammation of the peritoneum that covers the body of the uterus);

• Uterus - salpingitis (inflammation of the fallopian tubes);

• Oophoritis (ovarian inflammation);

• Salpingo (inflammation of the fallopian tubes and ovaries) or adnexitis;

• Adnekstumor (inflammatory swelling fallopian tubes and ovaries);

• Gidrosalpinks (inflammatory tumor of the fallopian tube accumulation of serous fluid in the lumen);

• Piosalpinks (inflammatory Bursiform fallopian tube tumor accumulation of pus in the lumen);

• Piovarum (inflammatory tumor of the ovary with its suppurative melting tissues);

• Perisalpinhit (inflammation of the fallopian tube retroperitoneal cover);

• Fiber pelvis - parametrit (inflammation of the tissue surrounding the uterus) - side, front and rear;

• Peritoneum pelvis - pelvioperitonit (pelvic peritonitis);

• Total peritonitis (diffuse or diffuse)

Properly formulated diagnosis must be clinical indications of flow, the localization process to determine the same principle of treatment duration, diagnostic features, the following tactics. Example:

- acute adnexitis;

- chronic salpingitis in remission;

- chronic salpingitis exacerbation trace the type of reaction;

- chronic adnexitis in toxic-infectious type.

Sometimes diagnosis is rendered next to the disease some of its symptoms due to their importance because they determine the clinical picture and treatment policy. Example;

- chronic adnexitis in remission. Sterility.

Etiology and pathogenesis of acute inflammatory diseases of genitals

The last decades are characterized by defined PID evolution of knowledge. This refers to the etiological factor and response of the patient woman.

Inflammation of the genitals of women is primarily infectious process in the origin of which can play the role of various microorganisms. Proved an overwhelming role in pathogenic staphylococci resistant to many antibiotics. Their etiological role installed when bacteriological tests in 53-56% of cases. Now etiology PID increased value of conditional pathogens (Escherichia coli, Mycoplasma hominis), which occur in isolation or in association with other organisms. Mycoplasma occur in 10-15% of patients with inflammation of the uterus, mixed aerobic and anaerobic flora - 26% aerobic - 27%. anaerobic - 18%. Significantly increased the role of anaerobes, including more frequent peptokokky, streptococci (33%), Clostridium (17%). Inflammatory diseases of the uterus caused by pathogenic anaerobes, occur most difficult tuboovarialnogo to form abscesses. There is also a tendency to increase the number of viral diseases. Inflammatory processes are caused by the herpes virus, cytomegalovirus, urogenital infection, only one percent of patients with severe acute course, there is other chronic diseases.

The increased possibility of bacteriological methods of research made available identification of microorganisms such as Chlamydia. The incidence of chlamydia secretions from the cervix is 5-40% of acute PID. Inflammation caused by chlamydia, clinically characterized by severe and less severe symptoms than other inflammatory etiology.

At the causative factor in the development of inflammation plays a significant role state microorganism and the set of conditions that act on the body simultaneously with the etiological factor. For example, E. coli, which under normal conditions does not cause inflammation, can cause severe peritonitis in patients with ectopic pregnancy, weakened large blood loss.

According to modern representations inflammation is primarily a defensive reaction in response to irritation and tissue damage (alteration), in the form of changes in tissue metabolism, cardiovascular reactions, phagocytosis, reproduction and formation of tissue cells.

At one time IV Davydovskyy formulated the thesis that there should be an epigraph to the entire medical practice: "Treatment can be successful only if it is etiopathogenetic." Excluding the medical complex etiology and pathogenesis of the highlights of the pathological process of treatment is symptomatic and therefore will not be successful.

It should always be remembered that the inflammatory process is not only the local process in the affected organ - the uterus, fallopian tube or other body of the reproductive system. Irritation and tissue damage related primarily to the most

dynamic structure - the nervous system receptor cells. Pathogenic stimuli has an impact not only in the localization of the inflammatory process, and remotely from it.

Highlights of the pathogenesis of acute inflammation are as follows: changes in the inflammation consisting primarily of carbohydrate metabolism, increase anaerobic glycolysis to form in the tissues of intermediate oxidized products (pyrovinohradnoyi, malic, succinic acid), the accumulation of fatty acids, ketone bodies in result of incomplete splitting of fats and proteins. Reducing the potential respiratory cells, reducing the buffer capacity are beginning to develop compensated and decompensated then ketoacidosis. Remembering that moment pathogenesis, the complex treatment drugs should be administered with detoxification and alkaline properties.

The second important point - changes in blood flow in the inflammation. Vasospasm, emerged first, further expansion of small arteries varies with increasing pressure in the capillaries - and the first development of arterial and venous blood pressure after standing boundary of leukocytes. Increased vascular permeability. Processes damage caused by the inflammatory agent apply to subcellular structures (mitochondria, lysosomes), which is damaging, emits large amounts of hydrolytic enzymes, the enzymes of glycolysis. With the destruction of lysosomes associated emergence of another group of biological compounds - prostaglandins. These biologically active substances improve vascular permeability for microbes and their toxins. Understanding the pathogenesis of inflammation that point requires the use in the treatment of patients in the acute phase inflammatory drugs that constrict blood vessels, reducing their permeability. Pathogenetically be caused by the use of inhibitors of proteolysis.

In the center stands a lot of inflammation kininov, together with prostaglandins responsible for the occurrence of pain in the affected organ. Pathogenetically conditioned anesthetic drugs are inhibitors of kinins and prostaglandins, which include preparations of acetylsalicylic acid (aspirin, indomethacin).

Violation of vascular permeability, vascular destabilization of membranes contribute to the fact that tissue out electrolytes (potassium, calcium, magnesium), so the correction of water-salt metabolism imperative.

Violation microcirculation standing boundary of leukocytes, increased aggregation formed elements transform the center of inflammation in chronic disseminated vnutrysudynnoho Center collapse. This point requires pathogenesis Antiplatelet agents used in the treatment.

The etiology and pathogenesis of chronic inflammation of genitals

If acute inflammation is the main factor microbial and definite etiological role that chronic inflammation that it does not matter. Etiological aspect of chronic inflammation can be any non-specific factors: aggravation of inflammation can be triggered by hypothermia, physical or psycho-emotional stress. But microbial factor. Knowledge of these features etiology of chronic inflammation radically changed approaches to the treatment of a large number of women suffering from this disease,

and led primarily to the failure of antibiotic therapy in chronic inflammation. However, in spite of the uniqueness of the relationship to the location microbial factors in the pathogenesis of chronic inflammation that characterizes today's level of knowledge, we must remember the possibility of the formation of inflammation in the heart of L-form bacteria,

Chronic PID to the fore the complex changes in the body that gradually get multisystem nature. Chronic inflammation of the genitals should be understood as a multisystem disease. There are changes in the nervous, endocrine, cardiovascular, immune, enzyme and other body systems.

Changes in the central and peripheral nervous system belongs to a leading role in the pathogenesis of common reactions inherent dovhodiyuchym inflammation of the uterus. Center inflammation in the genitals are the source of pathological impulses in the cerebral cortex, subcortical structures in the form of their painful dominant. Clinical manifestations of disorders of the nervous system doctor sees primarily in astenonevrotychnomu syndrome, emotional disorders. Changes function peripheral nervous system manifest themselves neuralgia, especially pelvic nerves steady hanhlionevrytamy that underlie sustainable pelvic pain syndrome.

It is important for the understanding and knowledge of proper treatment changes facing the vascular system. These changes relate to general and local, local reactions. There are significant regional circulation infringement in the form of shortage of blood supply and vascular dystonia small pelvis, are more pronounced in areas where a connective tissue, ie adhesions, scars. Vienna tubo ovarian plexus with irregular diameter, are convoluted, narrow, sklerozovani, varicose. If acute inflammation in vascular permeability centers increased inflammation, the process is chronic, by contrast, is reduced. This feature chronic inflammation explain the ineffectiveness of drug therapy in these diseases that are associated with the difficulty of penetration of therapeutic agents into the center of inflammation through a modified vessel wall. Changes in regional circulation accompanied by a slowing of blood flow, the formation of thrombosis that can cause sustained pelvic pain syndrome. Violation of venous outflow promotes varices small pelvis. On the other hand microcirculatory disorders contributes to the progression of disseminated intravascular coagulation syndrome. Deficiency of blood supply to the development of chronic hypoxic tissue eventually turns chronic inflammation center in the center of a potential cancer disadvantage. Understanding this point pathogenesis of chronic PID forced to abandon the tactics of prolonged conservative treatment of patients with inflammatory tumors. Common vascular reactions identified in vascular dystonia, vascular spasm with headache, pain in the heart. which can cause sustained pelvic pain syndrome. Violation of venous outflow promotes varices small pelvis. On the other hand microcirculatory disorders contributes to the progression of disseminated intravascular coagulation syndrome. Deficiency of blood supply to the development of chronic hypoxic tissue eventually turns chronic inflammation center in the center of a potential cancer disadvantage. Understanding this point pathogenesis of chronic PID forced to abandon the tactics of prolonged conservative treatment of patients with inflammatory tumors. Common vascular reactions identified in vascular

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Severe violations observed in the system of regulation of menstrual function, ie the system ovary, hypothalamus-pituitary-ovary. Dysfunction of this system is to change the production of gonadotropin hormone (follikulostymuyulyuyuchoho, LH), increased basal secretion, causing reduced production of sex hormones (estradiol and progesterone). Depressed function of the adrenal cortex.

In recent years, a great place in the pathogenesis of chronic diseases paid dysfunction of immune systems. Inhibition of T and B lymphocytes and their functional activity, the development of incomplete phagocytosis contribute to relapse process. Gaining importance not only of oppression reactivity, and her injury - develops autoalerhiyi phenomenon: the body ceases to recognize its own protein, modified microbial toxins and produces autoantibodies organic him. Organic circulating autoantibodies to tissue of the fallopian tubes, ovaries to respond antibody-antigen-antibody, which contributes to further destruction of the cells affected organ (tubes, uterus, etc.).

Much of set points in the pathogenesis of chronic inflammation is the result of research in recent years. This is largely changed attitude to the treatment of patients with chronic PID, namely one of the most common of them - chronic adnexitis. It became clear unreasonableness and even harmful antibiotics, calcium supplements, the need to stimulate or regulate the function of immune system, harm polypharmacy, especially against chronic autoalerhiyi PID.

The clinical picture of inflammatory diseases of the genitalia

In modern conditions PID have some features that significantly distinguish them from the clinical picture of disease 20 years ago. They are characterized by:

• erased clinical symptoms of the acute stage of the disease;

• advantage chronic processes, and in recent years the emergence of primary chronic diseases;

• resistant chronic relapsing course of processes;

• The most frequent localization of inflammation in the uterus;

• rare defeat parametrial tissue;

• purulent liquid development processes.

For classical picture of acute inflammation characterized by five classic signs of inflammation: calor, dolor, tumor, rubor, described Galen and funktia laesa, described Celsius. For inflammation of the uterus, the most frequent localization of genital inflammation characteristic temperature rise to 38-39 C below the belly pain radiating to the inner thighs, the waist. When vaginal study determined appendages enlarged, painful, swollen.

The presence of these signs of an acute inflammatory process pathognomonic, but no one of them should make the doctor think about the possibility of other pathologies and more carefully make a differential diagnosis.

However, in practice gynecologist dominated patients with chronic inflammatory diseases, the most frequent lesion of the uterus, vaginal mucosa, cervix. These patients make up 85% of all patients with genital inflammation. In this complaint often do not meet the changes that are an objective study of the reproductive system. If there malovyraznyh changes (slight compaction, minor pain, minor limitations in mobility with no increase organ) patients complain of significant deterioration, impaired sexual, menstrual, generative function. This feature consists of a clinical picture of chronic inflammation of the genitals. Patients suffering poliskarhiyeyu often by patients and many specialists, neurologists, gastroenterologists and surgeons.

If acute inflammation characteristic identified five signs of inflammation, it manifests a chronic process itself persistent painful syndrome and dysfunction of the affected organ and other regulatory systems. Of pain is the leading symptom of chronic inflammation, regardless of its location. Its morphological basis - it fybrotyzatsiya, sclerosis tissue involvement in the process of development of pelvic ganglia hanhlionevrytiv and the same experiences in distant organs (solarium and others.). Pain is a different character, dull, aching, pulling, increasing, constant or intermittent.

For chronic inflammation characterized by pain reflex (reperkusyvni) arising on the mechanism and vistserosensornyh viscero-kutannyh reflexes. Pain below the belly is diffuse, often localized in the right lion or groin area in iradiyuye sacrum, vagina, rectum, in the back, in the lower limbs. There are areas of increased skin sensitivity (zone Zaharyina-Ged) in inflammation of the genitals. They spread from the breast to X IV lumbosacral (lumbar) vertebrae (ovary - chest X, fallopian tubes - XI chest, uterus - IV lumbar).

There is a frequent headache (fronto-temporal lobe, neck), sometimes diffuse as migraine (in the second half of the menstrual cycle). Sometimes it bothers pain in the cervical spine, arms, between the shoulder blades, hands, feet. For patients PID characteristically unstable mood, tendency to depression.

Functional disorders confined to specific changes in sexual function disorders of the central and peripheral nervous system dysfunction of vital organs (liver, kidney).

Menstrual dysfunction appears hypermenstrual, less hypomenstrual, premenstrual syndromes. Menstrual dysfunction can occur without clinical manifestations, but the special survey (functional diagnostic tests, quantification of the hormones that are required for these patients) often luteal phase deficiency, frequent anovulatory cycles. Chronic anovulation in modern gynecology regarded as a precancerous condition, hence understandable bound onkonastorozhenosti out for patients with chronic PID.

Inflammatory diseases of the genital organs are the most common causes of abuse generative function, resulting in infertility, miscarriage, advancing threat of interruption of pregnancy. The main cause of infertility - a violation of tubal patency due process of adhesion, breach of morphological and functional properties and motility of epithelial tube. The cause of infertility can be peritubarnyh development of compounds with the formation of bends, deformation tube that extends and complicates the transportation of a fertilized egg and can cause ectopic pregnancy. The development process of adhesive around the ovary prevents its further progress towards the fallopian tube. The cause endocrine infertility (often it is accompanied by anatomical changes fallopian tubes) for inflammation of the genitals is anovulation, LPD. Considerable importance in breach of generative function play cervicitis, vaginitis, changing physical and chemical properties of cervical mucus. It should be remembered when examining women with infertility nekrotoksychnyy impact on vaginal microflora during its inflammation in the sperm.

There is a violation of sexual function in patients with chronic adnexitis. There are often situations where the patient is not able to express complaints taught, and whether the doctor forgets or does not add to this disease since neglected, leaving the patient alone with their suffering. And often these abnormalities cause sexual function disorders and family tragedies. Fryhydnist, sexual dissatisfaction should be taken into account when compiling the history and patients should be consulted relevant experts.

For chronic adnexitis characteristic lesion of neighboring organs, the most frequent are organs of the gastrointestinal tract. It should be remembered that these diseases often accompany each other, with bowel disease (colitis) may be primary, or vice versa. Regulation impaired bowel function, which manifests itself especially

constipation if the bowel wall becomes easy to penetrate bacteria and their toxins are particularly necessary for people with genital inflammation.

Diagnosis PID in the acute stage arranged on the anamnesis and objective research (five classical features, characteristic changes in blood: increased erythrocyte sedimentation rate, left shift formula of white blood cells), non-specific biochemical changes characteristic of blood (CRP increase seromucoid, syalovyh acids) rapid regression of clinical manifestations during antibiotic therapy.

Differential diagnosis in the acute stage is carried out with an ectopic pregnancy, acute abdominal disease voids (acute appendicitis), sometimes cancer patients.

Many problems can arise when diagnosing inflammatory diseases in a chronic stage that flows by type of trace reaction. The absence of pathognomonic manifestations characteristic changes in blood biochemical indicators of demand from the doctor is very thorough examination, differential diagnosis and shift the bulk of the auxiliary paraclinical diagnosis methods (methods of functional testing, laparoscopy, metrosalpynhohrafiya, virological and bacteriological methods of research). Constant pelvic pain syndrome may be exposed colitis proktosyhmoiditam (proctology offer a diagnosis of "irritable bowel syndrome") for varicose veins ovarian, uterine plexus (remember varicose veins, revealing a sense of weight, intense pain) with endometriosis (constant pain amplified with the beginning of menstruation), which may exist independently, but often develops in chronic inflammation centers and supported by some of its pathogenetic moments (autoalerhiya). Chronic adnexitis should be differentiated from chronic cystitis, chronic appendicitis, Alain-Masters syndrome (wide gap rear leaf uterine binding), specific inflammation (tuberculosis genitals). Availability complaints of pain below the belly still gives cause for the diagnosis of "chronic adnexitis." Alain-Masters syndrome (wide gap rear leaf uterine binding), specific inflammation (tuberculosis genitals). Availability complaints of pain below the belly still gives cause for the diagnosis of "chronic adnexitis." Alain-Masters syndrome (wide gap rear leaf uterine binding), specific inflammation (tuberculosis genitals). Availability complaints of pain below the belly still gives cause for the diagnosis of "chronic adnexitis."

Modern principles of treatment of inflammatory diseases of genitals

Modern PID treatment strategy should be based on all of the following principles:

1. Accurate diagnosis stages of disease (acute and chronic), its type (acute toxic on the type of infection or illness, the type of trace reaction);

2. Targeting a turnover of changes in inflammation and centers of decision-making on conservative treatment (non-operational) in turnover and surgery with irreversible structural changes. The latter include processes such as piosalpinks, piovarum, Gidrosalpinks in the absence of positive clinical dynamics after a rational long-term treatment and long existing presence of inflammatory tumors of the uterus, which can be benign or malignant ovarian tumors. Lack of objective or subjective surround speakers with the existence of the formation in the pelvis, which is regarded as inflammatory tumor, should be an indication for surgery. The presence of such formation in women over 40 years should be an absolute indication for surgery.

3. Strict clinical studies, rational antibiotic therapy. Etiological justified in acute inflammation is the use of drugs with antibacterial action. In the chronic stage (during remission and exacerbation with no signs of acute inflammation) antibiotics are not used. Exceptions to chronic process are two clinical situations where antibiotics are used all the same:

a) if this patient is not used or if used inefficiently (insufficient dose, wrong selection of antibiotic irrational route of administration);

b) an exacerbation of the inflammatory process that occurs on the type of toxic-infectious inflammation if accompanied by objective signs of subjective symptoms (exudation, pain in the two-handed study, increased body temperature, increased sends, the number of white blood cells).

4. Priority eliminate chronic pelvic pain that accompanies chronic inflammation. This pain pathogenesis is very complex, negatively affects many aspects of life of the organism, directly on the centers of inflammation, prevents defibrotyzuyuchiy of drugs. Leading role in addressing chronic pelvic pain are playing non-drug therapies.

5. Treatment oligosymptomatic forms of inflammation of the uterus and appendages. It is important for the prevention of infertility, miscarriage and other disorders specific functions and preventing the transition process in local multisystem disease.

6. The base role of non-drug methods of treatment of chronic inflammatory diseases.

7. Destabilization pathological homeostasis by chronic activation process to enhance clinical efficacy of treatment (bacterial polysaccharides: prodigiozan, pirogenal in conjunction with antibiotics, especially in the presence of extra-inflammation).

8. The need to evaluate the initial hormonal ovarian function. This principle is common in the treatment of any pathology genitals. Genitals are the target organs for their actions. In identifying the relative hiperestrohenemiyi should abandon the medicines that increase steroidogenesis (production of estrogen and progesterone). In carrying out the treatment without considering this factor is possible to optimize the conditions for hormone-dependent diseases - uterine fibroids, endometriosis, endometrial hyperplasia, mastitis. Recovery of ovarian function in its decline, with a disabled luteal phase, anovulation when appropriate to implement without hormones. It is easier to manage in younger women, with little duration of inflammation (up to 5 years), or the absence of infantilism initial endocrine disorders.

9. Compulsory union practices overall impact on the body in order to correct altered function of therapeutic agents with local authorities on the reproductive system.

10. Treatment of chronic inflammation centers extragenital localization.

11. Mandatory compliance phasing treatment, hospital (acute inflammation of chronic treatment process should be at least 3 weeks) - antenatal clinic (patient continues undertaken in hospital physiotherapy) - Resort (for rehabilitation of affected systems in 4-6 months acute stage of the disease).

The main treatments for inflammatory diseases of genitals

Based on the basic provisions of the etiology and pathogenesis of basic principles and approaches to the treatment of acute inflammation, treatment is performed as follows:

1. Treatment is required in a hospital. Daily bed. The patient - in bed with raised head end (to prevent the spread of per continuitatem). Local dosed hypothermia (hardware or lead to 10 after 10 minutes for 2 hours three times a day).

2. Antibiotic therapy is antibiotic group nitrofuranovogo drugs (furadonin, furazolidone) sulfanilamides (short, medium and prolonged duration of action) that have self-importance - and a number of drugs metronidazole (metronidazole, Metrogyl, trihopol). Antibiotics will take place in major medical complex. At the onset, if laboratory data on the nature of the pathogen and its sensitivity absent recommended to prescribe antibiotics prescribed focusing on the etiology of the disease. Assign semisynthetic penicillins (methicillin - 6.12 g / day, oxacillin - 3-6 g / day, Ampicillin - 4-6 g / day, ampioks - 2-4 g / day); cephalosporins (tsefaloridyn, fefalozolin, kefzol - up to 4.6 g / day); aminoglycosides (kanamycin - up to 2 g / day gentamicin - 1,60-2,40 g / day). Ways input: internally ' muscle, intravenous, directly through the rear appendages vaginal vault. The duration of a course of antibiotics - at least 7 days.

Given the high frequency of association of aerobic and anaerobic flora is recommended prescribe metronidazole series (trihopol 4 tablets a day for 5 days in Metrogyl / 100ml tively) hyperbarooksyhenatsiyu (HBO).

Some principles antibiotic contradictory. For example, in practice the doctor often assign multiple antibiotics, given associativity flora - the causative agent. However, there is opinion - his defending microbiologists - the more appropriate and justified logically combining antibiotics in time: after 4 days if the flora begins to get used to the antibiotic should be replaced with another. It is advisable to combine antibiotics with sulfonamides, especially when administered penicillin, sulfonamides inhibit penicillinase, thus enhancing the effect these antibiotics. It also makes it possible to reduce the dose of penicillin.

Remember that antibiotics being necessary preparations, caring for the body. Along should definitely prescribe vitamin B, vitamin With prolonged use of antibiotics, antifungal drugs (Nystatin, levorin, multivitamins).

3. Detoxification therapy is carried low molecular weight plasma substitutes: reopolyglukine, gemodez, neokompensan, 5% sodium bicarbonate district 200 ml district of glucose 5% - 500 ml saline. The total volume of fluid introduced into the body, depending on the weight and position is defined by 40-45 ml per 1 kg of the patient.

4. Mandatory use of drugs that improve blood rheology. This action is inherent in the group of low plasma substitutes. Suitable heparin at a dose of 2,5-5,0 thousand. From 2-4 times, aspirin.

5. Protease inhibitors (hordoks, kontrikal, zymofren, aminocaproic acid).

6. Immunomodulators (timalin, timohen, splenin, levamisole), plasma preparations (dry, native, hiperimunizovana, antistaphylococcal, antykoli-plasma antyesherihiyi -

plasma - at 100-150 ml / 3-5 times daily or every other day range - 3 doses of globulin within 3 days 3 times.

7. Analgesic effect is intended aspirin dosage hypothermia, laser therapy.

8. Local treatment is performed by assigning baths, washing, douching disinfectant solution (furatsillina, dimeksid, dyoksydin, chlorophyllipt) Herbal decoctions (celandine, marigold, rose petals, chamomile, sage, yarrow, and others.).

9. With the stabilization of inflammation and no signs of festering 10-12 days can assign physiotherapy treatment: eritemoterapiya ultraviolet, magnetic, dynamic currents.

Treatment of chronic inflammation

Recall again: not prescribe antibiotics, drugs 10% solution of calcium. Drug therapy should be minimized.

1. Elimination of pain: micro enema with warm 0.25% novocaine solution for 6-7 days; micro enema with a 5% solution of potassium iodide, especially when the adhesive process in the pelvis, presakralna novocaine blockade; analgesic tablets, prostaglandin inhibitors (aspirin, indomethacin and other non-steroidal anti-inflammatory drugs).

2. Extensive physical therapy appointments (preformed physical factors):

- galvanization (electrophoresis KJ, Ag, vaginal, intrauterine, cervical);
- HF (darsonvalization, diathermy, inductothermy); UHF and microwave;
- Ultrasound, phonophoresis, peloyidofonoforez;
- magnet;
- phototherapy;
- acupuncture;
- natural physical factors (climate balneotherapy).

3. Sedatives.

4. Correction of hormonal background, electrical cervical 5 to 23 day menstrual cycle, endonasal electrophoresis with vitamin B1, laser stimulation, vitamin (vitamin U1-1 ml per day in the cycle and phase of vitamin C - in the second phase), non-hormonal therapy after failure appointed by sex and gonadotrophin depending on the type of menstrual dysfunction.

5. Desensitizing therapy: diphenhydramine on 1 tab., Tavegil on 1 tab., Suprastin on 1 tab., 2 times a day for 7-10 days.

6. Antiplatelet agents - drugs that improve the microcirculation in the vessels of the pelvis and the whole body (gemodez 100-200 ml / v, reomakrodeks 100-200 ml / v, 3-5 times a year; aspirin on 1 tab. 3 times 7 days).

7. Protein drugs, amino acids and mixtures (alvezin, polyamine, aminosterol); to destabilize the pathological center - bacterial polysaccharides (prodigiozan 0.5 ml / m at intervals of 3-5 days pirogenal / m ranging from 25-50 MPD 1 time in 2-3 days, increasing the dose at each input of at 25- 50 MTD depending on the response, the course of 10-15 injections. when the temperature is accompanied by changes in the

blood picture, prescribe antibiotics. in the absence of changes in the blood picture, fever should be regarded as inflammatory reaction center, the patient does not require appointments antibiotic therapy can assign etc. intolerance hyperthermia and fever-reducing drugs (aspirin tablets or injections aspizol in.).

8. Remediation Center inflammation vaginal phonophoresis dimexide - 6 ml, chlorophyllipt - 2 ml, novocaine - 2 ml; intrauterine electrophoresis aloe, magnesium sulfate, zinc sulfate.

9. Immunotherapy (plasma / v, autovaccine, stimulators - aloe torfot, vitreous, mabistin, peloyidodistilat a month).

10. When infertility associated with obstruction of the fallopian tubes - enzymes (32-64 lidasa from, himotrypsin 5-10 mg injections, ronidaza using phonophoresis on the lower abdomen). Given the fact that enzymes are in direct contact with tissue, optimal way of administration of these drugs are injected through the back or set their input into the void uterus using hidrotubatsiy.

11. Spa treatment (with obligatory accounting hormonal background) that combines the performance of many factors: health regime (with the exception of daily life and work environment, peace, good food), climate (climatotherapy), a ray of sunlight (heliotherapy) mud with thermal factors (natural or artificial heat mud), vaginal irrigation mineral bath (carbonate, chloride, sodium, which are composed of arsenic, brackish), which broadly act on the body, destabilizing the pathological center polipshuyut b circulation rates, increase ovarian estrogen activity. Wide use is made of hydrogen sulphide and radon baths. Mud combined with physiotherapy, potentsiyuyuchy each other.

In addition to the treatment of acute and chronic inflammation of the genitals, belonging to the conservative and surgical methods used.

Indications for emergency surgery for acute genital inflammation are:

- diffuse peritonitis;
- piosalpinks gap;
- No effect 24 hours after abdominal drainage voids by laparoscopy.

Routinely is done in the presence of purulent inflammation appendages, Bursiform inflammatory tumors. The optimum time for the operation is the remission process. The volume of transactions depends on the nature and spread of the destructive process, the patient's age, medical history, potential onkonastorozhenosti. When performing the operation should be most carefully treat ovarian in all ages of women, observing parallel onkonastorozhenosti maximum. At a young age the operation is limited to the removal of the affected organ (usually fallopian tubes), and after the age of 45 years - expanding the volume of transactions (removal of the uterus, ovary possible).

Prevention of genital inflammation

Prevention consists primarily:

- of personal hygiene, sexual health;

- detection and treatment of chronic inflammatory extra-centers of origin, especially bowel disease;

- preventing unwanted pregnancies, which interrupts the body inflicts irreparable harm women because it leads to reproductive tract infection, menstrual dysfunction, infertility;

- rational organization of work and life with the exception of hypothermia, physical or mental overstrain;

- balanced diet that will prevent vitamin deficiencies, hypoproteinemia.

Inflammatory diseases of the genitals is one of the most common diseases of the genital organs. The most common form of the clinical flow is chronic, and localization - chronic adnexitis. The disease pathogenesis is very complex, requiring timely, well-reasoned, pathogenetic due treatment to prevent serious complications (infertility, malignancy, menstrual dysfunction) and invalydizatsiyi women.

Students who have received the data for independent work, supervise patients, dismantle and analyze history data, interpret the data.

5. Materials of student activization during lecture:

Questions:

1. What classification of ectopic pregnancy do you know?
2. What causes of ovarian apoplexy do you know?
3. What diagnostic methods are used to diagnose an ectopic pregnancy?
4. What is pelvioperitonitis?
5. What differences do you know between trichomoniasis and gardnerellosis?
6. What laboratory tests should be used to diagnose chlamydia?
7. What general methods of treatment of inflammatory diseases in gynecology do you know?

6. Self-control questions on the topic:

1. Inflammatory diseases of female reproductive organs: classification, aetiology, pathogenesis. Features of the course in different age periods.
2. Inflammation of the external genital organs and vagina (vulvitis, bartolinitis, vaginitis): clinical features, diagnosis and treatment.
3. Inflammation of the internal reproductive organs (endocervitis, endometritis, adnexitis, parametritis, pelvioperitonitis): clinical features, diagnostics, treatment, general practitioners' strategies.
4. Sexually Transmitted Diseases (trichomoniasis, gonorrhea, ureaplasmosis, mycoplasmosis, chlamydia, viral lesions): general practitioners' strategies in the detection of sexually transmitted diseases. Clinical features, diagnosis and treatment.
5. Ectopic pregnancy – clinical features, diagnostics, emergency care, general practitioners' strategies.
6. Ovarian apoplexy: clinical features, diagnostics, emergency care, general practitioners' strategies.

RECOMMENDED LITERATURE

Basic:

1. Obstetrics and Gynecology: in 2 vol.:textbook. Volume 2. Gynecology / V.I. Gryshchenko, M.O. Shcherbina, B.M. Ventskivskyi et al.; edited by V.I. Gryshchenko, M.O. Shcherbina. — 3th edition. – K.: AUS Medicine Publishing, 2022 – 352 p.
2. Obstetrics and Gynecology: in 2 vol.:textbook. Volume 1. Obstetrics / V.I. Gryshchenko, M.O. Shcherbina, B.M. Ventskivskyi et al.; edited by V.I. Gryshchenko, M.O. Shcherbina. — 2th edition. – K.: AUS Medicine Publishing, 2018 – 392 p.
3. Oats, Jeremy Fundamentals of Obstetrics and Gynaecology [Text]: Liewellyn-Jones Fundamentals of Obstetrics and Gynaecology / J. Oats, S. Abraham. – 10th ed. – Edinburgh [etc.]: Elsevier, 2017. – VII, 375 p.
4. Llewellyn-Jones Fundamentals of Obstetrics and Gynaecology (10th Ed). Jeremy Oats, Suzanne Abraham. Elsevier. 2016. – 384 pp.
5. 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. Modern technical teaching aids (see appendix to the work program of the 4th year)
2. 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)
3. Normative documents of the Ministry of Health of Ukraine on obstetrics and gynecology:

- Order No. 676 of 12/31/2004 "On approval of clinical protocols for obstetric and gynecological care"
- Order No. 782 dated 12.29.2005 "On the approval of clinical protocols for obstetric and gynecological care"(as amended in accordance with the orders of the Ministry of Health)
- Order No. 502 dated August 29, 2008, "On approval of the clinical protocol for antibacterial prophylaxis in surgery, traumatology, obstetrics and gynecology"
- Order No. 417 dated 15.07.2011 "On the organization of ambulatory obstetric and gynecological care in Ukraine"
- Order No. 955 dated 05.11.2013 "Procedurecarrying out emergency post-contact prevention of HIV infection among employees in the performance of professional duties".
- Order No. 59 dated 21.01.2014 On the approval and implementation of medical and technological documents on the standardization of medical care for family planning.
- Order No. 236 dated 02.04.2014 "Papproval and implementation of medical and

technological documents on the standardization of medical care for dysplasia and cervical cancer".

- Order No. 319 dated 06.04.2016 "On the approval and implementation of medical and technological documents on the standardization of medical care for genital endometriosis"
- Order No. 353 dated 04/13/2016 "On the approval and implementation of medical and technological documents on the standardization of medical care for abnormal uterine bleeding"
- Order No. 869 dated 05.05.2021 "On approval of the unified clinical protocol of primary, secondary (specialized), tertiary (highly specialized) medical care "Endometrial hyperplasia"

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