opuholy[Malignant tumours] 2014, №1, pp.39-46.

- 3. Belyakov I. S. Anurova O. A. Snigur P. V. Mutacii genov c-kit I PDG-FRA I kliniko- morfologicheskie osobennosti stromalnih opuholey geludochnokishechnogo trakta [Gene mutations c-kit and PDGFRA and clinical morphological features of stromal tumours of the gastrointestinal tract]. Voprosy oncologii [Oncology issues]. 2007, V. 53, № 6, pp. 677-681.
- 4. Seryakov A. P. Gastrointestinalnie stromalnie opuholi [Gastrointestinal stromal tumours]. Rossiiskiy gurnal gastroenerologii, gepatologii, koloproctologii [Russian Journal of Gastroenterology, Hepatology, Coloproctology]. 2010, V.20, № 4, pp.49-57.
- 5. Ciganova I. V Anurova O. A. Mazurenko N. N. Morfologicheskie osobennosti i kriterii prognosa stromalnyh opuholey GKT [Morfological features and criteria for the prediction]. Archiv patologii [Patology archive]. 2011, V.73, № 6, pp. 37-42. https://doi.org/10.17650/2313-805X.2015.2.2.29-40
- 6. Antman K. Crowley J. Balcerzak S. et al. J An intergroup phase III randomized study of doxorubicin and dacarbazine with or without ifosfamide and mesna in advanced soft tissue and bone sarcomas.. Clin. Oncol. 1993; 11(7): 1276-1285.
- 7. Antonescu C.R. Sommer G. Sarran L. Association of KIT exon 9 mutation with nongastric primary site and aggressive behavior: KIT emulation analysis and clinical correlates of 120 gastrointestinal stromal tumours. Clim.Cancer Res. 2003. N9. P.3329-3337. http://dx.doi.org/10.4061/2011/708596
- 8. Corless C.L. Fletcher J.A. Heinrich M.C. Biology of gastrointestinal stromal tumors // J. Clin. Oncol. 2004. Vol. 9. P.3329-3337.https://doi.org/10.1007/s00428-010-0891-v

- 9. Cross-sectional study of imatinib plasma trough levels in patients with advanced gastrointestinal stromal tumors: impact of gastrointestinal resection on exposure to imatinib. Yoo C. Ryu M.H. Kang B.W. et al. 1 Clin. Oncol. 2010; 28: 1554-1559. http://dx.doi.org/10.1200/JCO.2009.26.5785
- 10. CT and PET: early prognostic indicators of response to imatinib mesylate in patients with gastrointestinal stromal tumor. Holdsworth C.H. Badawi R.D. Manola J.B. et al. Am J Roentgenol. 2007; 189: 324-330.DOI:10.2214/AJR.07.2496
- 11. Effect of rifampicin on the pharmacokinetics of iraatinib mesylate (Gleevec, ST1571) in healthy subjects. Bolton A. Peng B. Hubert M. et al. Cancer Chemother Pharmacol. 2004 Feb;53(2): 102-106. DOI:10.1007/s00280-003-0722-9
- 12. Fletcher J. A. Corless C. L. Dimitrijevic S. Proc. Mechanisms of resistance to imatinib mesylate in advanced gastrointestinal stromal tumors. Am. Soc. Clin . Oncol . 2003; 22: 815 (A3275).
- 13. Imatinib plasma levels are correlated with clinical benefit in patients with unresectable /metastatic gastrointestinal stromal tumors. Demetri G. Wang Y. Wehrle E. et al. J Clin Oncol. 2009; 27:3141-3147. DOI:10.1200/JCO.2008.20.4818
- 14. Kantarjian H.M. The MD Anderson Manual of Medical Oncology .— 2nd. McGraw-Hill, 2011. ISBN 978-0-07-170106-8.
- 15. Miettinen M. Lasota J. Gastro-intestinal stromal tumors (GISTs): definition, occurrence, pathology, differential diagnosis and molecular genetics. Pol J Pathol. 2003; 54: 3–24.
- 16. Mudan S.S. Woodruff J.M. Brenan M. F. Ann. Surg. 2000. V.231. P. 51-58. http://dx.doi.org/10.1097/00000658-200001000-00008

- 17. Nonadherence to imatinib treatment in patients with gastrointestinal stromal tumors; the ADAGIO study. Mazzeo F. Duck L. Joosens E. et al. Anticancer Res. 2011;31:1407-1409.
- 18. Patel S. Managing progressive disease in patients with GIST: factors to consider besides acquired secondary tyrosine kinase inhibitor resistance. Cancer Treat Rev. 2012; 38(5): 467-72.http://dx.doi.org/10.1016/j.ctrv.2011.10.001
- 19. Rubin B. P. Gastrointastinal stromal tumours: an update // Histopatology. 2006. Vol. 48. P.83-96.DOI: 10.1111/j.1365-2559.2005.02291.x
- 20. Stromal tumours (GIST). Review on morphology ,molecular pathology, prognosis and differential diagnosis // Arch. Pathol. Lab. Med. 2006. Vol. 130 P.1466-1477. https://doi.org/10.1007/978-88-470-5310-6_8
- 21. Von Mehren M. Widmer N. Correlations between imatinib pharmacokinetics, pharmacodynamics, adherence, and clnical response in advanced metastatic gastrointestinal stromal tumor: an emerging role for drug blood level testing? Cancer Treat Rev 2011; 37: 291-299.Doi 10.1016/j.ctrv.2010.10.001

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THE IMPLEMENTATION OF LIQUID-BASED CYTOLOGY TO IMPROVE DIAGNOSTICS OF CERVIX UTERUS DISEASES

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ABSTRACT

A comparison of cytological results obtained by the method of liquid-based (LBC), implemented in practice on the basis of the laboratory of pathology, histology and cytology of the Clinic of MI M.K. Ammosov NEFU, and the traditional method is done.

It has been confirmed that the diagnostic value of the liquid-based cytology method in the diagnosis of cervical pathology is generally higher compared with TM. It is recommended to supplement the cytological study with a molecular method for the detection of human papillomavirus (HPV testing), which will improve diagnosis and subsequent treatment.

Keywords: cervical cancer, diagnostics, liquid-based cytology, screening.



Relevance. Cervical cancer (CC) is one of the few nosological forms of malignant tumors that meet all the requirements for population-based screening. The disease is widespread and important health issue which has a reliably recognizable preclinical phase and a long period of development. It is possible for further verification of the diagnosis and effective treatment methods, and there is a reliable screening test - cytological examination of smears taken from the cervix and cervical canal [4].

The one of the principal methods in the early detection of precancerous and tumor processes of the cervix is cytological method. It makes to evaluate of epithelium state, to check the presence or absence of cellular response to various effects, and to identify the inflammatory process and some infectious agents [3]. The essential factor in effective cervical cancer screening is the sensitivity of cytological screening. According to various researchers, it ranges from 66% to 83%. The cause of false-negative cytological responses in 70-90% of cases is poor material sampling for cytological examination, and only in 10-30% of cases is a misinterpretation of cytological data [6]. The most commonly nondiagnostic material is obtained in smears from the cervical canal. The absence of endocervical epithelium cells in smears is noted in 8-18% of cases. As a result, it is glandular and adenosquamous CC that is most often missed during the screening

It is necessary to use modern methods and to implement new clarifying diagnostic for maximum optimization of cervical pathology diagnosis and the avoidance of subjective intraoperative measurement of the location and size of plot neoplasia. Today, highly effective method of liquid cytology (LBC) are gaining ground, which give a thin representative monolayer drug with a minimum content of blood, bacteria and neutrophilic leukocytes. Wet fixation enhances the clarity of structures, common artifacts are absent. The sensitivity of the cytological method in the application of LBC increases to 85% [1]. Also, the LBC peculiarity is in fact, that one material sampling is able to give 6 «serial» (the same cell composition) smears. It makes possible to use additional research methods, for example, HPV testing, immunocytochemical determination of tumor markers [2]. Taking it into account, the liquid technology of cervical samples production was introduced into clinical practice on the basis of the Laboratory of Pathomorphology, Histology and Cytology of the Medical

Institute Clinic of NEFU. Yakutsk from August 2018. However, LBC is highly specific and should be supplemented by molecular diagnostic methods. Detection of human papillomavirus DNA has more sensitivity to the diagnosis of precancerous and CC than to cytology, which is then able to detect early precancerous changes of the cervix, therefore, reduces the risk of developing CC [5, 7].

The purpose of the study is to use the embedded method of liquid-based cytology to conduct a comparative analysis of the results of cytological examination of material from the cervix obtained by the traditional method and the method of liquid-based cytology.

Materials and methods. In the clinical laboratory of pathomorphology, histology, and cytology on the basis of M.K. Ammosov NEFU Medical Institute, 35 screening of cervical samples was conducted in the parallel with traditional method and liquid-based cytology with the preparation of a cytological drug on the automated system CellPrep Plus (Korea). The material was taken from the patients after examination and extended colposcopy in the «Malex+» clinic. The age of the patients ranged from 23 to 54 years. The diagnosis was conducted by Romanovskiy - Gimza stain method. Special attention in the screening was paid to the completeness of obtained material (the adequacy of the smear). Diagnostic accuracy of cytological material screening of the cervix depends largely on the quality of the material. If smears have cells of endocervical, flat and metaplastic epithelium, the material is adequate for the study. It is very important to take into account that such material should be obtained from the transformation zone - the area- where the tumor most often occurs. If the material is represented by a very small number of cells, a large number of blood elements, mucus, and the presence of artifacts, which makes impossible to properly assess the cytological picture,

it is considered inad-Cytological 45 equate. diagnosis was made 40 in accordance with 35 the clinicopathologic 30 classification of J. V. Bokhman (1976), and with the commonly accepted criteria for assessing the state 10 of the epithelium by Bethesda System (1999). Detection, typing (co-testing) of human papilloma virus (HPV) (6, 11, 16, 18,

26, 31, 33, 35, 39, 44, 45, 51-53, 56, 58, 59, 66, 68, 73, 82 serotypes) by PCR was performed on the basis of microbiological laboratory of the Medical Institute clinic based on NEFU.

The results and discussion. The percentage of background detection and precancerous pathology was estimated when comparing the traditional cytological study with the method of liquid-based cytology. It found a small difference between traditional smears and smears obtained by the LBC (Fig.1). The absence of intracellular lesions (cytogram without features) was revealed by traditional cytology in 10 (28.5%) patients, by LBC (NILM) in 23 (65.7%) patients, among them 9 (25.7%) patients with no pathology and 14 (40%) patients with reactive changes (squamous metaplasia, inflammation, moderate hyperplasia). Cervical pathology was revealed during the routine cytological examination in 71.4% of cases, and during liquid cytology in 74.3% of cases. Reactive changes in TM were 13 (37.1%) cases when in LBC were 14 cases, 40% of the total number of women studied.

The mild cervical dysplasia was established by the traditional method in 10 (28.5%) cases, in 2 (5.7%) cases of which have indirect signs of viral infection. Liquid-based cytology LSIL revealed in 11 cases (31.4 percent), of which CIN I in 7 (20%) cases, CIN I with koilocyte in 3 (8,6%) cases, and the presence of koilocytes with reactive changes in 1 case (2.8%) (Fig.2 (a, b)).

In 2 women (5.7%) revealed moderate dysplasia by TM, and in 1 case (2.8%) of the total number of women surveyed was recognized by LBC HSIL.

The use of co-testing confirmed HPV carriage in 3 women diagnosed by LSIL, of which 1 woman confirmed the presence of HPV 16,39 types; 1 woman was diagnosed with HPV 6 type; 1 woman HPV 68,39 types. 1 woman was diagnosed HPV 16 and 51 types by NILM. 3

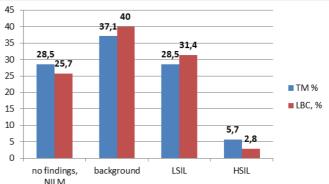
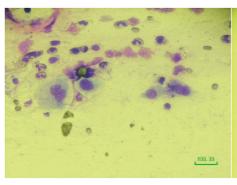


Fig.1. Comparative characteristics of cervix uterus disease diagnosis by the traditional method and the liquid-based cytology.



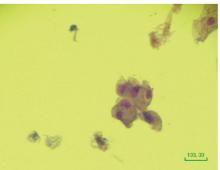


Fig.2. Binuclear or «kissing» nuclei in cervix smear for papillomavirus infection (conventional smear) (a) and koilocyte for liquid-based cytology (staining method by Romanovsky-Gimza), x400 (b) negative cases were identified in the di- of the reproductive organs from preven-

agnosis by LSIL, which indicates the beginning of a viral lesion or other causes

of dysplasia.

Thus, the diagnostic value of liquid-based cytology method in the diagnosis of cervical pathology is generally higher compared to the traditional method. The LBC method is more informative and can be used as an independent screening method for detecting cervical disease. Liquid-based cytology method in cervical cancer screening supplemented by a molecular method of virus detection (HPV testing) will enable to reveal the initial, precancerous stages and specific treatment in time.

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References

1. Kazaishvili T.N. Rannyaya diagnostika raka sheyki matki metodom zhidkostnoy tsitologii [Early diagnosis of cervical cancer using liquid cytology] Issledovaniya i praktika v meditsine [Research and practice in medicine]. Natsional'nyy kongress «Onkologiya reproduktivnykh organov ot profilaktiki i rannego vyyavleniya k effektivnomu lecheniyu [National Congress «Oncology

of the reproductive organs from prevention and early detection to effective treatment.»], Moscow, KVAZAR, 2004, p. 80-81.1

- 2. Kogan Ye.A. Monitoring bol'nykh, perenesshikh operatsivu konizatsii sheyki matki po povodu tservikal'noy intraepitelial'noy neoplazii (kliniko-morfologicheskiye i molekulyarno-biologicheskiye aspekty problemy) [Monitoring of patients undergoing cervical conization surgery for cervical intraepithelial neoplasia (clinical, morphological and molecular biological aspects of the problem)] Akusherstvo i ginekologiya [Obstetrics and gynecology]. Moscow, 2012, №1, p.70-74.
- 3. Mochalova M.N. Sovremennyye aspekty diagnostiki tservikal'noy neoplazii [Modern aspects of diagnosis of cervical neoplasia] Zabaykal'skiy meditsinskiy vestnik [Transbaikalian Medical Journal]. Chita, 2014, №2 (25), p.134-143.
- 4. Novik V.I. Faktory effektivnosti tsitologicheskogo skrininga raka sheyki matki [Efficacy factors for cytological screening for cervical cancer Prakticheskaya onkologiya [Practical Oncology]. Moscow, 2010, V.11, №2, p.66-71.
- 5. Anttila A. Rate of cervical cancer, severe intraepithelial neoplasia, and adenocarcinoma in situ in primary HPV DNA screening with cytology triage: randomized study within organized screening programme / A. Anttila, L. Kotaniemi-Tal-

onen, M. Leinonen [et.al.] // BMJ. – 2010. – Vol. 340. – P. 1804.

- 6. Cobb C.J. Suggested approaches to reporting benign cervical smears that lack endocervical columnar cells / C.J. Cobb // Acta Cytol. 1986. Vol.30. P.317-318.
- 7. Ronco G. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial / G.Ronco, P. Giorgi-Rossi, F. Carozzi [et.al.] // Lancet Oncol. 2010. Vol. 11, №3. P. 249–257.

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OPTIMIZATION OF AUTOPLASMA DONATION DURING PREGNANCY

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ABSTRACT

The article reflects the experience of autoplasma donation in pregnant women with threat of massive bleeding in the period from 2016 to 2018. Analysis of the statistics of massive bleeding according to the diagnosis is presented. According to the analysis, pathologies of pregnancy, related with the greatest risk of massive bleeding were identified. We also optimized the management of autoplasma donation in these groups of pregnant women.

Keywords: autoplasma donation, massive bleeding, obstetrics.