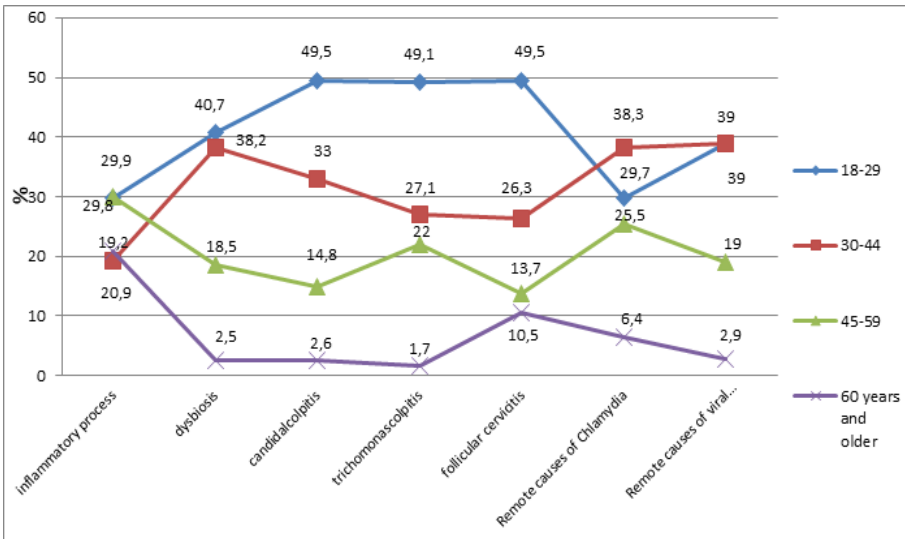

Fig.8. The rate of incidence of cervix inflammatory diseases among women of different age groups

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EVALUATION OF GLUTATHIONE SYSTEM INDICATORS IN THE BODY OF PATIENTS WITH LUNG CANCER

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ABSTRACT

Glutathione is very important in cells protecting, however, its high concentration in tumor cells can increase their survival by raising resistance to chemotherapeutic drugs and free radical oxidation. The effectiveness of chemotherapy treatment often depends on the individual genetic characteristics of the patient, his sensitivity to pharmaceutical drugs. According to scarce existing research it is indicated that tolerability of chemotherapy among Asians is lower compared to Caucasians. In this regard, we decided to evaluate the influence of ethnicity on the indicators of the glutathione system in patients with lung cancer and persons not suffering from oncopathology.

We examined 50 people with lung cancer, admitted to the Yakut Republican Oncology Center. The control group was selected based on age, gender and ethnicity and included 50 people. The main criterion for selection in the control group was the absence of cancer.

The concentration of reduced glutathione, TBA-active products, activity of glutathione reductase, glutathione-S-transferase, glutathione peroxidase were determined by the spectrophotometric method.

The results of our study showed that the concentration of reduced glutathione (Yakuts by 70.7, Russians by 52.4%), the activity of glutathione peroxidase (Yakuts by 34.4, Russians by 18.6%) in the body of patients had been decreasing. The activity of glutathione reductase in the body of patients with lung cancer decreased in Yakuts by 10.5%, while in Russians it increased by 13.0%. The results of our research testify to the depletion of the glutathione system in the group of cancer patients of the Yakut ethnicity, which is probably the reason for the severe tolerance of chemotherapy.

Keywords: glutathione peroxidase, glutathione reductase, glutathione-S-transferase, reduced glutathione, TBA-active products, glutathione system.

Introduction. Glutathione is an intracellular tripeptide consisting of the amino acids: L-glutamate, L-cysteine and L-glycine, it is present in the cells of all eukaryotes, including tumor cells. The concentration of glutathione in the cells is very high, reaching from 1 to 10 mM [15]. The main reservoirs of this tripeptide in the cell are: cytosol (90%), mitochondria (10%) and a small percentage falls to the share of the endoplasmic reticulum [13]. The glutathione metabolism proceeds fairly quickly, for example, in the liver of rats, the period of its half-life is only 2-3 hours [4].

Glutathione readily reacts with electrophilic compounds (carcinogens, drugs), reducing their toxicity [14]; in the nucleus, it promotes the repair of damaged DNA [3]; neutralizes free radicals and peroxides [11]; provides active transport of amino acids [6]; participates in the modulation of the immune response [8], regulates the redox state of the thiol proteins NFkB, caspase, which are involved in apoptosis [12]. It should be noted that glutathione is very important in cells protecting, however, a high concentration of glutathione in tumor cells can increase their survival by increasing their resistance to chemotherapeutic drugs and free radical oxidation [5].

The effectiveness of chemotherapy treatment often depends on the individual genetic characteristics of the patient, his sensitivity to pharmaceutical drugs [9, 16]. According to scarce existing research it is indicated that tolerability of chemotherapy among Asians is lower compared to Caucasians [7]. In this regard, we decided to evaluate the influence of ethnicity on the indicators of the glutathione system in patients with lung cancer and persons not suffering from oncopathology.

The **objective** of this study is to assess the level of glutathione levels in the body of patients with lung cancer.

Research materials and methods. 50 people with lung cancer, admitted to the Yakut Republican Oncology Center were under study. The diagnosis of lung cancer was confirmed histologically. The patients were divided into two groups according to ethnicity: the first group is the Yakuts, the second group is the Russians. The control group was selected based on age, gender and ethnicity and included 50 people. The main criterion for selection in the control group was the absence of cancer. The study material was venous blood, which was taken on an empty stomach from the ulnar vein.

The concentration of indicators of the glutathione system was determined in erythrocytes, and the level of TBA-AP in blood serum using SF-2000 spectrophotometer. The content of reduced glutathione was determined by the reaction with 5.5-dithiobis (2-nitrobenzoic acid) at 412 nm and was expressed in μM/gHb [2]. Glutathione reductase activity was determined by the oxidation rate of NADPH + in the presence of oxidized glutathione at 340 nm and expressed in μMGSSG/min * gHb. Glutathione-S-transferase activity was determined at 340 nm by the rate of formation of conjugates with 1-chloro-2.4-dinitrobenzene in the presence of reduced glutathione and expressed in μM GSH / min * g Hb [10]. Glutathione peroxidase activity was determined at 412 nm in the tertiary butyl hydroperoxide cleavage reaction using reduced glutathione as a substrate. The enzyme activity was expressed in μM GSH / min * gHb [1]. The level of TBA-AP was determined by the reaction of the end products of free radical oxidation of lipids with thiobarbituric acid to form a colored trimethine complex, which was measured at a wavelength of 532 nm and expressed in μM / L [17].

Statistical processing of the data was performed using the SPSS for Windows 10.0 application statistical software package. Standard methods of variation statistics were used: calculation of averages, standard errors, 95% confidence interval. The significance of differences between averages was evaluated using Student's t test for independent samples. The data in the tables are presented as M ± m, where M is the average, m is the average error. The probability of the validity of the null hypothesis was taken at $p < 0.05$.

Results and discussion. According to our data, the content of reduced glutathione in the group of relatively healthy people not suffering from oncopathology was 2.32 ± 0.09 μM / gHb. The concentration of reduced glutathione changed depending on ethnicity: in the first group it was 2.50 ± 0.05 μM / gHb, in the second - 2.04 ± 0.06 μM / gHb, that is, in the Yakuts it was higher by 18.4%, compared to the Russians.

Glutathione reductase activity was 6.8 ± 0.30 μM GSSG / min * g Hb. The level of the average activity of glutathione reductase in the first group (7.5 ± 0.10 μMGSSG / min * gHb) was 20% higher ($p < 0.05$) than in the second (6.01 ± 0.30 μMGSSG / min * hb).

Glutathione-S-transferase activity was 2.44 ± 0.07 μMGSH / min * gHb. We observed a decrease in the activity of glutathione-S-transferase in the first group (2.20 ± 0.06 μM GSH / min * gHb) by 9% compared with the second group (2.42 ± 0.03 μM GSH / min * gHb).

The level of glutathione peroxidase was 6.10 ± 0.005 μM GGSH / min * gHb. Depending on the ethnicity, differences in enzyme activity were noted: in the first group (6.50 ± 0.009 μM GGSH / min*gHb), it was significantly higher (by 35.4%) than in the second (4.20 ± 0.002 μM GH /min* ghb).

The concentration of the lipid peroxidation index - TBK-AP was equal to 1.61 ± 0.10 μM / l and depended on ethnicity. So, in the first group this indicator corresponded to 1.71 ± 0.16 μM / l, in the second - 1.38 ± 0.28 μM/l, i.e. in the first group, the level of TBA-AP was higher by 19.3% ($p < 0.05$).

Depending on the ethnicity of relatively healthy individuals, the indicators of the glutathione system change. In the Yakut group higher concentrations of reduced glutathione (18%), glutathione reductase activity (20%) and glutathione peroxidase (35.4%) are noted. We also noted the intensification of free radical oxidation of lipids in the body of Yakuts, as evidenced by an increase in the concentration of TBA-AP by 19.3%.

In the body of patients with cancer, the concentration of reduced glutathione was significantly lower (by 28.8%) compared with those not suffering from oncopathology and was equal to 1.65 ± 0.01 μM / gHb. This can probably be caused by a high rate of consumption and a low rate of its recovery. Maintaining a sufficiently high level of reduced glutathione by restoring its disulfide form is provided by glutathione reductase. Glutathione reductase activity in the group of patients

was less by 36.7% than in the control, and was 4.30 ± 0.05 μM GSSG / min * g Hb. Consequently, the regeneration of glutathione in the blood erythrocytes of patients with lung cancer at the proper level does not occur. We consider the most likely cause of this phenomenon an insufficient regeneration of $NADPH+H^+$ in the pentose phosphate pathway. The activity of glutathione-S-transferase did not actually differ from the control, it was equal to 2.42 ± 0.01 μM GSH / min * gHb. Glutathione peroxidase activity decreased by 68.8% (1.9 ± 0.001 μM GSH / min * gHb) than in the control group. In patients with lung cancer, a significant increase in free radical oxidation of lipids was noted. The average content of TBA-AP in the blood of patients with lung cancer was 32.6% higher than the control value and was 2.39 ± 0.32 μM/L.

In the group of patients, the concentration of the reduced form of glutathione, as well as the activity of glutathione reductase, did not have significant differences depending on ethnicity. In the first group of patients, the content of reduced glutathione was 34.4% less (P <0.05) compared with the control group (1.64 ± 0.01 μM / gHb), in the second group of patients it was 18.6% lower (P <0.05) (1.66 ± 0.009 μM / gHb). Glutathione reductase activity in the first group of patients was 10.5% lower (6.71 ± 0.09 μM GSSG / min * gHb), and in the second group of patients it was 13.0% higher than control (6.9 ± 0.15 μM GSSG / min * hb).

Significant differences in the activity of the enzyme performing the detoxification function in patients with lung cancer, depending on ethnicity, were not found. Glutathione-S-transferase activity in the first group of patients was 7.1% (2.37 ± 0.15 μM GSH / min * gHb), in the second group 3.0% (2.49 ± 0.25 μM GSH / min * gHb) above the control value.

An assessment of the enzymatic status of antioxidant protection in the blood of patients with lung cancer showed that glutathione peroxidase activity in both groups of patients was significantly reduced. In the first group, the glutathione peroxidase activity was 70.7% less than the control (1.90 ± 0.005 μM GSH / min * gHb); and in the second group - by 52.4% (2.00 ± 0.012 μm GSH / min * gHb).

At the same time, the intensity of free radical oxidation in the body of cancer patients increased, as evidenced by the increase in the content of TBA-AP in patients of the first group to 2.35 ± 0.12 μmM / l, which was 27.2% higher than the control (P <0.01), the second group was equal to 2.45 ± 0.25 μM / L, which exceeds the control indicators by 43.6% (P <0.05).

Conclusions. Thus, the results of our research have shown that in patients with lung cancer, indicators of the glutathione system vary depending on ethnicity. Among patients the concentration of reduced glutathione in the Yakuts decreased by 34.4%, Russians - by 18.6%, glutathione peroxidase activity - by 70.7 and 52.4%, respectively. The activity of glutathione reductase in the body of patients with lung cancer decreased in the Yakuts by 10.5%, while in the Russians it increased by 13.0%. The results of our research testify to the depletion of the glutathione system in the group of cancer patients of the Yakut ethnicity, which is probably the reason for the severe tolerance of chemotherapy.

This study was conducted in the framework of the research work "Epidemiological aspects of malignant tumors in the conditions of the Far North, the development of modern methods for early diagnosis, prevention using highly informative fundamental research methods" in the department of studying the adaptation mechanisms of the Yakut Science Center of Complex Medical Problems.

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ASSESSMENT OF CHANGE OF ERYTHROCYTES BY METHOD OF RASTER ELECTRONIC MICROSCOPY AT THE PERSONS WHO DIED OF FATAL HYPOTHERMIA

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ABSTRACT

Red blood cells (RBC) morphology of deceased from various causes (injury, hypothermia) was examined in this study by using scanning electron microscopy. The obtained data shows that the appearance of certain forms of cadaveric erythrocytes depends on the causes of death. Therefore, when death is caused by stabbing and gunshots RBC take acanthocyte forms and in cases of fatal hypothermia RBC take echinocyte forms. The results of an experiment carried out in vitro, at small negative temperatures,show the appearance of acanthocytes in observed blood samples. Based on theobtained data and on the ability of echinocyte to return to normal form, it can be concluded that the probability of restoring the vital activity of the frozen organismsare possible.

Keywords: red blood cells, erythrocytes,hypothermia, scanningelectron microscopy.

Introduction. Frostbite and hypothermiaare the most severe types of cold trauma, often leading to a high level of disability and death of the affected [1]. Till present time, the questions of death from freezing in conditions of extremely low temperatures (below -40°C) have not been fully examined in the world. In real conditions, people who died from hypothermia (by external signs) without carrying out resuscitation measures are delivered to the morgue. The key-point is that during the first 2 days when the victims are in a state of cold anabiosis (a very rare pulse, low blood pressure) it is may be possible to restore the vital activity of the organism(there are cases of preservation of the vital functions of the heart and other organs in frozen animals).The results of our work suggest a theoretical probability of the restoration of frozen tissues, organs, and also the revitalization of the frozen organisms.

At present time, in the literature available to the public, there are no data on the SEM study of the RBCs of people who diedfrom the cold temperatures.

Revealing the features of the morphology of the blood cells of the deceased from hypothermia may possibly supplement the idea of the cellular-molecular mechanisms of the process of general cooling of the organism and confirm the possibility of restoring the vital activity of the organism.

The purpose of this article is toexamine