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MORPHOMETRIC CHARACTERISTICS OF THE CERVIX IN THE NORM, WITH BACKGROUND AND PRECANCER DISEASES

(Literature review)

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Despite a significant number of works devoted to the study of the organs of the female reproductive system in different age periods, in our opinion, the quantitative morphological structural components of the cervix have not been studied enough. The characteristics of the morphological components of tissues and organs are not presented in publications, which determines the relevance of performing work on the morphological profile using morphometric methods in this direction.

Key words: stratified squamous epithelium (SSE), columnar epithelium (CE), cervical ectopia (CE), chronic cervicitis (CC), cervical intraepithelial neoplasia (CIN I, II, III).

The problem of protecting women's reproductive health remains extremely relevant today due to the continuing threat of depopulation. (1) Reproductive health indicators over the past decades indicate a steady increase in gynecological diseases With the development and improvement of modern methods of immunohistochemistry and molecular biology, new opportunities have appeared for assessing the morphogenesis of neoplasms, proliferative and secretory activity of cells. (2) Foreign pathologists are trying to answer a number of questions regarding background and precancerous changes in the cervical epithelium. At the same time, most of the works are devoted to the description of individual observations of rare morphological forms or to the clinical and morphological study of small groups of patients (3)

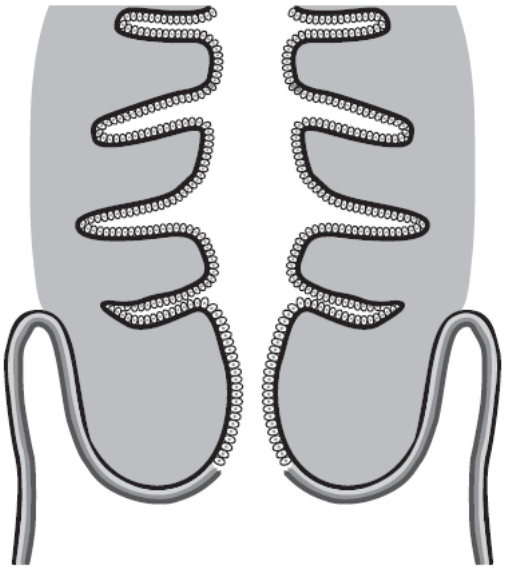
By the time of delivery, the uterus of newborns reaches a length of up to 38 mm, and then decreases somewhat due to a decrease in the level of estrogen hormones. From the moment of birth to the year of life, in parallel with a gradual decrease in the thickness of the wall of the uterine body and the size of myocytes, the area occupied by the main substance decreases, and the relative number of fibrous structures increases. At 4–7 years of age and further at 12–15 years, the uterine wall thickens, the area occupied by the main substance increases, and the relative amount of fibrous structures decreases.

In an adult woman, the uterus is on average about 7–8 cm long, 4 cm wide, and 2–3 cm thick. uterus is 4-6 cm3. In the age period of 16–47 years, the uterine stroma zones acquire a typical structure. At 48–55 years, the wall of the uterine body becomes thinner, in the first zone the number of elastic fibers increases; in the second, third and fourth zones, the number of elastic and collagen fibers also increases; in the fifth zone - only collagen and in the sixth zone - reticular fibers. At 75–90 years old, senile atrophy of the uterus occurs, which is accompanied by a decrease (up to 2.5%) in the area occupied by the main substance, a decrease in the number (up to 29.4%) of collagen fibers in all zones of the myometrial stroma [4,5,6.] .

In girls who have not reached puberty, the cervix has a conical shape, the same shape can be observed in infantile women. In women of childbearing age, the shape of the cervix, as a rule, is cylindrical;

As you know, the cervix is the caudal part of the uterus, located partially in the upper part of the vagina, 2–3 cm long. It is a smooth muscle organ formed by connective tissue (stroma) with vessels, as well as muscle and elastic fibers.

The border of the cervix and body of the uterus, where the cervical canal ends, is commonly called the internal os. The external opening of the canal, which opens into the vagina, is commonly called the external pharynx (Fig. 1). The anterior lip of the cervix is usually larger than the posterior lip. In girls, the cervix of the uterus is conical in shape with a punctate rounded pharynx, in those giving birth it is cylindrical in shape with a slit-like pharynx [7,8].

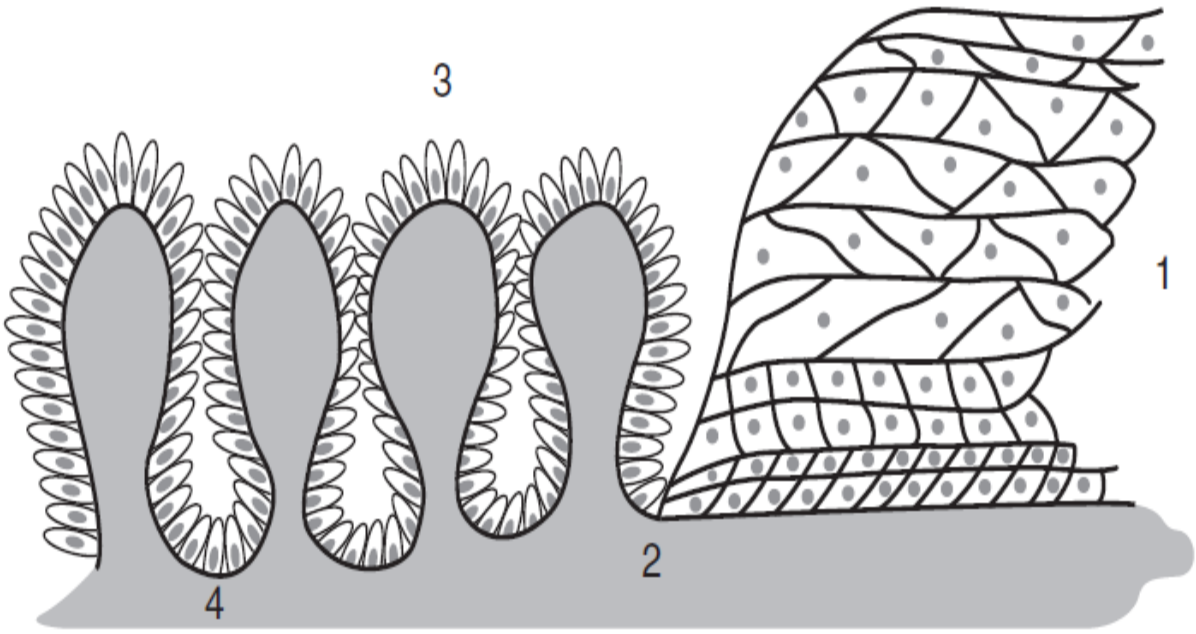


Pic. 1. The structure of the cervix is normal

The vaginal part of the cervix (exocervix) is a dense fibrous connective tissue (stroma), which is covered with stratified squamous epithelium (SSE).

The stroma under the MPE consists of collagen and, to a lesser extent, elastic fibers, among which are cellular elements: fibroblasts, histiocytes, lymphocytes, blood and lymphatic vessels, which intertwine and form complex plexuses. The content of muscle tissue is about 15% of the total mass of the tissue component of the cervix, it is located mainly in the upper third of the cervix, near the cervical canal (CC) and is represented by circularly arranged muscle fibers that provide a locking function. Connective tissue contains two types of fibers: collagen and elastin. The former create a strong frame, while the latter provide reversible changes in the size of the CMM. Blood and lymphatic vessels, as well as nerve fibers pass through the thickness of the wall. [7].

The MPE is thin, almost colorless, without vessels, as a rule, has a thickness of about 150–200 μm, and consists of 4 layers of cells (basal, parabasal, intermediate, and superficial). The MPE is capable of constant renewal due to the continuous desquamation of the surface layers (its renewal cycle averages 4–5 days). Its main function is protective. Normally, the MPE joins with the columnar epithelium of the cervical canal in the area of the external os. A schematic representation of the MPE structure is shown in pic.2.



Pic. 2. Schematic representation of the stratified squamous epithelium (1), columnar epithelium (3), covering the stroma (4), and their junction (2)

The basal layer of the MPE is located on the basement membrane separating it from the stroma. In histological analysis, the basal lower layer is represented by one row of rounded or low-cylindrical cells with a relatively large oval nucleus rich in chromatin. This layer is a reserve, thanks to it there is a constant replenishment of MPE cells. Melanocytes are sometimes found among the cells of the basal layer.

The parabasal layer consists of 2–3 rows of polygonal cells with large nuclei, basophilic cytoplasm, low glycogen content, and high mitotic activity.

Above it is an intermediate layer, which consists of large polygonal cells with small nuclei, light cytoplasm, and a high content of glycogen. The closer the layer is to the surface of the epithelium, the higher the differentiation of cells and the content of glycogen in the cytoplasm. The topmost layer of the epithelium is called the superficial. It has a cellular structure, and its nuclei are few and pycnotic, the cytoplasm is abundant, eosinophilic due to the high content of keratin microfilaments [9, 8].

MPE responds subtly to hormonal influences during the menstrual cycle and in various disorders. Estrogens stimulate the proliferation of the basal layers, the maturation of glycogen in the intermediate and keratin in the superficial layers [10].

The cervical canal has a fusiform shape, its mucous membrane is represented by numerous folds and ridges that form crypts with a depth of 4 mm or more. Histologically, they are called cervical glands. There are no true tubular glands in the cervical canal and exocervix. An element of the endocervix are pseudoglands or crypts, the cells of which secrete mucus, therefore, when viewed, the epithelium lining the endocervix always looks juicy, moist.

Normally, the canal is lined with a single-layered columnar epithelium (CE) lying on the basement membrane, with high cylindrical cells, basally located nuclei and a large number of vacuoles associated with mucus production. The secret of these cells is acidic and neutral mucins, the secretion of which is carried out using apocrine and merocrine types of secretion [7].

On the basement membrane under the environmental CE, pluripotent methods of reserve cells are called, following the study of the process of determining the epithelium. Differentiation of reserve cells can take place both in columnar and squamous epithelium [11]. The histological structure of CE and MPE is shown in photo 1, a (see color inset).

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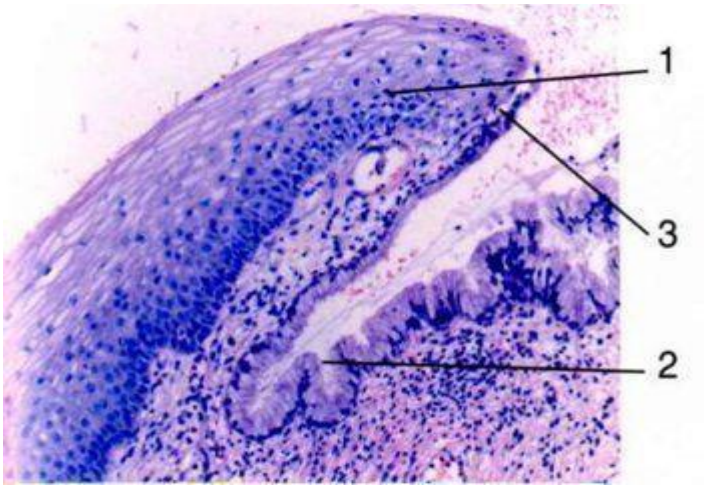
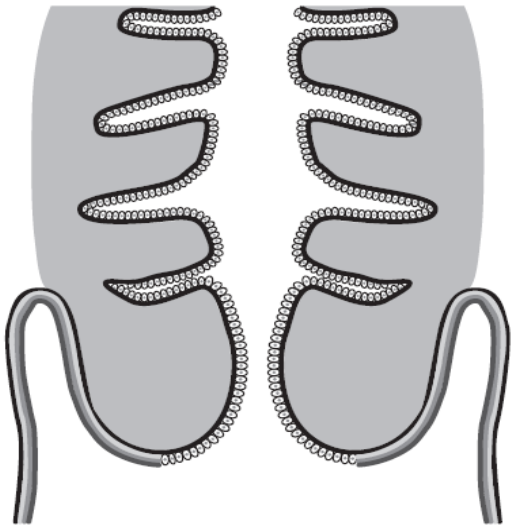


Photo 1, a Histological structure of the epithelium of the cervix. MPE (1) and CE (2) are joined (3). Stained with hematoxylin and eosin

In women of reproductive age, the junction of these two types of epithelium is normally located in the area of the external os, it can be located on the exocervix in young women, and inside the cervical canal in older women. The location of the CE on the exocervix is called ectopia (pic. 3).



pic. 3. The structure of the cervix with ectopia

"Problem within the problem" are also "benign" diseases of the cervix - morphological and functional changes in the mucous membrane of the cervix of an inflammatory, post-traumatic and dyshormonal nature, in which the stratification of the layers of the epithelium is preserved. Their frequency in the structure of gynecological diseases is 25-45%, while chronic cervicitis (ChC) (67.7%) (12.13)

EC is registered in 47.5–80.8% of women with ChC (11). ChC is one of the leading causes of the development of complicated EC and causes recurrence of the disease (14).

Among the factors causing CC, HPV-associated cervicitis is of great relevance due to their role in the development of precancerous processes and cervical cancer (12; 15; 16.17.). Inflammatory processes in the exo- and endocervix can lead to the development of endometritis and, consequently, impaired reproductive function (18). Many fundamental studies are devoted to the problem of complicated ESM (19; 20: 21). However, today it is necessary to clarify the spectrum of etiological factors leading to the occurrence of complicated ESM in modern women and to improve the treatment and diagnostic approaches for this pathology, taking into account the structural rearrangements of the endocervix.

Ectopia of the cervix (ESM) - displacement of the boundaries of the cylindrical epithelium on the vaginal part of the cervix [22.]. Normally, the area of transition of MPE to CE in a woman of reproductive age is more often localized in the area of the external uterine os, and in the postmenopausal period, the transition zone shifts to the lower third of the cervical canal [23]. In this case, ESM is defined as an atypical location of the CE on the exocervix [24.].

Atrophic changes in the cervix that develop with a deterioration in trophism against the background of a decrease in microcirculation are considered as a result of age-related estrogen deficiency. In 88% of patients, atrophic changes of a diffuse nature were observed, in 12% - focal. In addition, atrophic changes can be combined with an inflammatory reaction of the exocervix - atrophic nonspecific exocervicitis (70% of patients). The main difference between this process and inflammation of the cervix in women of reproductive age is the absence of edema and hyperemia, uneven thinning of the mucous membrane with easily damaged vessels of the subepithelial layer (25,26,27)

Precancerous conditions of the cervix epithelium include MPE dysplasia, endocervical epithelial dysplasia, and adenocarcinoma in situ. The term "dysplasia" is a morphological and at the same time a clinical concept and includes the process of cell proliferation with the appearance of atypia in them, especially nuclear, followed by a change in the entire structure of the epithelium, loss of the normal layered structure [28, 29].

It is believed that dysplasia, which is clinically manifested in the appearance of atypical (transformation zone) ST, occurs when HPV and other cofactors interfere with the process of normal metaplasia.

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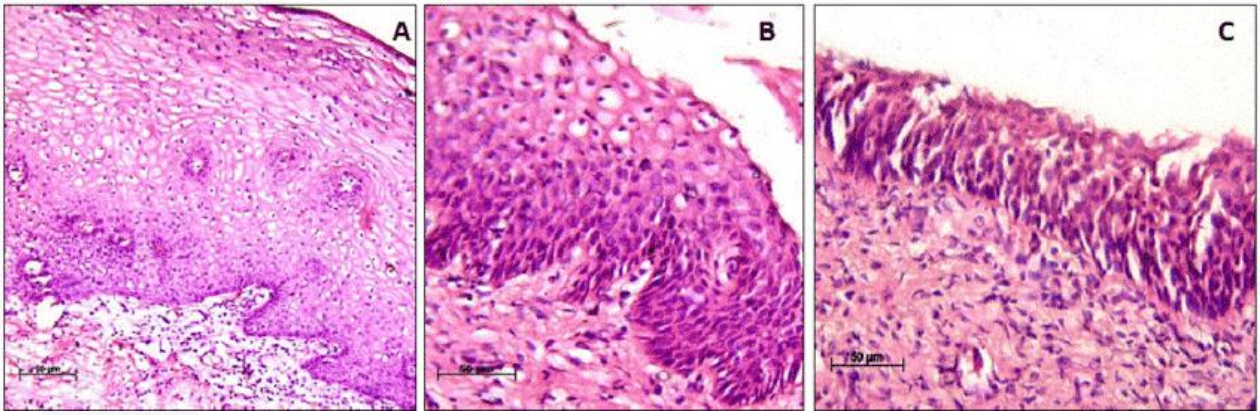
Depending on the intensity of cell proliferation and the severity of structural and cellular atypia in the epithelial layer, mild CIN I (photo A, see color insert), moderate CIN II (photo B, see color insert) and severe CIN III (photo C) are distinguished. , see color insert) dysplasia, characterized by the appearance of atypical cells first in the lower third, then in the lower two thirds, and finally in the entire thickness of the MPE, including the more superficial parts, respectively.



The modern paradigm of cervical cancer development is based on the stages of progression of dysplasia from mild to severe. In other words, all types of epithelial changes that precede the development of squamous cell carcinoma represent a single pathological process [28]. The condition when the expansion of atypical cells continues beyond the basement membrane is called invasive cancer (cancer).

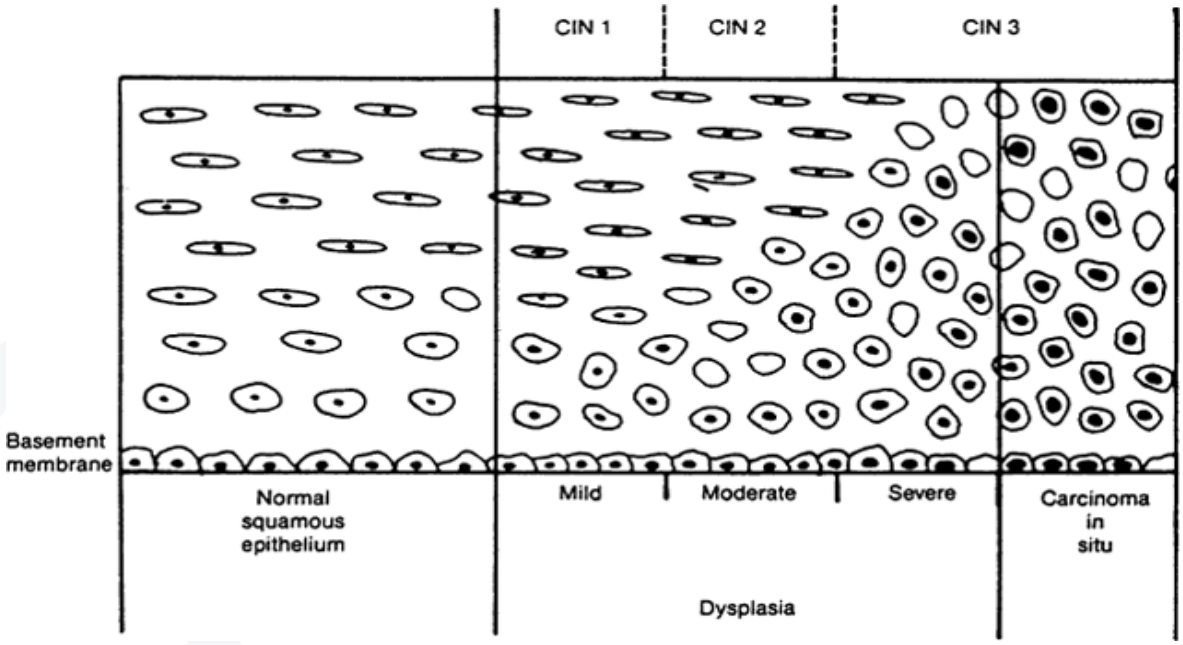
CC is the result of a multi-stage process of tumor conversion against the background of persistent papillomavirus infection, during which cervical intraepithelial neoplasia (CIN I, II, III), preinvasive and microinvasive cancer successively replace each other for several years and even decades [8].

There are still ongoing discussions about morphological criteria to determine the potential for malignancy of each of these conditions. The pattern of cell atypia (dyskaryosis) is thought to change and increase as the degree of CIN progresses.

Questions of terminology and classifications of precancerous conditions of cervix, vagina and vulva remain the subject of discussion. As William Farr said in 1856, “Classification is a method of communication.

Several classifications can be successfully used: the clinician, the pathologist, and the lawyer, each from his own point of view, can justifiably classify diseases and causes of death in a way that will most contribute to the solution of the issue under study and help to come to general conclusions” [30].

At the XI International Congress on the pathology of the cervix and colposcopy (1975), instead of the name "dysplasia and carcinoma in situ", the term "cervical intraepithelial neoplasia" (CIN) was proposed with the allocation of three degrees of severity: CIN I and CIN II degrees correspond to mild and moderate dysplasia , CIN III includes both severe dysplasia and preinvasive carcinoma (Fig. 4.). The combination of severe dysplasia and ip situ carcinoma in ClN III was associated with the similarity of their ultrastructural and cytogenetic features, as well as biological potency [7].



Pic. 4. Correlation of classifications for CMM lesions

At the end of the XX century. it was found that changes in the epithelium, characteristic of dysplasia, are observed during infection with HPV. In relation to such structural changes, the names "koilocytotic atypia", "koilocytosis", "condyloma flat" were used, which began to be combined with the terms "mild dysplasia", CIN I due to the similarity of their morphological features and difficulties in differentiation.

In order to better understand the essence of precancerous processes of the cervix, the National Institute for Research on Cancer (USA) developed their new cytological classification (Bethesda system, 1988, with subsequent revision in 1991).

In this classification, mild dysplasia is grouped with PVI (koilocytotic atypia, condyloma squamous) as low-grade squamous intraepithelial lesions (LSIL), and CIN II–III are grouped as high-grade squamous intraepithelial lesions (HSIL).

These concepts are gradually extrapolated to the histological criteria of precancer and clinical and colposcopic practice. In this edition, the Bethesda Terminology System

(TBS) is used to designate clinical and colposcopic situations, as has been customary in recent years in developed countries [30]

The localization of the process of cervical dysplasia also depends on the age of women. For young women, the most typical localization is the vaginal part of the cervix, with age there is a tendency to move to the endocervix. The maximum number of epithelial dysplasia against the background of ectopia is observed at the age of 36–45 years (8.5%). According to multicenter epidemiological studies, the maximum number of infectious lesions of the cervix occurs at 18–30 years, and the peak of dysplasia and preinvasive cancer occurs at 30–39 years [31.32.].

With the development and improvement of modern methods of immunohistochemistry and molecular biology, new possibilities have appeared for assessing the morphogenesis of neoplasms, proliferative and secretory activity of cells. Foreign pathologists are trying to answer a number of questions regarding background and precancerous changes in the cervical epithelium. At the same time, most of the works are devoted to the description of individual observations of rare morphological forms or to the clinical and morphological study of small groups of patients (33,34,35,36,37.)

Literature

1. Radzinsky, V.E. Obstetric aggression / V. E. Radzinsky. - M.: Status Praesens, 2011. - 688 p.
2. Greeley, C., S. Schroeder and S. G. Silverberg. Microglandular hyperplasia of the cervix: a true "pill" lesion Int J Gynecol Pathol, 1995. 14(1): p. 50-4
3. Hirama, T., C. W. Miller, S. P. Wilczynski and H. P. Koeffler. pl6 (CDKN2/cyclin-dependent kinase-4 inhibitor/multiple tumor suppressor-1) gene is not altered in uterine cervical carcinomas or cell lines. Mod Pathol, 1996. 9(1): p. 26-31. (1).
4. Gaivoronsky I.V., Berlev I.V., Kuznetsov S.V. Anatomical features of the uterine artery and parametric venous plexus. Vestnik Ross. VMA. - 2007. - - 1 (17). - P. 53–59.
5. Gracheva G.G. Clinical and topographic-anatomical aspects of intrafascial hysterectomy: author. dis. ... cand. honey. Sciences. - M., 2001. - 21 p.
6. Loit A.A., Kayukov A.V., Panshin A.A. Surgical anatomy of the chest, abdomen, pelvis. - St. Petersburg. : Peter, 2006. - 352 p.
7. Kondrikov N.I. Pathology of the uterus. –M.: Practical medicine, 2008.-334 p.
8. Minkina G.N., Manukhin I.B., Frank G.A. Precancer of the cervix.-M.: Airbrush-media, 2001.

9. Krasnopolsky V.I. Pathology of the cervix and vagina - M., 1997Dallenbach-Hellweg G., Knebel-Doeberitz M., Trunk M.J. Color atlas of histopathology of cervix uteri, 2004
10. Dallenbach-Hellweg G., Knebel-Doeberitz M., Trunk M.J. Color atlas of histopathology of cervix uteri, 2004
11. Mogirevskaya O.A. Clinical and morphological aspects of hyperplasia of the mucous membrane of the CC: Abstract of the thesis of a candidate of medical sciences.- M., 1997
12. [Prilepskaya, V.M. Possibilities of therapy for HPV-associated diseases of the genitals in women / V.M. Prilepskaya, E.R. Dovletkhanova, P.R. Abakarova // Obstetrics and gynecology. - 2011. - No. 5. - S. 123-128.,
13. Ovsyannikova, T.V., Diseases of the cervix. Clinic, diagnosis, treatment: a textbook for doctors / T.V. Ovsyannikova, N.O. Makarova, H.A. Sheshukova, N.A. Kulikov. - M.: MEDpress-inform, 2013. - 64 S.].
14. Rudakova E.B. Genital infection and age-related features of the pathology of the cervix. - IPTs OmGMA, 2004. - S. 86-102
15. Nazarova, N.M. N. M. Nazarova, N. V. Bestaeva, V. N. Prilepskaya, D. Yu. Trofimov, M. N. Kostava // Obstetrics and Gynecology. - 2012. - No. 5. - S. 10-16.
16. Letyaeva, O.I. Clinical and microbiological rationale for the complex therapy of inflammatory diseases of the urogenital tracts of non-gonococcal etiology in women of reproductive age / O. I. Letyaeva, I. I. Dolgushin // Obstetrics and Gynecology, 2013. - No. 6. - P. 60-64.
17. Rogovskaya, S.I. Clinical aspects of low-grade squamous intraepithelial lesions / S.I. Rogovskaya, L.I. Terebneva // Obstetrics and Gynecology. - 2013. - No. 2. - S. 136-143.
18. Voropaeva E.E. Spontaneous abortion: pathomorphosis, etiology, pathogenesis, clinical and morphological characteristics, rehabilitation: author. dis. ... MD - Chelyabinsk, 2011. - 45 p.
19. Rogovskaya S.I., Terebneva L.I. Clinical aspects of low-grade squamous intra-epithelial lesions.- Obstetrics and Gynecology, 2013. - No. 2.- P. 99-112
20. Rudakova E.B. Pseudo-erosion of the cervix (clinic, diagnosis, treatment): author. dis. ... Dr. med. nauk.- M., 1996.- 41 p.;
21. Rusakevich P.S. Background and precancerous diseases of the cervix. - Minsk. - 1998. - 368s.
22. Kulakov, V.I. Modern approaches to the diagnosis of papillomavirus infection of the genitals in women and their significance for cervical cancer screening

(literature review) / V.I. Kulakov, I.A. Apolikhina, V.N. Prilepskaya, A.I. Gus, G.T. Sukhikh // Prakt. gynecology. - 1999, Vol. 1. No. 2
23. Efremov, A.B. Etiopathogenetic aspects of pseudo-erosion of the cervix / A.V. Efremov, O.G. Pekarev, Yu. F. Luzyanin et al. // Obstetrics and Gynecology. - 2000. - No. 2. - S. 30-32.
24. Kondrikov, N.I. Classification of diseases of the cervix / N.I. Kondrikov // Genital infections and pathology of the cervix (clinical lectures) / ed. V.N. Prilepskaya, E.B. Rudakova. Omsk. - CPI OmGMA, 2004.-p. 79-86.
25. Bogdanova E.A. Gynecology of children and adolescents. - M.: Med. inform. Agency, 2000. - 330 p.
26. Bogdashkin N.G., Tuchkina I.A. Pediatric and adolescent gynecology: experience and perspectives
27. Parashchuk Yu.S. Infertility in marriage. - Kyiv: Health, 1994. - 208 p.
28. Kozachenko V.P. Cervical cancer // Modern Oncology. - 2001.-Vol.2. - No. 2. - S. 2-4.
29. Podistov Yu.I., Laktionov K.P., Petrovichev N.N. Epithelial dysplasia of the cervix (diagnosis and treatment). – M.: GEOTAR-Media, 2006
30. Gynecology. National leadership. - M .: GEOTAR-Media, 2008 p. 12-13
31. Mamedova L.T. Cancer of the cervix in women of elderly and senile age: Abstract of the thesis. dis. ... cand. honey. Sciences. - M., 2001. - 21 p.
32. Shoell W.M.J., Janicek M.F., Mirhashemi R. Epidemiology and biology of cervical cancer. // Seminars in Surgical Oncology. - 1999. - V. 16. - P. 203–211.
33. (Greeley, C., S. Schroeder and S. G. Silverberg. Microglandular hyperplasia of the cervix: a true "pill" lesion? Int J Gynecol Pathol, 1995. 14(1): p. 50-4.,
34. Hirama, T., C. W. Miller, S. P. Wilczynski and H. P. Koeffler. pl6 (CDKN2/cyclin-dependent kinase-4 inhibitor/multiple tumor suppressor-1) gene is not altered in uterine cervical carcinomas or cell lines. Mod Pathol, 1996. 9(1): p. 26-31.
35. Kyriakos, M., R. L. Kempson and N. F. Konikov. A clinical and pathologic study of endocervical lesions associated with oral contraceptives. Cancer, 1968. 22(1): p. 99-110.
36. Liang, M., M. Ueno, S. Oomizu, T. Arikawa, R. Shinonaga, S. Zhang, et al. Galectin-9 expression links to malignant potential of cervical squamous cell carcinoma. J Cancer Res Clin Oncol, 2008. 134(8): p. 899-907.
37. McCluggage, W. G. and P. Maxwell, bcl-2 and p21 immunostaining of cervical tubo-endometrial metaplasia. Histopathology, 2002. 40(1): p. 107-8.