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**MUTAGENIC EFFECT AND PRODUCTION FACTORS**

*Қарағанды облысы кеншілерінің ағзасына мутагенді эффектiлердiң және шаң-тозаңның әсерi туралы мәліметтер эксперименттi және табиғи зерттеулер нәтижесінде алынып сарапталды. Мутагенді әсерді анықтау үшін өндірістік ортаның микрородөңгейінің ұлғаюы мен бөлу айналымының бұзылуын қабылдайтын тест, ДНК-ң ролі көрсетілген. Бұл кеншілер әйелдерінің құрсақтарындағы ұрықтың өлуін көрсететін талдау, яғни, кеншілердің ағзасына мутациялық процестердің белсенді түрде әсер ететіндігін дәлелдейді.*

*Издаются полученные оригинальные данные по изучению в динамике роли мутационного эффекта при воздействии сочетанных факторов вибрации и пыли на организм как в эксперименте так и в натуральных исследованиях у шахтеров-угольщиков Карагандинской области. Для выявления мутагенного действия сочетанных факторов производственной среды установлено увеличение уровня микроядер и нарушение веретена деления, который является достаточно чувствительным тестом. Показана роль ДНК. Анализ внутриутробной смертности плода у жен шахтеров-угольщиков подтверждает и косвенно указывает на активизацию мутационного процесса у шахтеров-угольщиков.*

Due to the rapid development of technology, industry, today the problem of the impact of ecology became important, and in particular, the impact of production with its factors on the genetic apparatus of an organism. Therefore, great importance takes the assessment of genotoxicity of the industrial environment with the subsequent development of activities to protect heredity of the person [1–7].

We, in experimental conditions during modeling of a vibratory pathology (depending on terms of influence of vibration on the background of coal rock dust), studied the micronucleus analysis in polychromatocytes, which has shown that in 3 days of influence of vibration and dust there was observed significant increase of 38 % in frequency of cells with macronucleuses on average of  $0,47 \pm 0,04 \text{ ‰}$ ,  $P < 0,05$ ; in comparison with the control  $0,34 \pm 0,03 \text{ ‰}$  (Table 1 Figure 1). Basically, these changes occurred at the expense of micronucleuses (acentric fragments), the level of which has averaged  $0,43 \pm 0,04 \text{ ‰}$ ,  $P < 0,01$ ; that is 40 % more than in the control  $0,31 \pm 0,02 \text{ ‰}$ . Violation of maturation spindle, as evidenced by the presence of macronucleuses, increased by 67 % to  $0,05 \pm 0,0004$  in comparison with the control —  $0,03 \pm 0,0001 \text{ ‰}$ ,  $P < 0,01$  (Table 1, Figure 1.2). On day 7 of vibratory and dust impacts the quantity of cells with macronucleuses continued to raise with high degree of reliability in 2 times in comparison with control values, reaching  $0,70 \pm 0,05$ , as well as micronucleuses, which also increased in 2 times on average to  $0,62 \pm 0,03 \text{ ‰}$ , that considerably differed from the indicators of 3-day exposition — on 44 %,  $P < 0,0001$ . The num-

ber of violations of maturation spindle continued to increase in 2,7 times on average to  $0,08 \pm 0,05 \%$ ,  $P < 0001$  and by 60 % in comparison with 3-day exposition.

On the 10th day of an exposition we observed the further growth of frequency of cells with macronucleuses — in 2,3 times on average to  $0,79 \pm 0,07 \%$ ,  $P < 0001$ . It is same characteristic for the level of micronucleuses — i.e. their increase in 2 times to  $0,62 \pm 0,03 \%$ . With high degree of reliability in 5,7 times increased the number of violations of maturation spindle to  $0,17 \pm 0007 \%$ ,  $P < 0,001$ , in 2 times in comparison with 7-day experiment.

After 14 days of influence of local vibration and dust level of macronucleuses continued to increase statistically authentically in 3,2 times, reaching a value of  $1,07 \pm 0,10 \%$ ,  $P < 0,001$ . The number of violations of maturation spindle remains at level of 10th day and raises in 6 times to  $0,18 \pm 0,09 \%$  in comparison with the control,  $P < 0,001$ . The level of micronucleuses also continued to increase in 2,9 times to  $0,89 \pm 0,03 \%$ ,  $P < 0,001$ , and by 44 % in comparison with 10-day period.

Table

Data of micronucleus analysis of polychromatocytes in rats depending on duration of the impact of local vibration and dust (%)

Duration of the impact, days	n	Cells with macronucleuses	Micronucleuses	Violation of maturation spindle
0	6	$0,34 \pm 0,03$	$0,31 \pm 0,02$	$0,03 \pm 0,001$
3	6	$0,47 \pm 0,04$ *	$0,43 \pm 0,04$ **	$0,05 \pm 0,006$ **
7	6	$0,70 \pm 0,05$ *** ###	$0,62 \pm 0,03$ *** ###	$0,08 \pm 0,008$ *** ##
10	6	$0,79 \pm 0,07$ ***	$0,62 \pm 0,03$ ***	$0,17 \pm 0,007$ *** SSS
14	6	$1,07 \pm 0,10$ *** &	$0,89 \pm 0,03$ *** &&&	$0,18 \pm 0,09$ ***

Symbols — \* <0,05; \*\* <0,01; \*\*\* <0,001 — in comparison with the control;  
 ## <0,01; ### <0,001 — in comparison with 3-day term;  
 SSS <0,001 — in comparison with 7-day term;  
 & <0,05, &&& <0,001 — in comparison with 10-day term.

It is shown, that already on the 3rd day of the combined influence there was observed an increase in level of micronucleuses and violation of maturation spindle. Consequently, these indicators in erythrocytes are sufficiently sensitive test of detecting mutagenic activity of local vibration on the background of dust factor.

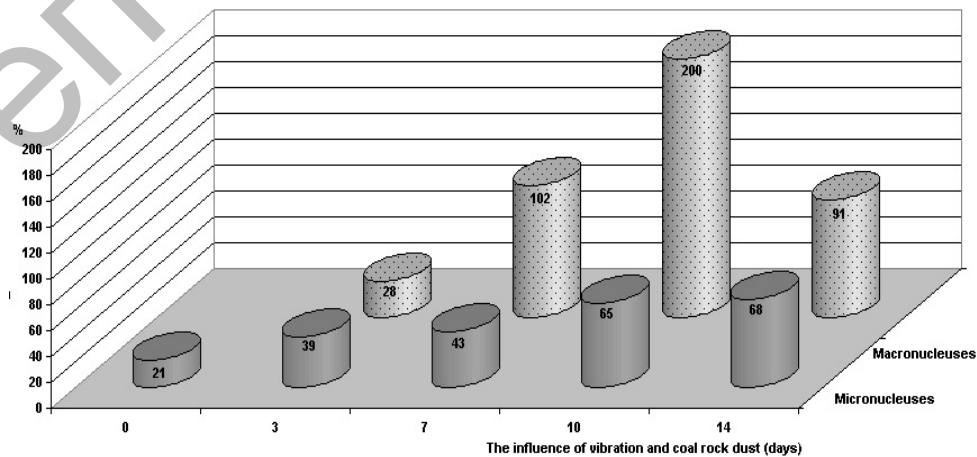


Fig. 1. Dynamics of changes in the frequency of erythrocytes with micro- and macronucleuses at rats under the influence of vibration and coal rock dust

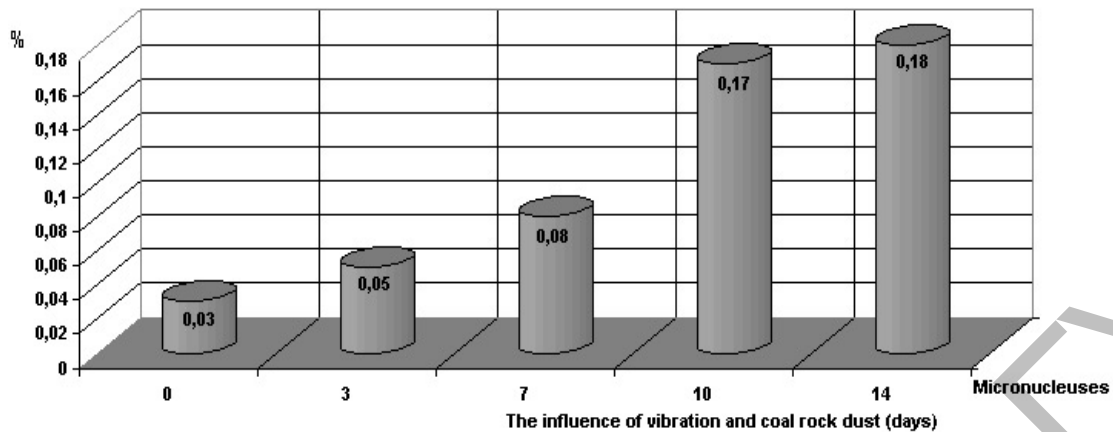


Fig. 2. Dynamics of violations of maturation spindle in erythrocytes of rats under the influence of vibration and coal rock dust

As the most sensitive indicator should be recognized the level of micronucleuses or acentric fragments. This parameter has shown positive and stable correlation with the data of cytogenetic analysis of chromosome aberrations ( $r \geq 0,9$ ). However, the level of violations of maturation spindle is most expressed on the 10th day of combined influence, which corresponds to the analysis data of genomic violations.

The metaphasic analysis of violations of chromosomes in the bone marrow cells, caused by the action of local vibration and dust: the cytogenetic analysis of violations in the bone marrow cells of experimental animals has shown authentic growth in the level of chromosome aberrations in the 3-day exposition on  $27\%$  to  $1,00 \pm 0,08\%$ ,  $P < 0,01$  in comparison with the control —  $0,79 \pm 0,05$  (Fig. 3). In general, as well as in the control group we observed simple violations (single and conjugated acentric fragments) with prevalence of damage of chromatid type. At the 3rd day of influence there were also outlined some changes in the spectrum of mutations. Symmetric exchanges of chromosomal type with the frequency of  $0,07 \pm 0,06\%$  and isochromatid fragments —  $0,09 \pm 0,08\%$  were found out. It is necessary to note the trend towards an accelerated growth of aberrations of chromosomal type in comparison with violations of chromatid. So, if the frequency of damage in the whole chromosome by the 3rd day of the experiment has increased by  $44\%$ , the second parameter has grown by only  $16,4\%$ . Higher rates of increase in the frequency of gaps of chromosomal type remained on the late terms of the experiment that testifies about greater susceptibility to mutations of chromosomes until their reduplication, i.e. immediately after mitosis.

Thus, on the 3rd day of vibratory influence we observed significant increase in the frequency of aberrations. The received results related to symmetric exchanges and isochromatid fragments have Poisson distribution, which is within the existing understanding of the dynamics of these types of aberrations in the passage of cell division. Discussed types of violations are rare due to its nature and therefore do not bring the essential contribution to the increase of the frequency of aberrant metaphases — the increase occurs basically due to conjugated and single fragments. This trend continues to remain on later terms of the experiment.

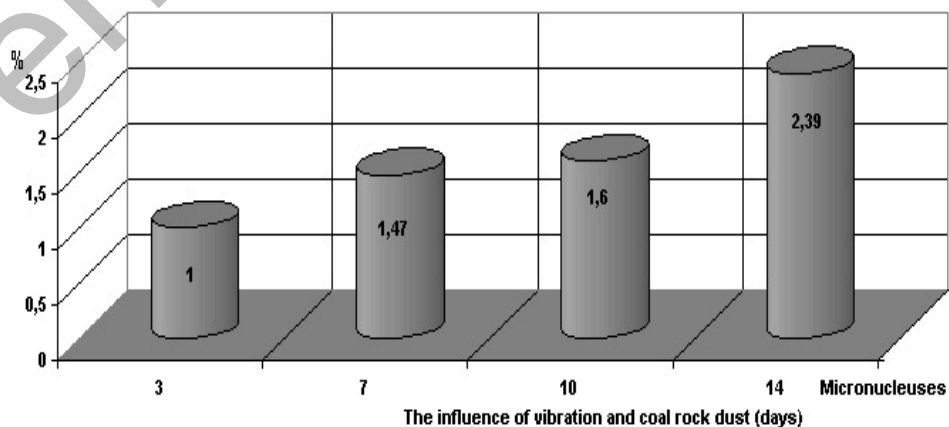


Fig. 3. Dependence of the frequency of violations in the structure of chromosomes of bone marrow cells from duration of influence of vibration and coal rock dust on experimental animals

After 7 days of influence the number aberrant metaphases authentically increased in 2,2 times on average to  $1,74 \pm 0,04$  %,  $P < 0,001$  in comparison with the control. Conjugated fragments still have predominated among aberrations of chromatid type, which frequency increased in 2,6 times to  $0,64 \pm 0,14$  % in comparison with the control. There were changes in the spectrum of chromosome violations due to the appearance of dicentrics —  $0,07 \pm 0,06$  %. The level of symmetrical chromosomal exchanges did not change statistically authentically. Gaps of chromosomal type are presented by the single fragments, which number increased by 46 % in comparison with the control —  $0,94 \pm 0,18$  %.

The gaps of chromatid type, but to a lesser extent, still prevailed over chromosome violations. The coefficient of chromosome gaps / chromatid aberrations was 0,84.

Thus, by the 7th day of influence the frequency of cells with structural chromosome violations continued to increase. We observed changes in the spectrum of aberrations manifestative in the appearance of dicentric anomalies. The tendency, which has outlined earlier to change of the ratio of chromosome and chromatid damages, remained.

On the 10th day of exposition some decrease in the number aberrant metaphases to  $1,60 \pm 0,08$  % in comparison with the data of 7-day experiment was revealed. However these sizes are statistically inauthentic as well as changes. The levels of aberrations of chromosomal type did not differ from the frequency of aberrations of chromatid type. The number of structural violations of chromosomes in the 14-day exposition increased in 3 times in comparison with the control group, reaching on average —  $2,39 \pm 0,12$  %. Basically they occurred at the expense of increase of the frequency of conjugated chromosomal fragments to  $0,69 \pm 0,13$  and dicentrics —  $0,30 \pm 0,13$  %.

Changes in the spectrum of violations are connected with the appearance of acentric rings with frequency of  $0,09 \pm 0,08$  and isochromatid fragments —  $0,20 \pm 0,08$  %. At this stage of influence symmetrical chromosomal exchanges are not revealed. The level of gaps of chromosomal type did not differ from the frequency of chromatid violations. These indicators increased in 4 and 2 times in comparison with the control to  $1,08 \pm 0,18$  and  $1,02 \pm 0,19$  % respectively,  $P < 0,001$ .

Based on the foregoing, it is possible to draw a conclusion that influence of local vibration and a dust causes increase in frequency of structural violations of chromosomes. During 3-day exposition mutations of chromatid type prevailed, but frequency of violations as a whole of the entire chromosome practically did not differ from control values. Taking into account the character of distribution of data related to symmetrical chromosome exchanges and the specific condition of the cell population, when we were observing 1st, 2nd and even 5–6th mitosis simultaneously, it is possible to assume that professional factors have influence mainly in the stages S and G1 of cell cycle. Expansion of the spectrum of aberrations, apparently, is due to the transformation of some types of violations in the other ones as a result of the passage of several cell divisions at later terms of the experiment.

It is known that the emergence of the gap needs to react to one locus of chromosome with one and (or) two particles of the mediator. It is possible to assume that in this case the chromosome reacted to influence of vibration and dust simultaneously as one — and double-stranded structure.

All above-stated gives the reason to claim the mediated influence of the studied factors. Apparently, the direct influence of vibration on the background of coal rock dust on DNA was reflected by the deviation towards functional double-strand. At the same time character of mutation spectrum allows to suggest nonspecific binding of the mediator with DNA molecule.

We had made an attempt of extrapolation of experimental data in natural researches on coal miners of the Karaganda coal basin. One of the data specifying the genetic disadvantage, caused from both ecological and professional factors, is the pathology of pregnancy and delivery (spontaneous abortions, mortinatality) [8–15].

Genetic consequences from the action of combined factors of production at the population level of the coal miners have been studied by the account of intrauterine mortality rate at their wives. With the help of a questionnaire the increase in 3 times of quantity of intrauterine mortality of a fruit at wives of the miners contacting on production with local vibration — to 8,9 % in comparison with the control (2,9 %) is revealed. For an exception of habitual miscarriages all families, in which there were 2 and more miscarriages, are excluded from the analysis. Due to the fact that the work of women was not linked with industrial hazard, it is possible to suggest that increased intrauterine mortality is explained only by mutational damage of men cells.

The influence of age of father and mother on an investigated indicator is excluded, in view of the fact that both samples did not differ statistically on the sign. No distinctions between samples on the average experience of father were revealed at the moment of conception. However this indicator in a group of miners contacting to local vibration by 90 % higher than in the control, which amounted to  $2,8 \pm 0,1$  years. It should

be noted that the sign in contact group tends to stabilize (the coefficient of variation is equal to 21 %), while in the control it varies quite widely. The correlation analysis has not shown dependence between the experience and quantity of intrauterine mortality rate of a fetus.

It is shown from the analysis of spontaneous abortions depending on the terms of abortion that the wives of miners, whose work is related to exposure to significant levels of local vibration, miscarriage occurs primarily in early terms of pregnancy. Whereas in the control group this apparent predominance has not been found. The frequency of spontaneous abortions in late terms of pregnancy of the wives of miners, who have had contact in the working process, has decreased in comparison with the control by 62 and 43 % after 9–15, 16–22 weeks.

On the basis of cytogenetic observation of the analysis material of spontaneous abortions, several researchers showed that the frequency of chromosome anomalies varies dramatically depending on the terms of the interruption of pregnancy: on the 2nd week, it is 78 %, on the 3rd — 60 %, on the 4th — 61 % (on average of 14 weeks of pregnancy 66 %).

Thus, we can assume that the natural abortion among the wives of coal miners is mainly due to genetic reasons.

The number of spontaneous abortions among the wives of coal miners is 50 % higher than in the control group. The level of congenital malformations in children born from miners was 0,31 %, while there were not observed congenital malformations in the control. The frequency of stillbirth is also equal to 0,31 %. There were found out no stillbirths in the control group. The level of early infant mortality of miners in this category amounted to 0,62 %, which is 70 % higher than the measure in the control. Integration measure of one mutation event among miners of vibration dangerous professions — 2,62 %, which is 80 % higher than in the control group. Analysis of intrauterine fetal mortality among wives of coal miners confirms and indirectly points at activation in the mutation process of coal miners.

Based on the above described experimental data one can claim about the role of mutational effect in the conditions of influence of vibration and coal rock dust by the analysis of macro- and micronucleuses, the violation of maturation spindle in polychromatic erythrocytes, identification of violations of the structure and function of cell membranes. Changes in the cell membrane, changing its resistance and destroying the structure of DNA, cause mutational instability, inducing an increase in the level of micronucleuses, the violation of maturation spindle in polychromatic erythrocytes of blood, and have a stable positive correlation with the data of cytogenetic analysis of chromosome aberrations. Analysis of distribution of chromosome aberrations in cells is characterized by the stages of mutation process. Increase of mitotic activity in bone marrow cells in the early stages of the experiment and the reduction — in the later correlated with the content of DNA. RNA, acidic DNK in cells of the blood. The negative trade factors, indirectly via the metabolism, induce molecular mechanisms of transformation of nuclear structures, which involved in the process of adaptation that found out an indirect confirmation among coal miners.

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### RESEARCHING OF GENETIC MODIFIED INGREDIENTS IN MEAT PASTES

*Қазақстан нарығында және ТМД елдерінің аумағында өндірілетін етті пащеттің 8 түрі құрамында генетикалық модификацияланған организмдер бар болуына зерттелді, үш «ПЛАНТ-СКРИН», «Терминатор Nos» және «ГИ-соя-40–3–2» тест-жүйе қолданылды. Полимераздық тізбекті реакциясы көмегімен біреуінен 40–3–2 генетикалық модификацияланған соя табылды.*

*Изучено 8 разновидностей мясных пащеттов, имеющих на рынке Казахстана и производимых на территории стран СНГ, на наличие генетически модифицированных организмов с использованием трех тест-систем «ПЛАНТ-СКРИН», «Терминатор Nos» и «ГИ-соя-40–3–2». Использован метод полимеразной цепной реакции. В одном из продуктов выявлена генетически модифицированная соя линии 40–3–2.*

All over the world the market of a foodstuff is flooded by the goods containing genetically modified organisms. In agricultures of many leading countries-exporters of a vegetative foodstuff and vegetative raw materials, plants with the changed genetic code for a long time already are grows up. Production of new transgene plants as yet one of perspective and most developing directions of biotechnology in agro production sphere [1, 2].

Transgene names those kinds of plants, in which gene (or genes) transferred from other kinds of plants or animals [3] is successfully functions.

Areas under GM-plant crops anniversarily increase approximately on 60 %. Apparent, now it exceeds 50 million hectares that makes about 3 %-5 % from the all areas of crops. In production of foodstuff 70 % GM-soya, 25 % GM-corn, and also a potato, rice, rape, tomatoes, a sugar beet are used. The general manufacturer of production which contains GMO — is USA that makes 68 % GM-products, 12 % Argentina, 6 % Canada, 5 % Brazil, 4 % China [4, 5, 6].

Now there is no the valid scientific information authenticates to any inherent danger of genetically modified organisms (GMO). However it does not prove full absence of the risks associated with ubiquitous introduction of GMO. Opponents of accelerated introduction GM-organisms declare that outcomes from the eating of such products have long-term character and shows through a few generations. As proofs experiences on animals, with amazing results are represented. Accounting a large quantity of population which consuming GM-soya, corn, rice, a potato, and other plants, the slowed down effects can lead to mass unwanted consequences [7, 8, 9].

The most part of genetically modified products is using for export. Now more and more countries accepts laws on required marking of such goods and even prohibition of it import to certain territories [10].

In Kazakhstan the question of GMO disturbs only certain organizations. The researches spent in this area are insignificantly and limits by detecting GMO in a foodstuff and nothing more. At least and this tests brings results. For example, established, that 60–75 % of all imported foodstuff in the country contains GM-components [11]. Absence of the necessary equipment in the country impedes to other kinds of research.

Expounded above confirms the necessity of researching foodstuff on presence GMO in it.

For today, the most effective method of monitoring for presence GMO in a foodstuff is method of PCR allowing not only to detect presence GMO in it, but also to define their quantity [12–19].