Russian Journal of Infection and Immunity = Infektsiya i immunitet
2023, vol. 13, no. 4, pp. 761–766

Инфекция и иммунитет
2023, Т. 13, № 4, с. 761–766

ASSESSING A RELATION BETWEEN COMPOSITION OF LUMINAL AND TISSUE MICROBIOTA AND CERVICAL INTRAEPITHELIAL CHANGES

S.M. Chechko[a,b], A.V. Lyamin[a], A.V. Kazakova[a], A.V. Yanchenko[a], N.V. Sapozhkova[b], E.S. Katorkina[c], M.E. Stolbova[d]

[a] *Samara State Medical University, Samara, Russian Federation*
[b] *Samara City Clinical Hospital No. 2 named after N.A. Semashko, Samara, Russian Federation*
[c] *Clinics of Samara State Medical University, Samara, Russian Federation*
[d] *Samara Regional Center "Dynasty", Samara, Russian Federation*

Abstract. The incidence of cervical cancer (CC) in Russia remains at a high level and ranks fourth among all cancers. CC is preceded by mild, moderate, and severe cervical intraepithelial neoplasia. Human papillomavirus (HPV) is known to be the main cause for its development being responsible for 99% cancer cases. Despite HPV infection, the oncological process occurs only under certain conditions. There are risk factors that indirectly affect the course and emergence of cervical dysplasia. In recent years, the role of cervico-vaginal microbiome for onset and progression of this pathology has been actively discussed. Many studies evidence that dysbiosis along with cervical intraepithelial dysplasia is associated with increased HPV viral load, additionally allowing to clarify a role of specific microorganisms. Despite the knowledge rapidly accumulating about the nature of vaginal microbiome in cervical precancerous processes, the level of its impact on disease course has not been fully investigated and is of great interest. Identification of microorganisms that affect emergence and progression of this pathology will allow to prevent and apply select approach to treatment of dysbiosis. The aim of our study was to identify a relation between cervical tissue and luminal culturome and severe cervical intraepithelial neoplasia. The study evaluated the microbiota of cervical and cervical canal mucosa biopsy in patients with cervical intraepithelial changes. According to the study results, the *Streptococcus* genus representatives were significantly more frequent in cervical biopsy specimens in severe dysplasia vs. no cervical intraepithelial changes, whereas cervical canal cultures provided comparable data. Bacteria from the *Corynebacterium* genus were found in cervical biopsy specimens 3 times more often than in smear from the cervical canal mucous membrane. The microbiota from cervical and cervical canal biopsy specimens differ qualitatively and quantitatively particularly regarding prevalence of *Streptococcus* spp. representatives being more common in patients with cervical dysplasia. *Corynebacterium* spp. were detected more often in cervical biopsy specimens than in cervical canal smears. Thus, the method of collecting biological material has a great influence on final results.

Key words: *cervical intraepithelial neoplasia, cervical microbiome, biopsy specimen of the cervix, bacteriological examination, Streptococcus spp., Corynebacterium spp.*

Адрес для переписки:
Янченко Анна Витальевна
443099, Россия, г. Самара, ул. Чапаевская, 89,
Самарский государственный медицинский университет.
Тел.: 8 963 116-31-51.
E-mail: pystnica131902@gmail.com

Contacts:
Anna V. Yanchenko
443079, Russian Federation, Samara, Chapaevskaya str., 89,
Samara State Medical University.
Phone: +7 963 116-31-51.
E-mail: pystnica131902@gmail.com

Для цитирования:
Чечко С.М., Лямин А.В., Казакова А.В., Янченко А.В., Сапожкова Н.В., Каторкина Е.С., Столбова М.Е. Оценка связи состава просветной и тканевой микробиоты с интраэпителиальными изменениями шейки матки // Инфекция и иммунитет. 2023. Т. 13, № 4. С. 761–766. doi: 10.15789/2220-7619-AAR-11258

Citation:
Chechko S.M., Lyamin A.V., Kazakova A.V., Yanchenko A.V., Sapozhkova N.V., Katorkina E.S., Stolbova M.E. Assessing a relation between composition of luminal and tissue microbiota and cervical intraepithelial changes // Russian Journal of Infection and Immunity = Infektsiya i immunitet, 2023, vol. 13, no. 4, pp. 761–766. doi: 10.15789/2220-7619-AAR-11258

DOI: http://dx.doi.org/10.15789/2220-7619-AAR-11258

ОЦЕНКА СВЯЗИ СОСТАВА ПРОСВЕТНОЙ И ТКАНЕВОЙ МИКРОБИОТЫ С ИНТРАЭПИТЕЛИАЛЬНЫМИ ИЗМЕНЕНИЯМИ ШЕЙКИ МАТКИ

Чечко С.М.[1, 2], Лямин А.В.[1], Казакова А.В.[1], Янченко А.В.[1], Сапожкова Н.В.[2], Каторкина Е.С.[3], Столбова М.Е.[4]

[1] ФГБОУ ВО Самарский государственный медицинский университет Минздрава РФ, г. Самара, Россия
[2] ГБУЗ СО Самарская городская клиническая больница № 2 имени Н.А. Семашко, г. Самара, Россия
[3] Клиники ФГБОУ ВО Самарского государственного медицинского университета Минздрава России, г. Самара, Россия
[4] ГБУЗ Самарский областной медицинский центр «Династия», Самара, Россия

Резюме. Заболеваемость раком шейки матки (РШМ) в России по-прежнему остается на высоком уровне и занимает четвертое место среди всех онкологических заболеваний. РШМ предшествует цервикальная интраэпителиальная неоплазия легкой, умеренной и тяжелой степени. Известно, что вирус папилломы человека (ВПЧ) служит основной причиной развития данной патологии и ответственен за 99% случаев развития рака. Несмотря на инфицирование ВПЧ онкологический процесс возникает только при наличии определенных условий. Существуют факторы риска, опосредованно влияющие на течение и возникновении дисплазии шейки матки. В последние годы активно обсуждается роль цервико-вагинального микробиома в возникновении и прогрессировании данной патологии. Многие исследования свидетельствуют о том, что дисбиоз, при наличии цервикальной интраэпителиальной дисплазии связан с повышенной вирусной нагрузкой ВПЧ, также уточняется роль конкретных микроорганизмов. Несмотря на быстро накапливающиеся знания о характере вагинального микробиома, при наличии предраковых процессов шейки матки, уровень его влияния на течение заболевания до конца не изучен и представляет большой интерес. Выявление микроорганизмов влияющих на возникновение и прогрессирование данной патологии позволит профилактировать и избирательно подходить к лечению дисбиоза. Целью нашего исследования было выявить связь между тканевым и просветным культуромом шейки матки и цервикальной интраэпителиальной неоплазией тяжелой степени. В исследовании оценивалась микробиота биоптата шейки матки и слизистой оболочки цервикального канала у пациентов с цервикальными интраэпителиальными изменениями. Согласно результатам исследования представители рода *Streptococcus* достоверно чаще встречались в биоптате шейки матки у пациенток с дисплазией тяжелой степени по сравнению с женщинами без интраэпителиальных изменений шейки матки, тогда как в посеве из цервикального канала эти результаты были сопоставимы, а бактерии из рода *Corynebacterium* обнаруживалась в биоптате шейки матки в 3 раза чаще, чем в мазке со слизистой оболочки цервикального канала. Микробиота биоптата шейки матки и цервикального канала качественно и количественно отличаются, в частности встречаемость представителей *Streptococcus* spp. отмечается чаще у пациентов с наличием дисплазии шейки матки, а *Corynebacterium* spp. — в биоптате шейки матки по сравнению с мазком из цервикального канала. Таким образом большое влияние на результат имеет способ сбора материала.

Ключевые слова: *цервикальная интраэпителиальная неоплазия, цервикальный микробиом, биоптат шейки матки, бактериологическое исследование, Streptococcus spp., Corynebacterium spp.*

Microbiota plays a key role in human physiology and maintenance of homeostasis. In recent years, knowledge about the microbiome has changed significantly [4]. It is known that the vaginal ecosystem is a metabolically and microbiologically complex environment. In most women, the vaginal microbiota is dominated by numerous varieties of *Lactobacillus* spp., which form the colonization resistance of the mucous membranes. Thus, the loss of dominance of *Lactobacillus* spp. promotes colonization by anaerobic bacteria and an increase in microbial diversity, which in some cases contributes to the progression of cervical intraepithelial neoplasia. The development of cervical cancer is known to be associated with persistent human papillomavirus (HPV) infection [3]. Most often, HPV infection is transient [5], but long-term persistence of HPV is associated with an increased risk of cervical intraepithelial neoplasia (CIN) and cervical cancer [5]. Dysbiotic changes in the vaginal microflora are a risk factor for the persistence of HPV infection [2, 7]. Recent studies show a relationship between cervico-vaginal microflora and the progression of CIN. With the advent of modern methods for diagnosing the state of microbiome and rapidly accumulating knowledge in this area, many issues require further study and systematization.

The purpose of the study was to reveal the connection of tissue and luminal culture of the cervix with severe cervical intraepithelial neoplasia.

The study was conducted on the basis of Samara State Medical University. The study involved 29 women of reproductive age (from 18 to 45 years). All patients were divided into two groups. The main group included women with severe intraepithelial lesions (10 people). The comparison group included women with no intraepithelial changes in the cervix (19 people).

The exclusion criteria for both groups were: pregnancy, HIV infection, hepatitis B, C, patients who received antibiotics within 15 days prior to taking a sample or who had intercourse/douching within 48 hours prior to sampling.

To study the cervical microbiota in women of both groups, a microbiological examination of cultures of the mucous membrane of the cervical canal and biopsy specimen of the cervix was carried out. The method of seeding the biopsy specimen of the cervix was conducted according to the author's method (patent for invention No. 2784053). Collection of material from cervical canal of the cervix was carried out with a sterile swab, biopsy of the cervix with a gynecological conchotome with endovideo control (patent for utility model No. 213605). After collection, the samples were placed in liquid Amies transport medium and delivered to the laboratory within 2 hours under isothermal conditions. In the laboratory, the material was placed on an expanded set of solid nutrient media: 5% blood agar (HiMedia, India), anaerobic agar (HiMedia, India), veillonella isolation agar (HiMedia, India), clostridium isolation agar (HiMedia, India), bifidobacteria isolation agar (HiMedia, India), lactobacilli isolation agar (HiMedia, India), universal chromogenic medium (Bio-Rad, USA). The cultures were incubated for 5 days at 37°C under aerobic and anaerobic conditions. Then, using MALDI-ToF mass spectrometry (Microflex LT, Bruker), all isolated microorganisms were identified.

The present study evaluated the qualitative and quantitative composition of tissue and luminal microbiota in the smear from the cervical canal and biopsy specimen of the cervix, as well as the association of microbiota with cervical intraepithelial changes in the cervix.

Statistical analysis was carried out using the StatTech v. 2.8.7 (developer — Stattech LLC, Russia). Comparison of percentages in the analysis of the four-field contingency tables was performed using Pearson's chi-square test, Fisher's exact test. The link between the signs was regarded as statistically significant at a significance level of $p < 0.05$.

Representatives of the following genera of bacteria were isolated from the obtained material (Table 1).

As a result of evaluating the frequency of isolation of *Streptococcus* spp. bacteria, depending on the presence of intraepithelial changes in the cervix, statistically significant differences were found ($p = 0.017$). In the biopsy specimen of the cervix with intraepithelial changes, bacteria of the genus *Streptococcus* were found in 70% of cases, whereas in the biopsy specimen without dysplasia — in 21.1% of cases.

The presence of *Streptococcus* spp. in the biopsy specimens in patients of the main group was detected 8.750 times more often than in the control group, the differences in chances were statistically significant (95% CI: 1.528–50.112).

Then a study of *Streptococcus* spp. in a smear from the mucous membrane of the cervical canal was conducted. In patients with cervical dysplasia, bacteria of this genus were detected in 50% of cases, without dysplasia in 47.4% of cases, while there were no statistically significant differences between the groups.

A study of the species composition of *Streptococcus* spp. in a biopsy specimen and in a smear from the cervical canal was also carried out (Table 2).

The data obtained suggest that the presence of *Streptococcus* spp. is a marker associated with the presence of cervical dysplasia. The greatest number and variety of strains of *Streptococcus* spp. was found in a biopsy specimen of the cervix in patients with dysplasia. The most common was *S. anginosus*, which, along with *S. oralis*, *S. mitis*, *S. sanguinis*, is part of the oropharyngeal microflora and these species cause oral pathology. The role of these microorganisms in the development of genital pathology is not fully understood. Their appearance in the vaginal microflora may be due to the prevalence of unprotected oral-genital contact. Thus, representatives of the genus *Streptococcus* are associated with the activation of many inflammatory cytokines and can affect the epithelial cells of the vagina and cervix, thereby contributing to the occurrence or progression of intraepithelial lesions of the cervix [6, 8, 12, 13, 14].

In comparing the qualitative characteristics of the microbiota of the biopsy specimen of the cervix and that of the cervical canal in the study groups, statistically significant differences were found for representatives of the genus *Corynebacterium* spp. These bacteria are able to adhere to vaginal cells and bind to extracellular matrix proteins such as fibronectin. When forming microbiocenosis in female reproductive tract, they affect the production of cytokines in the epithelial cells of the vagina. This allows them to compete with other microorganisms for adhesion sites and exist in the vaginal ecosystem both in health conditions and in various infectious diseases of the external and internal genital organs.

The data obtained by us indicate the ability of *Corynebacterium* spp. to invade, since they were significantly more common in the biopsy specimen of the cervix than in the smear from the cervical canal, which is an important result of the diagnostic search. However, there was no difference in the quantitative composition of *Corynebacterium* spp. in the biopsy specimen of the cervix of the main group (47.4%) and the comparison group (60%), as well as in the smear from the cervical canal — 15.8% and 20% respectively.

The species composition of *Corynebacterium* spp. is presented in Table 3.

The greatest variety of *Corynebacterium* spp. was found in the cervical canal of the cervix, which confirms the ability of this genus of bacteria to adhere. Colonizing the vaginal biotope, corynebacteria interact with various strains of microorganisms [1, 11]. Scientific publications show conflicting data about their role in the human body. *C. aurimucosum* causes urinary tract infection, *C. accolens* — pelvic osteomyelitis and granulomatous mastitis. In women with cervical cancer, *C. amycolatum* is found in the vaginal microbiome, but according to another study, this

Table 1. Inter-group qualitative characteristics of cervical and cervical canal biopsy microbiota

The genus of microorganisms	Cervical biopsy specimen (number of patients)		Cervical canal smear (number of patients)		P
	Comparison group (n = 19)	Main group (n = 10)	Comparison group (n = 19)	Main group (n = 10)	
***Staphylococcus* spp.**	14 (73.7)	8 (80.0)	9 (47.4)	8 (80.0)	0.155
***Photobacterium* spp.**	0 (0.0)	0 (0.0)	1 (5.3)	1 (10.0)	0.473
***Escherichia* spp.**	4 (21.1)	1 (10.0)	5 (26.3)	1 (11.1)	0.664
***Enterococcus* spp.**	9 (47.4)	3 (30.0)	10 (55.6)	5 (50.0)	0.632
***Rothia* spp.**	0 (0.0)	0 (0.0)	1 (5.3)	1 (10.0)	0.473
***Haemophilus* spp.**	1 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	0.554
***Klebsiella* spp.**	0 (0.0)	0 (0.0)	2 (10.5)	0 (0.0)	0.236
***Morganella* spp.**	0 (0.0)	1 (10.0)	1 (5.3)	1 (10.0)	0.575
***Candida* spp.**	2 (10.5)	0 (0.0)	1 (5.3)	0 (0.0)	0.532
***Enterobacter* spp.**	1 (5.3)	1 (10.0)	0 (0.0)	0 (0.0)	0.473
***Microbacterium* spp.**	1 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	0.554
***Stenotrophomonas* spp.**	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0.180
***Brevibacterium* spp.**	1 (5.3)	0 (0.0)	1 (5.3)	0 (0.0)	0.779
***Gardnerella* spp.**	5 (26.3)	1 (10.0)	4 (21.1)	3 (30.0)	0.705
***Cutibacterium* spp.**	2 (10.5)	0 (0.0)	0 (0.0)	1 (10.0)	0.367
***Actinomyces* spp.**	0 (0.0)	1 (10.0)	1 (5.3)	1 (10.0)	0.575
***Campylobacter* spp.**	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0.180
***Fusobacterium* spp.**	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0.180
***Peptostreptococcus* spp.**	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0.180
***Kocuria* spp.**	1 (5.3)	0 (0.0)	1 (5.3)	0 (0.0)	0.779
***Aerococcus* spp.**	0 (0.0)	0 (0.0)	1 (5.3)	0 (0.0)	0.554
***Peptoniphilus* spp.**	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0.188
***Bifidobacterium* spp.**	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0.180
***Acinetobacter* spp.**	0 (0.0)	0 (0.0)	1 (5.3)	0 (0.0)	0.554
***Dermabacter* spp.**	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0.180
***Metamycoplasma* spp.**	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0.180
***Dialister* spp.**	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0.180
***Alloscardovia* spp.**	0 (0.0)	1 (10.0)	0 (0.0)	1 (10.0)	0.268
***Citrobacter* spp.**	1 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	0.554
***Micrococcus* spp.**	2 (10.5)	0 (0.0)	0 (0.0)	0 (0.0)	0.236
***Streptococcus* spp.**	4 (21.1)	7 (70.0)	9 (47.4)	5 (50.0)	0.017*
***Corynebacterium* spp.**	9 (47.4)	6 (60.0)	3 (15.8)	2 (20.0)	0.043*

Note. *Significant differences ($p < 0.05$).

Table 2. Inter-group *Streptococcus* spp. species composition

Species of *Streptococcus* spp.	Biopsy specimen of the cervix (number of patients)		Smear from the cervical canal (number of patients)	
	Comparison group (n = 19)	Main group (n = 10)	Comparison group (n = 19)	Main group (n = 10)
Streptococcus vestibularis	–	–	1	–
Streptococcus oralis	1	2	1	–
Streptococcus anginosus	2	7	4	2
Streptococcus mitis	–	1	–	–
Streptococcus sanguinis	–	1	–	–
Streptococcus pseudopneumonia	–	–	–	1
Streptococcus galloliticus	–	–	–	–
Streptococcus agalactiae	–	1	2	1

Table 3. Inter-group *Corynebacterium* spp. species composition

Species of *Corynebacterium* spp.	Biopsy specimen of the cervix (number of patients)		Smear from the cervical canal (number of patients)	
	Comparison group (n =19)	Main group (n = 10)	Comparison group (n =19)	Main group (n = 10)
Corynebacterium aurumucosum	1	1	1	2
Corynebacterium amylocatum	5	3	4	2
Corynebacterium tuberculostearicum	1	2	2	2
Corynebacterium simulans	–	–	1	1
Corynebacterium pyruviciproducens	–	–	1	–
Corynebacterium mucifaciens	–	1	–	–
Corynebacterium coyleae	–	1	1	1
Corynebacterium riegelii	–	–	1	–
Corynebacterium accolens	–	–	–	1

strain is considered as a probiotic, so the role of the *Corynebacterium* genus in the vaginal microbiome is not fully understood [1, 4, 9].

No connection between the remaining identified microorganisms and intraepithelial changes in the cervix was found.

In our study, we have identified an association between the presence of *Streptococcus* spp. in the biopsy specimen of the cervix and the presence of dysplasia. These results are consistent with the previous studies that have shown a correlation between impaired cervical microbiota and the development of cervical dysplasia [5, 14].

However, we found no statistically significant differences in the presence of *Streptococcus* spp. in a smear from the cervical canal in patients of both groups, which may indicate the ability of *Streptococcus* to adhere to the mucous membrane with further invasion. The conducted study clearly demonstrates the decisive importance of the method of collecting material. The resulting microflora qualitatively and quantitatively differs in the biopsy specimen of the cervix and the smear from the cervical canal. The data obtained confirm the need for further research in this area.

References

1. Гладышева И.В., Черкасов С.В. Коринебактерии вагинального микробиома — потенциальные патогены или перспективные пробиотики? // Бюллетень Оренбургского научного центра УрО РАН. 2019. № 3. 20 с. [Gladisheva I.V., Cherkasov S.V. Corinebacteria of vaginal microbiom — potential pathogens or perspective probiotics? *Byulleten' Orenburgskogo nauchnogo tsentra UrO RAN = Bulletin of the Orenburg Federal Research Center UB RAS, 2019, no. 3, 20 p. (In Russ.)*] *doi: 10.24411/2304-9081-2019-13022*
2. Clarke M.A., Rodriguez A.C., Gage J.C., Herrero R., Hildesheim A., Wacholder S., Burk R., Schiffman M. A large, population-based study of age-related associations between vaginal pH and human papillomavirus infection. *BMC Infect Dis., 2012, vol. 12: 33. doi: 10.1186/1471-2334-12-33*
3. Cogliano V., Baan R., Straif K., Grosse Y., Secretan B., El Ghissassi F. WHO International Agency for Research on Cancer. Carcinogenicity of human papillomaviruses. *Lancet Oncol., 2005, vol. 6, no. 4: 204. doi: 10.1016/s1470-2045(05)70086-3*
4. Gladysheva I.V., Khlopko Y.A., Cherkasov S.V., Kataev V.Y. Genome sequence of Corynebacterium amycolatum ICIS 99 isolated from human vagina reveals safety and beneficial properties. *Arch. Microbiol., 2022, vol. 204, no 4: 226. doi: 10.1007/s00203-022-02852-7*
5. Ho G.Y., Bierman R., Beardsley L., Chang C.J., Burk R.D. Natural history of cervicovaginal papillomavirus infection in young women. *N. Engl. J. Med., 1998, vol. 338, no. 7, pp. 423–428. doi: 10.1056/NEJM199802123380703*
6. Kang G.U., Jung D.R., Lee Y.H., Jeon S.Y., Han H.S., Chong G.O., Shin J.H. Potential association between vaginal microbiota and cervical carcinogenesis in korean women: a cohort study. *Microorganisms, 2021, vol. 9, no. 2: 294. doi: 10.3390/microorganisms9020294*
7. Linhares I.M., Summers P.R., Larsen B., Giraldo P.C., Witkin S.S. Contemporary perspectives on vaginal pH and lactobacilli. *Am. J. Obstet. Gynecol., 2011, vol. 204, no. 2: 120.e1–5. doi: 10.1016/j.ajog.2010.07.010*
8. Liu J., Luo M., Zhang Y., Cao G., Wang S. Association of high-risk human papillomavirus infection duration and cervical lesions with vaginal microbiota composition. *Ann. Transl. Med., 2020, vol. 8, no. 18: 1161. doi: 10.21037/atm-20-5832*
9. Manzanares-Leal G.L., Coronel-Martínez J.A., Rodríguez-Morales M., Rangel-Cuevas I., Bustamante-Montes L.P., Sandoval-Trujillo H., Ramírez-Durán N. Preliminary identification of the aerobic cervicovaginal microbiota in mexican women with cervical cancer as the first step towards metagenomic studies. *Front. Cell Infect. Microbiol., 2022, vol. 12: 838491. doi: 10.3389/fcimb.2022.838491*
10. Mendling W. Vaginal microbiota. *Adv. Exp. Med. Biol., 2016, vol. 902, pp. 83–93. doi: 10.1007/978-3-319-31248-4_6*
11. Smith S.B., Ravel J. The vaginal microbiota, host defence and reproductive physiology. *J. Physiol., 2017, vol. 595, no. 2, pp. 451–463. doi: 10.1113/JP271694*

12. Tao Z., Zhang L., Zhang Q., Lv T., Chen R., Wang L., Huang Z., Hu L., Liao Q. The pathogenesis of Streptococcus anginosus in aerobic vaginitis. *Infect. Drug. Resist., 2019, vol. 12, pp. 3745–3754. doi: 10.2147/IDR.S227883*
13. Wu M., Gao J., Wu Y., Li Y., Chen Y., Zhao F., Li C., Ying C. Characterization of vaginal microbiota in Chinese women with cervical squamous intra-epithelial neoplasia. *Int. J. Gynecol. Cancer, 2020, vol. 30, no. 10, pp. 1500–1504. doi: 10.1136/ijgc-2020-001341*
14. Zhang C., Liu Y., Gao W., Pan Y., Gao Y., Shen J., Xiong H. The direct and indirect association of cervical microbiota with the risk of cervical intraepithelial neoplasia. *Cancer Med., 2018, vol. 7, no. 5, pp. 2172–2179. doi: 10.1002/cam4.1471*

Авторы:

Чечко С.М., ассистент кафедры акушерства и гинекологии Института педиатрии ФГБОУ ВО Самарский государственный медицинский университет Минздрава России, г. Самара, Россия; врач акушер-гинеколог отделения оперативной гинекологии ГБУЗ СО Самарская городская клиническая больница № 2 им. Н.А. Семашко, г. Самара, Россия;
Лямин А.В., д.м.н., директор Научно-образовательного профессионального центра генетических и лабораторных технологий ФГБОУ ВО Самарский государственный медицинский университет Минздрава России, г. Самара, Россия;
Казакова А.В., д.м.н., доцент, зав. кафедрой акушерства и гинекологии Института педиатрии ФГБОУ ВО Самарский государственный медицинский университет Минздрава России, г. Самара, Россия;
Янченко А.В., специалист Научно-образовательного профессионального центра генетических и лабораторных технологий ФГБОУ ВО Самарский государственный медицинский университет Минздрава России, г. Самара, Россия;
Сапожкова Н.В., зав. отделением оперативной гинекологии ГБУЗ СО Самарская городская клиническая больница № 2 им. Н.А. Семашко, г. Самара, Россия;
Каторкина Е.С., зав. отделением гинекологии Клиник ФГБОУ ВО Самарский государственный медицинский университет Минздрава России, г. Самара, Россия;
Столбова М.Е., врач акушер-гинеколог ГБУЗ Самарский областной медицинский центр «Династия», г. Самара, Россия.

Authors:

Chechko S.M., Assistant Professor, Department of Obstetrics and Gynecology, Institute of Pediatrics, Samara State Medical University, Samara, Russian Federation; Obstetrician-Gynecologist, Department of Operative Gynecology, Samara City Clinical Hospital No. 2 named after N.A. Semashko, Samara, Russian Federation;
Lyamin A.V., DSc (Medicine), Director of Research and Educational Professional Center for Genetic and Laboratory Technologies, Samara State Medical University, Samara, Russian Federation;
Kazakova A.V., DSc (Medicine), Associate Professor, Head of the Department of Obstetrics and Gynecology, Institute of Pediatrics, Samara State Medical University, Samara, Russian Federation;
Yanchenko A.V., Specialist of Research and Educational Professional Center for Genetic and Laboratory Technologies, Samara State Medical University, Samara, Russian Federation;
Sapozhkova N.V., Head of the Department of Operative Gynecology, Samara City Clinical Hospital No. 2 named after N.A. Semashko, Samara, Russian Federation;
Katorkina E.S., Head of the Department of Gynecology, Clinics of Samara State Medical University, Samara, Russian Federation;
Stolbova M.E., Obstetrician-Gynecologist, Samara Regional Medical Center «Dynasty», Samara, Russian Federation.

Поступила в редакцию 20.05.2023
Принята к печати 28.08.2023

Received 20.05.2023
Accepted 28.08.2023