The probability of preterm birth in genital infection (table 2) and intrauterine infection (IUI) is analyzed in women with the genotypes IL-6(-174GC)/TNFa(-308GG), IL-6(-174GG)/TNFa(-308GG) and IL-6(-174CC)/TNFa(-308GG).

Table 2 - The proability of preterm birth in patients with the genotypes IL-6(-174GC)/TNFa(-308GG), IL-6(-174GG)/TNFa(-308GG) and IL-6(-174CC)/TNFa(-308GG) in the presence of genital infection, n, p%, 95%CI_p

Genotype	Preterm labor		OR, 95%CI, p
	genital infection	no infection	
IL-6(-174GG)/TNFa(-308GG) N=21	9 (43%; 22-66)	1 (5%; 0-24)	OR=15,0, 95%CI 1,7-133,6, p=0,01
IL-6(-174GC)/TNFa(-308GG) N=53	24 (45%; 32-60)	2 (4%; 1-13)	OR=21,1, 95%CI 4,7-95,8, p<0,0001
IL-6(-174CC)/TNFa(-308GG) N=12	8 (67%; 35-90)	1 (8%; 0-39)	OR=22,0, 95%CI 2,1-236,1, p=0,01

With IUI, the probability of preterm delivery is higher in patients with the IL-6(-174GG)/TNFa(-308GG) genotype - 8 (89%; N=9) to 2 (17%; N=12) women with this genotype and no IUI (OR=40,0, 95%CI 3,1- 524,9, p=0,005).

Conclusions. With genital infection the chance of preterm delivery is increased in patients with the genotype IL-6(-174CC)/TNFa (-308GG), IL-6(-174GC)/TNFa(-308GG) and IL-6(-174GG)/TNFa(-308GG). With genotype IL-6(-174GG)/TNFa(-308GG) and the realization of intrauterine infection, the chances of premature birth are 40 times higher.

Allelic polymorphism of the promoter regions in the human IL-6 and TNFa genes reflects the functional state of the immune system and can be used for timely diagnosis and prevention of preterm labor in patients with genital infection.

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PROLIFERATIVE-APOPTOTIC PROCESSES IN TESTICULAR SEMINOMA

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Testicular tumors, though being equal up to 1% out of all the male neoplasms all over the world, are the most frequent among white men within the period from puberty up to the age of 40 in industrially advanced countries [1]. At that, testicular germ cell tumors (TGCT) amount to more than 90% of all the testicular tumors and seminoma amounts about 50% of them [2]. Objectives: to study the proliferative-apoptotic processes in testicular seminoma.

Materials and Methods. Material was collected in Pathological Anatomy Department of Kharkiv Regional Clinical Centre of Urology and Nephrology named after Shapoval V.I. We analyzed 13 cases of testicular seminoma which were obtained with orchifuniculectomy. Immunohistochemical (IHC) examination was performed by indirect immunoperoxidase reaction. For estimation of proliferative-apoptotic processes the following primary antibodies were used: Mo a-Hu Ki-67 (Monoclonal Antibody, clone MIB-1, «DAKO», Denmark), Rb a-Hu Bax (Polyclonal Antibody, «Thermo Fisher Scientific Inc.», USA), Mo a-Hu Bcl-2 (Monoclonal Antibody, clone100/D5, «Thermo Fisher Scientific Inc.», USA) and Mo a-Hu p53 (Monoclonal Antibody, clone DO-7, «DAKO», Denmark). The reaction was visualized using Ultra Vision Quanto Detection Systems HRP Polymer («Thermo Fisher Scientific Inc.», USA).

For the most vivid comparison of IHC characteristics all observations were divided into groups depending on the degree of tumor progression. Thus, guided by WHO and pathological pTNM classifications [3], the following groups were formed: group «1» – tumors of this group corresponded to the stages $T_1N_0S_{0-2}$ (n=4), group «2» – $T_2N_{1-3}S_{0-2}$ (n=5), group «3» – $T_3N_{1-3}S_{0-2}$ (n=3) and group «4» – $T_{2-3}N_{0-3}S_{0-2}$ with the presence of distant metastasis (n=1). IHC stained histological sections of seminomas were recorded using an Olympus BX-41TF microscope (Japan) and a digital camera Olympus C3040-ADU (Japan). For the morphometric measurement of the relative area of immunopositive structures determined in % the received photos were processed in Matlab software using standard digital image processing tools. Counting of mentioned parameter was performed in 10-30 randomly selected fields of vision of the microscope Olympus BX-41TF with magnification ×200 ($3{,}12\times10^{-7}$ m^2) in each case.

All values are expressed as means and standard error of the mean for statistical analysis. Spearman's rank correlation coefficient (r) was counted for measure of the strength of relationship between paired data. The accepted level of significance was $p\leq0.05$.

Results. The average relative area (ARA) of Ki-67 expression in the observations of group «1» was low and comprised 1.17±0.07%. At that, expression of Ki-67 was identified predominantly in tumor cells, but was also present in cells of the immune infiltrate. In the group «2» ARA of Ki-67 expression (1.56±0.13%) was not significantly different from the same in the group «1» ($p>0.05$). As well as in the previous group, the expression of Ki-67 was predominantly located in tumor cells. In the group «3» the ARA of Ki-67 expression (1.91±0.05%) was greater than the same index in the group «1» ($p<0.05$) and did not differ significantly from it in the group «2». In a single observation of the group «4» the ARA of Ki-67 expression was 1.91±0.1%.

In the group «1» ARA of Bax expression was 2.74±0.1% and in the group «2» and group «3» – 5.35±0.07% and 6.0±0,06% respectively. Comparison of these values showed increasing of ARA of Bax expression in the groups «2» and «3» relative to the same index in group «1» ($p<0.05$ and $p<0.05$ respectively). Besides, the ARA of Bax expression in the group «3» was greater than the same in the group «2» ($p<0.05$). In a single observation of group «4», the ARA of Bax expression was 5.93±0.1%. Expression of Bax was identified predominantly in the cytoplasm of tumor cells and in single cells of immune infiltrate.

As regards the anti-apoptosis marker bcl-2, it was detected only in single tumors: in one of five observations in the group «2», in one of three observations in the group «3» and in a single case of group «4». Immunopositive staining was detected only in the cytoplasm of single cells of the immune infiltrate. Expression of bcl-2 was absent in tumor cells.

Expression of p53 was absent in all observations of the group «1» and in two of five cases of the group «2» (respectively, in three, there was a positive staining of single tumor cells). In groups «3» and «4», all observations were characterized by a positive reaction with p53, but only in single tumor cells.

Statistical analysis showed a high positive correlation between the relative area of Ki-67 and relative area of Bax and p-53 expression ($r=+0.83$ and $r=+0{,}70$ respectively). Also moderate positive correlation between the relative area of Bax and p-53 expression ($r=+0.62$) was identified. Valid correlation between the relative area of Bcl-2 and other investigated markers was absent.

Prospects for further research. Further investigation of proliferative-apoptotic processes in other germ cell tumors is planned with the detection of differences between them.

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MOLECULAR-BIOLOGICAL MARKERS OF IMPLANTATION DISORDERS IN PATIENTS WITH INFERTILITY AND EXTERNAL GENITAL ENDOMETRIOSIS

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The effectiveness of the IVF program as one of the most effective methods of infertility treatment is 12.5% in case of external genital endometriosis (EGE) of the 1st-2nd stage, compared to 28.6-37.4% in case of tubal-peritoneal infertility factor (TPF). There is still no clear opinion on whether endometrial receptivity changes in patients with this disease and the expression of which morphological and molecular markers is impaired. The aim of this study was to study the molecular-biological peculiarities of endometrium in patients with infertility and stage 1-2 of the NEGP during the "implantation window".

Materials and Methods. A total of 72 infertile patients were studied: 23 with stage 1-2 of the NEG, 32 with tubal-peritoneal factor (TPF) and 17 with male infertility factor (MF). All patients underwent endometrial aspiration pipelle biopsy on the 6th-8th day after ovulation followed by histological and immunohistochemical examination. The number of pynopodia, the level of expression of estrogenic (EPa) and progesteronic (PR-A) receptors in the stroma and endometrial epithelium, the ratio of EP/EP in the stroma using mouse monoclonal antibodies to EPa (clone 1D5 RTU "DAKO", Denmark) and EP-A (clone 636 RTU "DAKO", Denmark) were determined.

Results. The average age of the patients of the main group was 34.17±0.69 years and did not statistically differ from the patients of the comparison group (32.63±0.72 years; p=0.138) and the control group (33.4±1.05 years; p=0.544). In the main group the expression of EPa in the endometrial stroma of the early and middle stages of secretion was low with a tendency to increase and averaged 50±12.25 and 62.27±19.45 points, respectively. In the endometrial epithelium of this group of patients, both early and middle stage of secretion, a moderate EPa expression with a tendency to decrease was noted and averaged 183.75±21.54 and 109.09±16.48 points, respectively. In the comparison group, the expression of ERa in the endometrial stroma of the middle stage of proliferation was moderate (140±20 points), and in the endometry of the early, middle and late stages of secretion, low expression was noted and averaged 40.56±12.68.39.94±7.92 and 70 points, respectively. The expression of EPa in the epithelium of endometrium of the middle stage of proliferation and early stage of secretion was moderate (180±20 and 106.11±18.41 points, respectively), with a tendency to decrease, and in the endometrium of the middle and late stage of secretion there was a low expression of EPa in the epithelium and an average of 70.75±13.24 and 70.0 points, respectively. In the control group the expression of EPa in the endometrial stroma of both early and middle stages of secretion was low (50±20.0 and 60±17.61 points), in the endometrial epithelium the moderate expression of EPa in the early stage of secretion (105.0±35 points) and low (70±15.04 points) - in the middle stage of secretion. When comparing the nature of ERE expression in endometrium of patients with different types of infertility, a higher level of ERE expression in the endometrium of patients with NGE and its increase from early to middle stage of endometrial secretion (p=0.031) was revealed. Expression of ERa in epithelium significantly decreased depending on the phase of endometrial development in all groups (p=0.038), but the average ERa level in epithelium was statistically higher in patients with NGE (p=0.027).