

or if the mother's life was in danger ( $\chi^2=47,676$ ;  $P<0.001$ ). When comparing the willingness of female students to have an abortion under different circumstances of pregnancy, depending on religiosity, a statistically significant difference was proved in the following circumstances: in the case of "abortion on demand", regardless of the reason ( $\chi^2=11,908$ ;  $P=0.012$ ), teenage pregnancy ( $\chi^2=33,308$ ;  $P<0.001$ ) and if pregnancy interferes with the mother's career ( $\chi^2=35,897$ ;  $P<0.001$ ). Non-religious students expressed more liberal views [11].

**Conclusion.** Social research on the study of the attitude of the population to artificial termination of pregnancy (abortion) is relevant. It is especially important to know the opinion of young people of reproductive age, since the attitude to abortion in different societies cannot be called certain. The frivolous attitude of young people towards abortion may lead to significant demographic problems in the country in the future. In our study, the majority of young people not only condemn abortions (31.3%), but also believe that it is possible to allow artificial termination of pregnancy only for strict medical reasons (26%), legislative prohibition is supported by 7.7% of respondents, 29.3% adhere to liberal views on abortion. We did not find a connection between the attitude to abortion and the marital status of the respondents, but the presence of children determines the negative attitude of re-

spondents to the artificial termination of pregnancy.

## Reference

1. Bravina R.I. Konceptiya zhizni i smerti v kul'ture etnosa: na materiale traditsij saha [The concept of life and death in the culture of an ethnic group: based on the traditions of Sakha. Novosibirsk: Nauka. 2005: 307 (In Russ.).]
2. Kononova E. N. Problema otnosheniya k abortam u sovremennoj molodezhi [The problem of attitude to abortion among modern youth]. Aktual'nye voprosy social'noj raboty s razlichnymi kategoriyami naseleniya: materialy IV mezhdregion. nauch. konf., Kirov, 31 marta 2017 g./ Kirov: Izd-vo Kirovskogo gosudarstvennogo medicinskogo universiteta, 2017 [Topical issues of social work with various categories of the population: materials of the IV inter-region. Scientific conference, Kirov, March 31, 2017/ Kirov: Publishing House of the Kirov State Medical University, 2017 (In Russ.).]
3. Makraus YA. V. Problemy psihologicheskogo soprovozhdeniya sovremennoj sem'i: otnoshenie studencheskoj molodezhi k abortam [Issues of psychological support of the modern family: the attitude of students to abortions]. Sociokul'turnye i psihologicheskie problemy sovremennoj sem'i: aktual'nye voprosy soprovozhdeniya i podderzhki: materialy III Vseross. nauch. konf. Tula, 23–24 noyabrya 2017 g. [Socio-cultural and psychological problems of the modern family: topical issues of support and support: materials of the III All-Russian Scientific Conference. Tula, November 23–24, 2017/ Tula: Publishing House of L.N. Tolstoy TSPU, 2018 (In Russ.).]
4. Novikov A.G. O mentalitete saha. Yakutsk: Analit. centr pri Prezidente Resp. Saha [About the mentality of Sakha. Yakutsk: Analyt. Center under the President of the Rep. Sakha. 1996.147p. (In Russ.).]

5. Hodarina YU.I., Hvostova M.A., Kryuchkova A.V., Kondusova YU.V. Otnoshenie sovremennoj molodezhi k moral'no-eticheskim problemam aborta [The attitude of modern youth to the moral and ethical problems of abortion]. Molodezhnyj innovacionnyj vestnik [Youth Innovation Bulletin. 2017; 6 (2): 383-385 (In Russ.).]

6. Kononova S.K. [et al.] Otnoshenie molodykh lyudej reproduktivnogo vozrasta k eticheskimi spornym voprosam prenatal'noj diagnostiki nasledstvennykh boleznej [The attitude of young people of reproductive age to ethically controversial issues of prenatal diagnosis of hereditary diseases. Yakut Medical Journal, 2023;2: 53-57 (In Russ.).]

7. Otnoshenie sovremennoj molodezhi k probleme abortov. Negativnye yavleniya v molodezhnoj srede i profilaktika zdorovogo obraza zhizni [Elektronnyj resurs] [The attitude of modern youth to the problem of abortion. Negative phenomena in the youth environment and prevention of a healthy lifestyle [Electronic resource]. - Access mode: URL: <http://www.sociodone.ru/codos-734-1.html> (In Russ.).]

8. Tyrylgina M.A. Istoki fenomenal'noj zhiznesposobnosti naroda saha [The origins of the phenomenal vitality of the Sakha people. Yakutsk: Publishing house of Bichik. 2000: 304 (In Russ.).]

9. Kononova S., Vinokurova D., Barashkov NA, Semenova A., Sofronova S., Oksana S., Tatiana D., Struchkov V., Burtseva T., Romanova A., Fedorova S. The attitude of young people in the city of Yakutsk to DNA-testing. Int J Circumpolar Health. 2021;80(1):1973697. doi: 10.1080/22423982.2021.1973697.

10. Ravindran J. Unwanted pregnancy—medical and ethical dimensions. Med J Malaysia. 2003;58:23-35.

11. Trninić Z, Bender M, Šutalo N, Kozomara D, Lasić V, Bevanđa D, Galić G. Attitudes of Students of Medicine, University of Mostar According to Induced Abortion. Psychiatr Danub. 2017;29:866-871.

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## THE PRACTICAL IMPLEMENTATION OF THE IMMUNOCYTOCHEMICAL RESEARCH METHOD IN THE DIAGNOSIS OF PRECANCEROUS DISEASES OF THE CERVIX

Patients with cervical pathology were analyzed by cytological, immunocytochemical and molecular genetic tests. Among the selected groups, 78 women were more likely to have low-grade dysplasia, or LSIL (16.3%). In more than half of the cases (60.2%) in women who were tested, positive HPV tests were observed. The majority of positive HPV tests in the were for high oncogenic risk (32%), with 16 (19.1%) and 31 (8.5%) being the most common types. It was found that the frequency of double staining of p16ink4a/Ki67 was noted in women with a high degree of intraepithelial lesion (37%), and the detection of HPV type 16 was prevailed - 19.1%. The number of cases in the group of women without pathology, but with latent HPV infection, cases with a positive HPV test and a negative result of p16/Ki67 protein expression prevailed was 94.1%. It was found that the number of p16-positive cells was higher in women of group 1 with LSIL (55.8%) and group 2 (44.4%) with HSIL. In the group of women without cervical pathology, but with latent HPV infection, indicators of weak expression of p16ink4a were most frequently recorded (57.1%).

**Keywords:** cytology, diagnostics, human papillomavirus, dysplasia.

**Relevance.** Currently, there is an increase in the number of patients with cervical cancer (CC) each year. According to the available data available for the year 2021, The incidence of CC in Russia has increased from 113.1 in 2011 to 126.7 per 100 thousand females in 2021. In recent years, the incidence CC has been in the second position after uterine body cancer in the structure of genital cancers in the country [1]. At the same time, in terms of prevalence in women in the age category from 35 to 49 years, it took the second place [3]. According to Minkin G.N., cervical pathology is a prevalent gynecological disease among women in their reproductive years, ranging from 10% to 15% [1,6]. There are a number of background processes that are noted for the development of CC, in particular, condylomas, dysplasia of varying severity and cancer in situ. The accessibility of malignant neoplasms of the cervix and the possibility of using various diagnostic measures should help reduce the incidence of cervical cancer. Early detection and timely treatment of precancerous diseases can prevent most cases of cervical cancer [7]. It is known that the most important factor in cervical carcinogenesis is infection of women with human papillomavirus (HPV). In turn, early sexual activity, frequent changes of sexual partners, non-compliance with sexual hygiene, sexually transmitted diseases, immunodeficiency, smoking and contact with toxic substances create condition for HPV infection, thereby increasing the risk of developing CC [2,6].

More than 15-20% of women are infected with HPV, but only a few develop dysplasia of varying severity or cervical cancer, according to studies [10]. In this regard, early detection of background and precancerous cervical diseases associated with HPV is important. In addition to the detection of high-risk HPV (HR), numerous foreign studies have shown that research data based on markers of proliferation, methylation in HPV infection, and their introduction into clinical practice are carried out [4,9,13].

It is known that cytological examination is the main method of screening for cervical cancer and precancerous diseases. Despite the general availability, reliability, and widespread use of this method, there are several disadvantages: the lack of standard methods for sampling biomaterial for research, which can lead to false negative results in 20-30% of cases, the probability of false positive results in 5-70% of cases, and the problems associated with repeated sampling of material. In recent years, the method

of obtaining smears using the method of liquid cytology has been improved, which makes it possible to perform additional molecular types of research, one of which is immunocytochemical examination (ICC) [5].

The immunocytochemical method is a method of molecular immunological diagnostics that allows the identification of cellular and tissue antigen molecules as a result of their binding to antibodies and the formation of an "antigen-antibody" complex. In modern diagnostics, CC ICC is a combination of cytological and enzyme immunoassay methods. It detects the pathological process directly in the cell under study, and also determines the parameters of HPV aggressiveness. The determining factor in the pathological process is the presence of cancer proteins p16ink4a and Ki-67, whose concentrations increase in response to the viral assault [8]. The index of proliferative activity of p16ink4a and Ki-67 expression should be determined by the immunocytochemical method for the differential diagnosis of the severity of cervical lesions, according to the data of the All-Russian public organization "Russian Society of Specialists in the Prevention and Treatment of Tumors of the Reproductive System" [11]. The immunocytochemical analysis of the p16ink4a cancer protein permits the precise distinction between tumor and non-tumor dysplasia, as well as demonstrating a high degree of specificity. It is known that the expression of this protein is associated with mild (CIN I), moderate (CIN II) and severe dysplasia (CIN III), as well as intraepithelial cervical cancer. It's rare to find it in the cells of the squamous epithelium without signs of dysplasia. According to the results of studies by different authors, it seems important to find out if the p16ink4a protein is expressed by immunocytochemical method in addition to the routine method of liquid cytology and Pap smear staining [5,15]. A marker of proliferation, Ki-67, is an antigen of a cancerous tumor that is detected in a cell when it divides, but it is not detected in the resting phase of the cell cycle. The aggressiveness of a malignant tumor and unfavorable prognosis can be predicted by this feature of Ki-67, which is a useful indicator of the prognosis of its behavior [14,16].

There are a number of studies that present data that the diagnostic value is not only the mono-expression of p16ink4a and Ki-67 proteins, but their simultaneous detection (co-expression) in the form of double staining. Some authors say that the cytological method of double staining is recommended for addition-

al examination of HPV-positive patients during primary HPV screening because it makes cytology being a more specific test for sorting HPV-positive women [12,17].

**The purpose of the study.** To evaluate the results of expression of p16ink4a and Ki-67 protein in cytological samples by immunocytochemical method in women with cervical pathology associated with HPV.

**Materials and methods of research:** the research used a comprehensive cytological, immunocytochemical and molecular genetic examination of 245 women aged 22 to 56 years and older. It was performed on the basis of the Yakut Scientific Center for Complex Medical Problems. The obtained material from each woman was examined by the method of liquid cytology (LC) on the automated CellPrepPlus system (Korea), as an independent highly informative method that contributes to the improvement and standardization of all stages of cytological examination. Glass staining by the Romanovsky-Giemsa method was used for traditional smears and Pap staining for smears by liquid cytology. The interpretation of the results was in line with the terminology of the Bethesda System, 2015[16], which is based on the introduction of the term SIL (Squamous Intraepithelial Lesion) – squamous intraepithelial lesion. It is divided into categories: NILM (negative for intraepithelial lesion or malignancy) – characterizes the clinical norm, i.e. the absence of pathology or the presence of benign changes due to reparative and reactive changes. LSIL (low-grade squamous intraepithelial lesion): These lesions are changes in the squamous epithelium that are typical of HPV infection and mild dysplasia CIN I. HSIL (high grade squamous intraepithelial lesion) - intraepithelial lesions of the squamous epithelium of a high degree, the group covers moderate and severe dysplasia, CIN II, CIN III, ASCUS- atypical squamous epithelial cells of unclear significance, ASC-H – atypical squamous epithelial cells that do not allow to exclude HSIL, CIS – carcinoma in situ, SIL - squamous intraepithelial lesion.

Immunocytochemical examination of smears for the protein p16ink4a and Ki-67 was performed using the CINtec PLUS kit (Germany). The nuclear and cytoplasmic reactions were evaluated, and the nuclear reaction was compared to the cytoplasmic reaction (pic.3). The results of liquid cytology were compared with the results of traditional cytology.

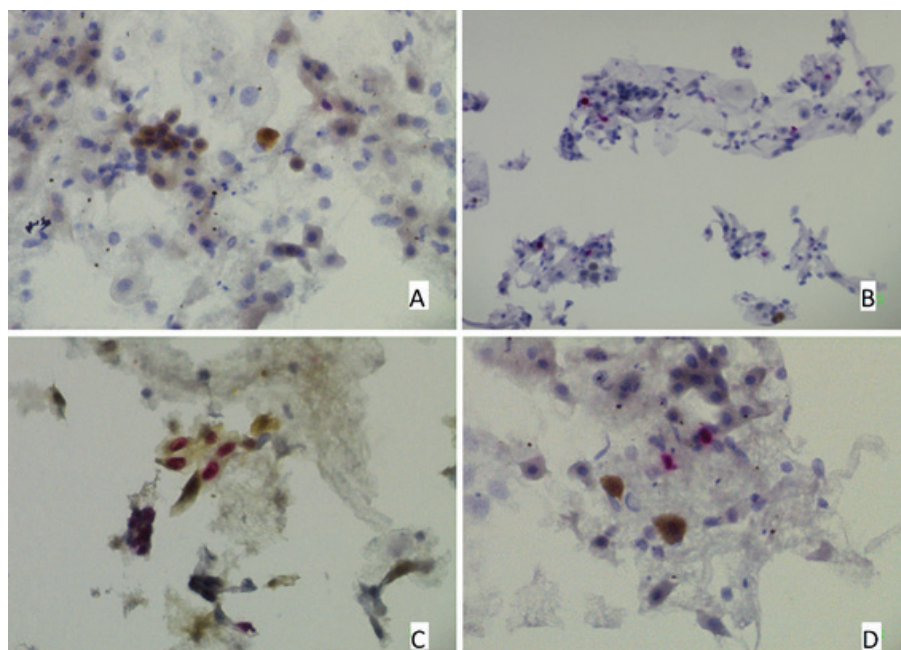
The HPV typing was conducted using a PCR test referred to as "Kvant-21"

(Moscow, Russia) on the basis of the microbiological laboratory of the NEFU Clinic. The real-time PCR method can quickly tell what type of HPV it is by measuring the amount of virus and comparing it to other samples. It can also tell the difference between 21 different types of HPV (6,11, 16, 18, 26, 31, 33, 35, 39, 44, 45, 51, 53, 56, 58, 59, 66, 68, 73, 82, serotypes). Including high- and low-oncogenic types.

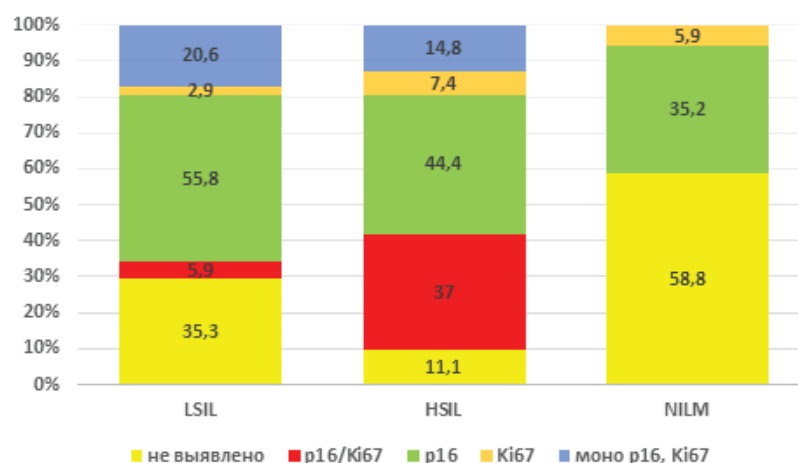
Relative indicators (P) and their errors (m) were calculated and intergroup and intragroup differences were estimated. The calculation was performed using the SPSS Statistics 19 package. The differences were considered statistically significant at  $p < 0.05$ .

**Results and discussion.** The absence of intracellular lesion (NILM) was detected in 171 women, which was 69.8% of all women studied, according to the results of cytological examination by liquid cytology. The prevalence of squamous intraepithelial lesions of low (LSIL) and high (HSIL) degree was observed in 28.6% of cases, with LSIL detected in 40 cases (16.3%), HSIL detected in 30 cases and accounting for 12.2% of the total number of women studied. In 1 case (0.4%), ASCUS, ASC-H, SIL and CIS were diagnosed. Patients with HPV-associated CIN and patients without cervical pathology, but with a latent form of HPV infection, were selected for the study. A total of 78 women were examined. The average age of women was  $44.27 \pm 11.7$  years. Three distinct groups were established: group 1 comprised patients with LSIL (mean age  $47.32 \pm 12.1$ ) ( $n=34$ ), group 2 comprised patients with HSIL (mean age  $42.19 \pm 12.5$ ) ( $n=27$ ), and group 3 comprised patients who did not have cervical pathology but had latent HPV-infection with a diagnosis of NILM (mean age  $41.47 \pm 8.31$ ) ( $n=17$ ).

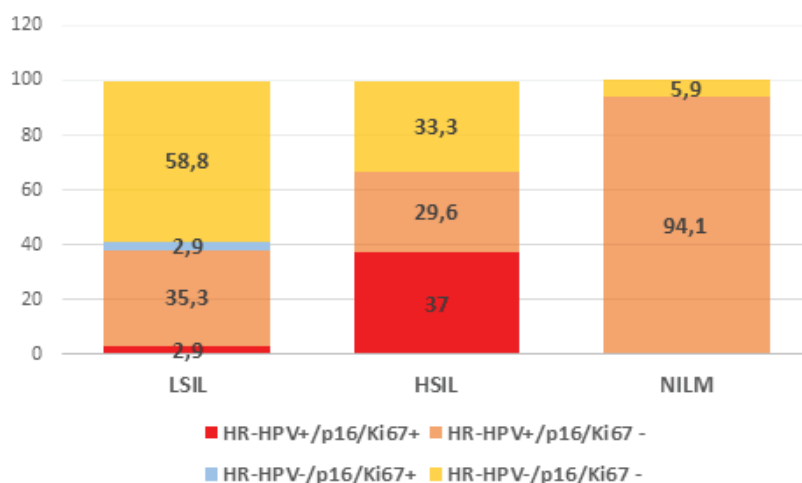
Given the role of HPV in the development of cervical cancer, HPV testing is currently the most important moment of screening, [7, 13]. The results of the study showed that 47 women had confirmed HPV carrier status, which was 60.2% of all surveyed women. The presence of oncogenic HPV types of high oncogenic risk was detected in 25 women and amounted to 32%. The most common types were highly oncogenic HPV types 16 and 31 (19.1 and 8.5%, respectively). Papilloma-virus infection was found to be monoinfection (68%) or coinfection (31.9%) on a quantitative basis. The evaluation of the indicators revealed statistically significant patterns among the analyzed groups, as well as a favorable response to the HPV test ( $r=0.444$ ,  $p=0.000$ ).



**Fig. 1.** Positive ICC reaction to p16ink4a and Ki-67 (Pap staining, x200). A- expression of p16ink4a protein, B – expression of Ki-67 protein, C –coexpression p16ink4a/Ki-67, D– monoexpression p16ink4a and Ki-67



**Fig. 2.** Evaluation of detection of expression of proteins p16ink4a and Ki67



**Fig. 3.** Combination of HR-HPV infection detection results and p16ink4a/Ki67 protein detection



The simultaneous co-expression of p16ink4a and Ki67 in the same cell indicates a violation of the regulation of the cell cycle characteristic of HPV transformation and the development of dysplasia of cervical epithelial cells. The frequency of positive results from double staining of p16ink4a/Ki67 by immunocytochemical examination in 78 examined patients revealed that co-expression of p16ink4a/Ki67 was detected in 12 examined women, representing a percentage of 15.4%. As depicted in Pic. 1, it can be observed that in patients belonging to group 1 with LSIL, there were two instances of double staining of p16ink4a/Ki67, which accounted for 5.9% of the total cases. In contrast, in group 2 with HSIL, the frequency of p16ink4a/Ki67 cases increased with the severity of dysplasia, reaching a total of 37%. The correlation analysis between the examined groups and the positive p16ink4a/Ki67 test revealed the presence of a negative correlation ( $r=-0.391$ ,  $p=0.000$ ). There was no expression of the studied marker in any material among patients without cervical pathology (group 3).

Positive expression of p16ink4a protein was detected in 37 examined women and amounted to 47.4%. It was discovered that the highest prevalence were observed in the first group of women, which was 55.8%. Moreover, in 44.1% of cases, the expression was considered moderate, in 8.8% of cases, it was severe, and in 2.9%, it was considered weakly expressed. In group 2, the p16ink4a protein was found in 44.4% of cases, 26% of them were moderate, 7.4% were severe and 11.1% were weakly expressed. In group 3 - 35.2% of cases, weakly expressed p16 protein expression prevailed the most - 57.1% and in 11.7% of cases - moderate. Thus, a direct correlation was also established between the positive p16ink4a test between the groups of the examined ( $r=0.401$ ,  $p=0.000$ ). The expression of the Ki67 protein cell proliferation marker was detected in 2.9% of women from group 1, 7.4% of women from group 2, and 5.9% of women from group 3.

Various combinations of p16ink4a/Ki67 expression with the presence or absence of HR-HPV, depending on the severity of cervix epithelial dysplasia, are presented in Pic.2. The difference between the selected subgroups was statistically significant ( $r=-0.924$ ,  $p=0.000$ ).

In group 1, patients with LSIL pathology were most often characterized by the absence of HR-HPV- / p16/Ki67- -58.8% (20 cases), in 35.3% (12 cases) - HR-HPV+/p16/Ki67- and in 1 case (2.9%,

respectively) HR-HPV+ was detected/ p16/Ki67+ and HR-HPV-/p16/Ki67+. In group 2, cases with overexpression of HR-HPV+/p16/Ki67+ prevailed in HSIL - 10 cases (37%), while 8 (29.6%) cases with HR-HPV+/p16/Ki67- and 9 (33.3%) cases with absence of HR-HPV+/p16/Ki67- prevail. It should also be noted that with a high intraepithelial lesion of the cervix, the detectability of HPV type 16 in the presence of p16/Ki67 coexpression was higher and amounted to 19.1%, while the detectability of other HPV types varied from 4.2 to 2.1% of cases. The frequency of cases in the group of women without pathology but with latent HPV infection was dominated by cases with HR-HPV+/p16/Ki67- - 16 cases (94.1%) and in 5.9% with a negative result of the presence of the virus and the expression of the protein p16/Ki67.

It's important to know that if a group of women with latent infection have the p16ink4a marker, they might have dysplasia even if they don't have any symptoms or signs of cancer at the time of the study. This means more research should be done with these women.

Thus, the predominance of NILM in cytological samples (69.8%) compared with intraepithelial lesions of the cervix (28.6%) was revealed. Among the these groups, low-grade dysplasia - LSIL (16.3%) was more common. 60.2% of women had positive HPV tests. The majority of positive HPV tests revealed high oncogenic risk (32%), while HPV of 16 (19.1%) and 31 (8.5%) types were most common. It was discovered that the frequency of double staining of p16ink4a/Ki67 was observed in women with a high degree of intraepithelial lesion (37%), while the detection of HPV type 16 prevailed at 19.1%. The frequency of cases with a positive HPV test and with a negative result of p16/Ki67 protein expression was highest (94.1%) in the group of women without pathology but with latent HPV infection. It was found that the proportion of p16-positive cells was higher among women belonging to group 1 with LSIL (55.8%) and group 2 (44.4%) with HSIL. Among the group of women without cervical pathology, but with latent HPV infection, indicators of low expression of p16ink4a (57.1%) were most often recorded. This may suggest a threat of dysplasia in the absence of clinical and cytological signs of the lesion.

**Conclusion.** A comprehensive examination of women with various cervical pathologies was carried out with the inclusion of a molecular diagnostic method. The evaluation of the expression of the protein p16ink4a and Ki-67 in the tissues

of the cervix revealed the presence of precancerous changes.

The aim of early detection of cervical pathology is achieved through cytological and PCR-based diagnostics of the human papillomavirus. Screening diagnostics provide additional opportunities for the prevention of cervical cancer at an early stage, which determines the basis for the prospects of preserving women's health.

## Reference

1. Donnikov A.E., Markelov M.I., Pestrikova T.Y. [et al.] Analiz rasprostranennosti i virusnoj nagruzki razlichnyh tipov virusa papillomy cheloveka v regionah Rossijskoj Federacii [Analysis of the prevalence and viral load of various types of human papillomavirus in the regions of the Russian Federation]. *Akusherstvo i ginekologiya* [Obstetrics and gynecology. 2019; 4:39-47 (In Russ.).]
2. Davydov M.I., Axel E.M. Statistika zlokachestvennyh novoobrazovaniy v Rossii i stranah SNG v 2008 g. [Statistics of malignant neoplasms in Russia and CIS countries in 2008]. *Vestnik RONC im. N.N. Blohina* [Bulletin of the N.N. Blokhin Russian Research Center. 2010. Vol.21 (In Russ.).]
3. Kaprin A.D., Starinsky V.V., Shakhzadova A.O. Zlokachestvennye novoobrazovaniya v Rossii v 2021 godu (zabolevaemost' i smertnost') [Malignant neoplasms in Russia in 2021 (morbidity and mortality)]. M.: MNIIOI im. P.A. Gercena - filial FGBU «NMIC radiologii» Minzdrava Rossii [P.A. Herzen Institute of Medical Research - branch of the Federal State Budgetary Institution National Medical Research Radiological Centre of the Ministry of Health of Russia. 2022: 252 (In Russ.).]
4. Minkina G.N. Cervikal'nyj skrining: menyaem ideologiyu [Cervical screening: changing ideology. Statuspraesens. 2013; 4:83-87 (In Russ.).]
5. Klinyshkova T.V., Karatyuk T.I., Mozgovoy S.I., Pritykina T.V. Osobennosti ekspressii p16ink4ai metabolitov estradiola pri VPCB-associirovannyh ploskokletochnykh porazheniyah shejki matki [Features of expression of p16ink4ai estradiol metabolites in HPV-associated squamous cell lesions of the cervix]. *Voprosy ginekologii, akusherstva i perinatologii* [Issues of gynecology, obstetrics and perinatology. 2011;10(2):45-9 (In Russ.).]
6. Kotov V.A., Raskin G.A., Protasova A.E. [et al.]. Primenenie zhidkostnoj citologii i immunocitohimicheskogo opredeleniya onkomarkerap16ink4a dlya skrininga, diagnostiki i vybora taktiki lecheniya zabolevaniy shejki matki: uchebnoe posobie [Application of liquid cytology and immunocytochemical determination of cancer marker p16ink4a for screening, diagnosis and choice of tactics for the treatment of cervical diseases: textbook. St. Petersburg, 2009: 23 (In Russ.).]
7. Pestrikova T.YU., Ismaylova A.F. Celesoobraznost' immunocitohimicheskogo issledovaniya kak markera proliferativnoj aktivnosti pri cervikal'noj intraepitelial'noj neoplazii [Expediency of immunocytochemical research as a marker of proliferative activity in cervical intraepithelial neoplasia]. *Ginekologiy* [Gynecology. 2020;24 (1):47-50 (In Russ.).]
8. Prilepskaya V.N. VPCB-associirovannye zabolevaniya shejki matki, metody obsledovaniya, principy lecheniya [HPV-associated diseases

of the cervix, methods of examination, principles of treatment]. *Ginekologiya* [Gynecology. 2019; 21(3):6-8 (In Russ.).]

9. Rogovskaya S.I. Papillomavirusnaya infekciya u zhenshchin i patologiya shejki matki [Papillomavirus infection in women and pathology of the cervix. M.: GEOTAR-Media, 2008: 188 (In Russ.).]

10. Mingaleva N.V., Degtyareva O.G., Abramashvili Yu.G., Metelev N.S. Tyazhest' cervical'nyh porazhenij po dannym citologii i ih vzaimosvyaz' s vyavleniem virusa papillomy cheloveka vysokoonkogenogo riska u zhenshchin do 30 let i starshe [Severity of cervical lesions according to cytology and their relationship with the detection of human papillomavirus of high-oncogenic risk in women under 30 years and older]. *Kubanskij nauchnyj medicinskij vestnik* [Kuban Scientific Medical Bulletin. 2016; 1(156): 88-95 (In Russ.).]

11. Cervikal'naya intraepitelial'naya neoplaziya, eroziya i ektropion shejki matki. Klinicheskie

rekommendacii Rossijskogo obshchestva akusherov-ginekologov (ROAG), Obshcherossijskoj obshchestvennoj organizacii «Rossijskoe obshchestvo specialistov po profilaktike i lecheniyu opuholej reproduktivnoj sistemy (ROSORS) [Cervical intraepithelial neoplasia, erosion and ectropion of the cervix. Clinical recommendations of the Russian Society of Obstetricians and Gynecologists (ROAG), the All-Russian public Organization "Russian Society of Specialists in the Prevention and Treatment of tumors of the Reproductive System (ROSORS). M.2020 (In Russ.).]

12. Areán-Cuns C, Mercado-Gutiérrez M, Paniello-Alastruey I, et al. Dual staining for p16/Ki67 is a more specific test than cytology for triage of HPV-positive women. *Virchows Arch.* 2018;473(5):599-606.

13. Cuschieri K., Ronco G., Lorincz A, et al. Eurogin roadmap 2017: Triage strategies for the management of HPV-positive women in cervical screening. *Int J Cancer.* 2018; 143(4):735-45

14. Schmidt D, Bergeron C, Denton KJ, Ridder R; European CIntec Cytology Study Group. p16/Ki-67 dual-stain cytology in the triage of ASCUS and LSIL Papanicolaou cytology. Results from the European Equivocal or Mildly Abnormal Papanicolaou Cytology Study. *Cancer Cytopathol.* 2011;119(3):158-66.

15. Thomas CWJr, Behrens CM, Ranger-Moore J, et al. Triage of HPV-positive women with p16/Ki-67 dual-stained cytology: Results from a sub-study nested into the ATHENA trial. *Gynecol Oncol.* 2017;144(1):51-6.

16. Wright TC, Stoler MH, Behrens CM, et al. Primary cervical cancer screening with human papillomavirus: end of study results from the ATHENA study using HPV as the first-line screening test. *Gynecol Oncol.* 2015;136(2):189-97.

17. Wright TC Jr, Behrens CM, Ranger-Moore J, et al. Triage of HPV-positive women with p16/Ki-67 dual-stained cytology: Results from a sub-study nested into the ATHENA trial. *Gynecol Oncol.* 2017;144(1):51-6.

## HYGIENE, SANITATION, EPIDEMIOLOGY AND MEDICAL ECOLOGY

L.D. Olesova, A.P. Chevychelov, P.I. Sobakin, E.D. Okhlopova, T.E. Popova, S.I. Sofronova, A.N. Romanova

### THE STATE OF THE ADAPTIVE POTENTIAL OF THE WORKING POPULATION IN THE ZONE OF INCREASED RADIATION EXPOSURE

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A radiological and medical-biological study of the population of Aldan and Tommot of the Aldan region of South Yakutia, located in the zone of increased natural radiation, was carried out. The annual individual effective exposure dose to the population turned out to be 2 times higher in the city of Aldan (6.22 mSv). The contribution of radon and its decay products in the city of Aldan was 59.5%, in the city of Tommot - 48.3%.

Assessment of the adaptive potential (AP) of the circulatory system of the population showed a high percentage of the occurrence of functional stress of adaptation mechanisms, especially among residents of the city of Aldan (86.5%). The correlation showed a negative role of an increase in the level of triglycerides, urea, the activity of LDH, CK, and a decrease in the activity of alkaline phosphatase on AP. The presence of GBL dysfunction and, especially, fatty hepatosis was also associated with a decrease in AP.

**Keywords:** radon, radiation, adaptive potential, Yakutia, fatty hepatosis.

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**Introduction.** Natural sources of ionizing radiation, as a constant physical environmental factor, dominate the collective effective dose, causing the main harm to public health (about 70%), and cause reasonable concern among the population in areas with an unfavorable radioecological situation. In the Republic of Sakha (Yakutia), in the Aldan region, there are 2 uranium-bearing provinces, where the main uranium reserves of the Russian Federation are concentrated. The Elkon uranium ore region with an area of 1,500 km<sup>2</sup> is located 50 km east of the administrative center, the city of Aldan, with a population of more than 20,000 people. and 40 km southeast of the city of Tommot with a population of more than 7 thousand people. The fed-

eral highway Neryungri -Yakutsk passes through the central part of the district from south to north with a high traffic intensity [2].

According to the Gosatomnadzor of the Far Eastern District of the Russian Federation, in the process of large-scale geological prospecting since 1959, more than 1 million tons of mining and ore mass containing about 2000 tons of uranium have been extracted from the bowels and stored on the day surface in the form of dumps. There were centers of radioactive contamination with high DER values (equivalent dose rate), reaching 1500-2000 µR/h. In 2022, in 40 premises of public buildings in the Aldan district, the values of ERVA (equivalent equilibrium volumetric activity) of radon exceed-