Open Journal of Social Sciences, 2018, 6, 48-65
http://www.scirp.org/journal/jss
ISSN Online: 2327-5960
ISSN Print: 2327-5952

Children's, Adult's and Family's Emotional Stress in Context of Genomic Instability

Faina Ingel[1], Elena Krivtsova[1], Nadezhda Urtseva[1], Tatiana Legostaeva[2]

[1]The Laboratory of Genetic Toxicology of Federal State Organization "Centre for Strategic Planning and Management of Biomedical Health Risks" of the Ministry of Health of the Russian Federation, Moscow, Russia
[2]Nosov Magnitogorsk State Technical University, Russian Federation, Magnitogorsk, Russia
Email: fainaingel@mail.ru

How to cite this paper: Ingel, F., Krivtsova, E., Urtseva, N. and Legostaeva, T. (2018) Children's, Adult's and Family's Emotional Stress in Context of Genomic Instability. *Open Journal of Social Sciences*, **6**, 48-65.
https://doi.org/10.4236/jss.2018.66005

Received: April 23, 2018
Accepted: May 20, 2018
Published: May 23, 2018

Abstract

Scientific data concerning the impact of emotional stress to human genomic instability very seldom describes in literature. For many scientists this connection is not supposed to be obvious, although oncologists and psychologists know that a prolonged state of heightened emotional tension is fraught with serious problems for the nervous-immune-endocrine system of the organism. Moreover, oncologists know that cancer is often the result of resentment and loneliness. At the same time, the role of genome instability in processes of tumor induction and progression is proved very correctly. In the report will be paying attention to 3 aspects of human life in context of emotional stress expression and its connection with genomic instability: environmental pollution, genomic predisposes, ethic and social-economic problems. The report will contain data from literature and results of own research directed to the analyzing the impact of the degree of emotional stress expression on the children's and adults' genomic instability. Special attention will be paid to the investigation how emotional state of parents and teachers impact on young children's genomic instability. Methods. For evaluation of stress expression levels we used the complex of standard psychological tests: questionnaires—for adults and 8-coloured M. Luscher's test—for children. Estimation of genomic instability was carried out in blood cultures by test on chromosome aberration and micronuclei test with Cytochalasin B. Alteration of biochemical indices were detected by standard methods.

Keywords

Component, Formatting, Style, Styling, Insert

1. Introduction

The term "genomic instability" describes complex of various molecular mechanisms and their effects leading stable genome of normal cell to unstable, characteristic for tumors [1]. European investigations demonstrated that detection of increased frequencies of chromosome aberrations as well as cells with micronucleus in human blood correlated with increased risk of tumor development [2] [3]. This direction of study is very important because in 2015 about 8.8 million people died from cancer—near 1 of 6 global deaths. WHO prognoses 12 million cancer deaths worldwide in 2030 [4]. Cancer death as well as cancer rejuvenation observing in all countries stimulated our interest to revealing of the reasons of children's and adult's genomic instability.

More often we could hear that "stress harms health"—this phrase we found out even in WHO publication [5]. In this publication we will consider stress syndrome (synonyms—general adaptive syndrome, stress reaction, stress) in accordance to H.Selye's concept [6] [7] [8] [9]:

- is a nonspecific response of the total body to any demands made upon it;
- is a part of daily life and can't be avoided;
- is a mechanism of acute and chronic adaptation necessary for evolution and survival;
- the integrated stress response is a part of the homeostatic balance, and the dysfunction of this response may contribute to disease.

Biological role of stress is to increase resistance and adopt organism to environmental impacts. Stress reaction develops by excretion of neurotransmitters, what triggers, practically, all of biochemical reactions, including response of the neural system, immune response and endocrine reactions. So, stress is normal reaction of all organisms and life is impossible without it.

Now it is admitted to distinguish two different levels of stress expression [6] [7] [8] [9]:

1) normal level of stress expression is the responding reaction, arising within individual norm of reactivity of the organism and necessary for its normal functioning;

2) non-adaptive (abnormal) stress or distress—the response, which level of expression exceeds adaptive potential of an organism and lead to tension or breakdown of adaptive systems' work and diseases. The main targets of distress in mammalian and human organisms are neural, cardio-vascular, immune and endocrine systems as well as gastrointestinal tract. So, the main trigger or real reason of, practically, all of diseases may be abnormal stress expression (distress). In all of our studies we adhere namely to this concept.

2. Results

2.1. Human Emotional Stress and Environmental Pollution

Statement of the problem concerning principal possibility of environmental pollution to increase level of human emotional tension lead us to idea to compare levels of stress expression between people living in one areas of Moscow but at different distance from the major car road. Results of the study had shown that the closer to the road, loaded with transport, the higher levels of stress expression in the inhabitants of these houses.

In **Figure 1** it is seen that with increasing of air samples toxicity the proportion of respondents who were in a state of psychological comfort significantly decreased (R = −0.65). It should be emphasized that in the area with maximal pollution almost all residents who were asked to undergo anonymous psychological testing refused it in sharp form, while residents of areas with lower levels of air toxicity were more friendly and mostly agreed to answer to our questionnaires (testing at all areas in each district was carried out by the same group of specially trained scientists, who used the same questionnaires and interviewed people by common rules).

Then comparative investigations were carried out in 4 Russian industrial towns[1]. Groups of adults for these studies were formed in: Diadkovo Town—workers of Crystal plant and citizens (men and women); Chapaevsk Town (Russian dioxin town)—workers of agricultural poisons plant and citizens (women); Yaroslavl Town—workers of oil refinery and machinery plants (men); Moscow—workers of oil refinery and citizens (men); Moscow (scientists, toxicologists (women). In total were examined 279 persons. Program of the investigations included: 1) evaluation of total toxicity and total mutagenisity of air samples, collected in work area and living zones or evaluation of dioxin in blood and /or contents of heavy metals in hairs of surveyed persons; 2) level of chromosome aberration (CA) and coefficient of UV-induced DNA reparation (Cuv UDS) in human blood lymphocytes; 3) evaluation of levels of emotional stress expression (ESL) by standard psychological questionnaires detected different kinds of emotional tension – psychological depression, anxiety and overfatigue.

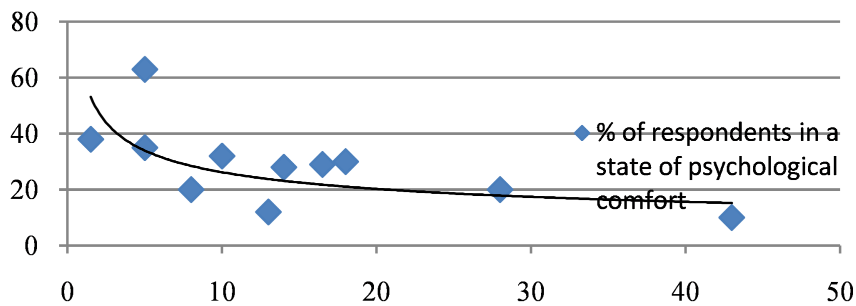

Figure 1. The proportion of residents of 4 districts of Moscow who were in a state of psychological comfort at the time of examination, depending on the levels of toxic effects of air samples (“Ekolum 005”, open air, sample volume 100 m^3) taken in the places of surveyed people residence. R = −0.65. 562 adults were interviewed. On the abscissa axis—the ratio of luminescence extinguishing.

[1]All of the studies were permitted by Ethical Committee in Administration of the Cities, the Main Pediatricians and written resolution of all volunteers and parents of all children.

The differences between workers and citizens by levels of genomic instability in each town were not detected (**Figure 2**), but very significant were differences between people in state of psychological comfort, but living in different towns (**Figure 3**), what allow use this complex approach to select the priority of risk assessment in the surveyed towns.

Summarizing all the data obtained in this work, it should be said that human ESL correlated with level of CA ($P \leq 0.05$), with Cuv UDS ($P \leq 0.01$) and with blood dioxin contents ($P \leq 0.001$) [10]. Moreover, people in state of distress, as a rule, had higher level of CA and abnormal DNA reparation in blood lymphocytes than people living in state of psychological comfort. Repeated studies showed that people in stress had higher susceptibility of genome to environmental mutagens as well as their blood lymphocytes—to in vitro mutagenic loads, what is in good agreement with results of our prolonged murine experiments [10] [11]. So, level of emotional stress expression may be useful as the indicator and measure of level of toxic and/or genotoxic exposure.

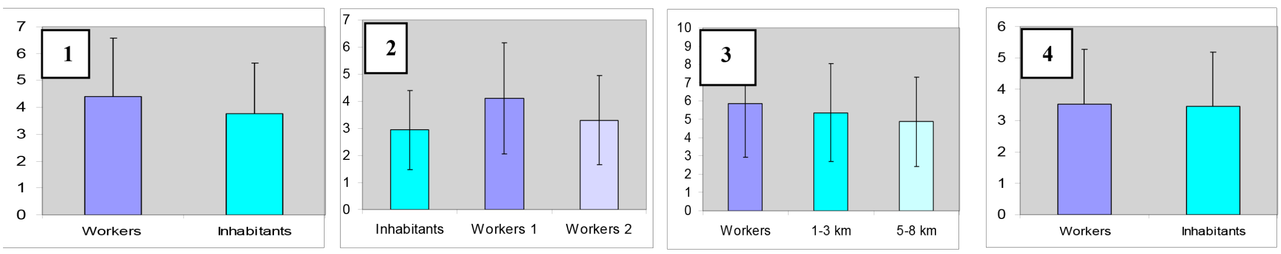

Figure 2. The average frequencies of chromosome aberrations in blood of peoples, living in different Russian industrial towns: 1—Chapaevsk, 2—Moscow, 3—Diat'kovo, 4—Yaroslavl (workers 1—mechanical plant, workers 2—oil refinery plant).

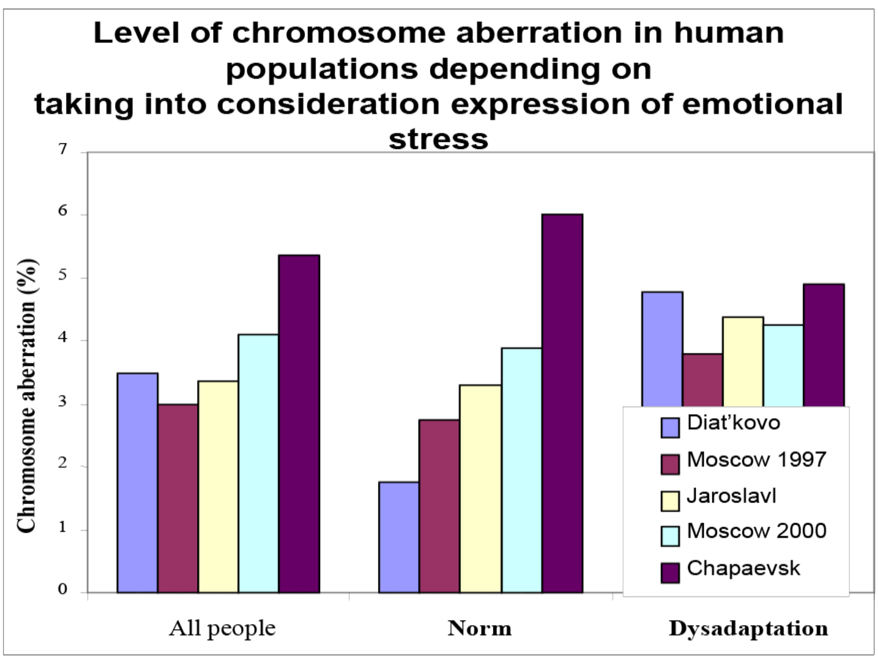

Figure 3. The experimental approach for prioritization the risk assessment of human genome instability from the analysis of the air pollution impact.

So, our data demonstrate that level of emotional stress expression significantly modifies genome susceptibility to environmental mutagens and, consequently, is an important risk factor, have to be included into system of genetic monitoring: 1) people with high level of chronic stress have to be included into groups of increased genetic risk; 2) levels of genetic damage (CA and MN) detected only among people living in state of psychological comfort allow evaluate levels of genetic damage and DNA reparative activity being free of social and economical factors impact. This procedure can be useful for correct comparison of genetic effects between groups, departments, plants, and etc.

2.2. Genomic Instability and Susceptibility of Children from Aral Sea Basin in Respect of Emotional Stress

It is well known that children are most sensitive to environmental pollution [12] [13]. To understand the role of emotional stress in this problem we carried out the international study in Aral Sea Basin in frames of INTAS 1005 project (2002-2003)[2] [14] [15]. Before providing this study it was concluded that the environmental problems in the Aral Sea region in Kazakhstan were of near catastrophic proportions because of high concentrations of industrial pollutants such as PCB-compounds, salts of heavy metals and pesticides have accumulated not only in water, but also into soil to an unknown extent and have been deposited over large areas by atmospheric transport. The expansion of irrigation and achievement of self-sustainability in cotton for the USSR as a whole was found to have been reached at the expense of the region's food sustainability. Socio-economic processes causing a decline of the quality of life, deterioration of health, growth of unemployment and emigration are associated with this region, too. These consequences became even more complicated by the painful economic transition in the new independent states. The deterioration of human health with increasing infant mortality rate, declining life expectancy at birth and increasing prevalence of serious infectious diseases in former Soviet Republics is thought to be due to a combination of several factors such as inadequate nutrition, poor sanitation, collapse of the health care system and pollution from Soviet agriculture and industries. Among this complex of problems on the maiden place, unconditional, problem of health of children leaves. And the greatest problem is children's genome stability, because it is closely connected with health of future generations.

For detail analysis of the situation with children health we created especial complex approach for verifying the hypothesis that not only bad ecology, but, possibly, social and, connecting with this, emotional disturbances are leading factors damaged children heath in Aral Sea region (Aralsk-town) in comparison with Akchi, located in relevantly cline Kazakh area. In the frames of this approach we determined: 1) environmental pollution in air, soil and water in com-

[2]In the project took part scientific teams from Russia, Kazakhstan, Germany and Austria. Coordinator of the study Dr. Lothar Erdinger.

plex with detecting of total mutagenicity of these samples; 2) social and emotional statuses of children and members of their families, 3) children somatic health by medical examination; 4) children immunologic status by saliva analysis; 5) children genetic health by evaluation of genomic instability; 6. heavy metals, PSBs and DDE blood contents. Here we briefly present the main results of evaluation of children genomic instability. For better understanding them, below we'll shortly enumerate the main results of children' medical examination and the data [14]. So, for example, we detected that children living in Aralsk are characterised with higher morbidity than ones, living in settlement Akchi—the control population. Especially for children of 5 - 8 years old, frequency of the main pathologies—anemia and chronic respiratory diseases was significantly higher in Aralsk. Additionally, it was observed that 36% of young children from Aralsk were in status of oligotrophy (in Akchi—2.9%). For those children from Aralsk the frequency of anaemia, chronic respiratory, infectious and ccardiovascular diseases, dysfunction of the immune system as well as common morbidity correlated with family social status. From the other hand, children' anxiety expression correlated with both stress expression of their parents, family social status and with monthly income provided by 1 family member. Additionally, it was observed that anxiety among children from Aralsk was expressed more often than in Akchi and correlated with the frequency of oligotrophy, anaemia, chronic respiratory diseases and dysfunction of the immune system ($P \leq 0,05$). From all of these data we concluded that Aral Sea Basin is the region of social catastrophe.

For the study we chose method for blood cell cultivation with cytochalasine B usually used for detection of micronuclei in binuclear cells [16]. In this study we wide the ability of the method, taking into consideration, practically, all types of cells, micronuclei in them, apoptosis and mitotic activity (**Figure 4**). For detecting of individual genome susceptibility we, additionally, measured radiosensitivity and adaptive response to gamma-irradiation of blood cells in vitro [17]. In this study we supposed that emotional dysadaption may correlates with increased susceptibility of genome, what could be appear as increased number of children with absence or with inverted adaptive response—in Aralsk above in Akchi. Blood samples were collected from 5 - 8 years old children living in Aralsk (44 persons) and Akchi (34 persons). Groups of sex-matched healthy children were selected from randomized excerpts of the data of the previous medical and psychological (8-cjlored M.Luscher's test) examination. After stained with Romanovsky-Giemsa stain the slides they were coded, with decoding only after finish of all of cytogenetic analysis.

Results demonstrated that the frequency of binuclear cells with MN was lower in blood of children from Aralsk compared to Akchi (15.4 ± 2.74 and 38.2 ± 9.17, respectively). This effect was equally expressed for the background level of binucleated cells with MN and for binucleated cells with multiple MN. Similarly, the radiosensitivity of blood cells from Aralsk was lower compared to those from

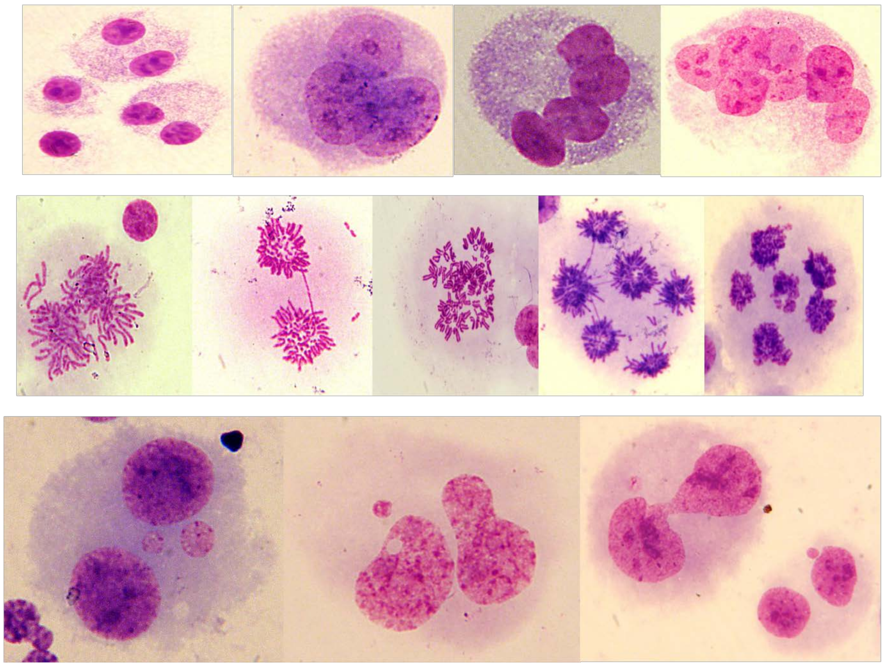

Figure 4. Micro-nuclear test on human blood lymphocytes cultivated with Cytochalasin B. The most common signs of genome instability. Microphotos, visible light, 10×100, oil immersion.

Akchi. Taking into consideration only the parameters which are used for standard evaluations [6], the genetic health of children from Aralsk would have to be estimated as significantly better compared to Akchi.

Since, however, the mitotic activity was significantly higher in blood cultures from Aralsk, we supposed, that fraction of genetically altered cells could have a shorter cell cycle and, consequently, divided more often during cultivation (or were eliminated). If this was correct, MN should be found predominantly in more rapidly dividing cells, which should also undergo more than one mitosis during cultivation with Cytochalasin B, and should therefore be detectable in cells with more than 2 nuclei (**Figure 5**). If it was correct the second conjecture—fractions of rapidly dividing cells haven't contain more MN then bi-nuclear cells.

To verify this hypothesis we counted the total number of cells with micronuclei in each culture, including cells with 1, 2, 3, 4 and more nuclei (**Figure 6(A)**), and evaluated the number of cells in each fraction separately (**Figure 6(B)**).

As a result no differences between Aralsk and Akchi by total number of cells with MN were found—for background as well as—for irradiated cultures (**Figure 6(A)**). At the same time, however, the number of cells in fractions of dividing cells (**Figure 6(B)**) was1.5 times higher than in Akchi in comparison to Aralsk. Additionally, number of cells in fractions of rapidly dividing cells (*i.e.* cells with 3, 4 and more nuclei) was significantly higher in samples from Aralsk, too. Thus, the data in **Figure 6(B)** support the assumption that the duration of the cell cycle in blood cultures from Aralsk was shorter than in ones from Akchi. Analysis of MN in rapidly dividing cells (**Figure 6**) further demonstrated that cells

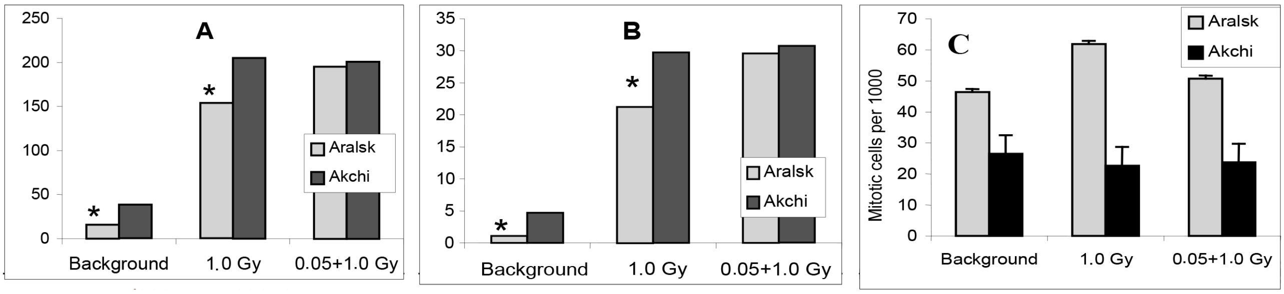

Figure 5. Number of: binuclear cells with MN (A); binuclear cells with multiple MN (B); mitotic index (C) per 1000 cells analyzed in blood cultures of children from Aralsk and Akchi. Ordinate: Number of each type of cells per 1000. *the differences are significant at $p \le 0.05$.

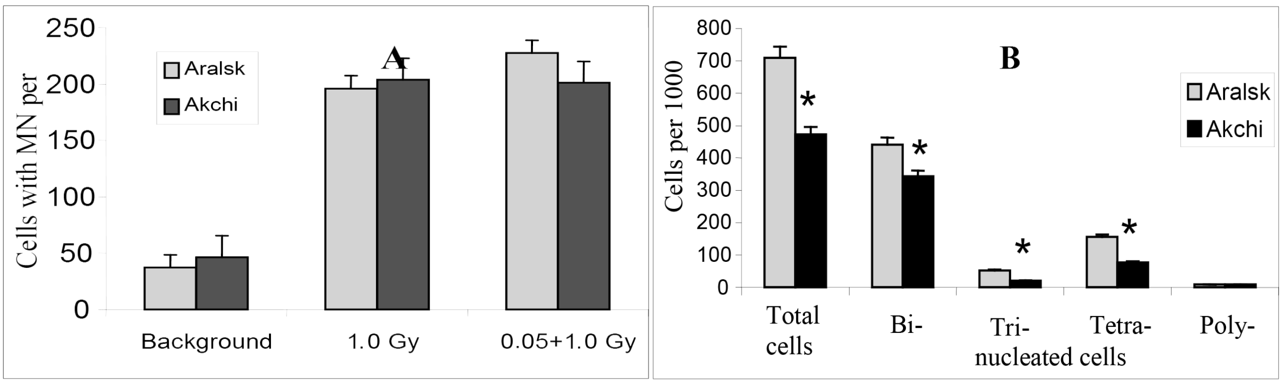

Figure 6. The total number of cells with micronuclei (A) and the number of cells in each fraction of dividing cells in blood cultures from Aralsk and Akchi.

in cultures from Aralsk had a greater frequency of MN than the ones from Akchi under all treatment regimens.

Adaptive response is the term for determination the ability of a low-priming-dose of ionizing radiation to modify the effects of a subsequent higher or challenge dose. This experimental approach is directed mainly to the evaluation of the activity of apoptosis, because the role of the low-priming-dose of ionizing radiation, which itself, practically, doesn't induce detectable levels of genetic damage, is, mostly, to induce apoptosis [10]-[16].

In children's biosubstrates (blood, urine) we evaluated concentrations of some organic compounds: PCBs (138, 153, 180), HCB, DDE, as well as come inorganic ions: Hg and As[3] (**Figure 7**).

Results of the analysis demonstrated the absence of the differencies between Aralsk and Akchi by all of concentrations of these compounds. But the concentrations, had been detected, correlated with children's anxiety (**Figure 8**). These data support that the exposure with toxic compounds may lead to increased expression of emotional stress.

Because earlier we have shown children's health correlated with quality of interpersonal relation in their families [14], the aim of the next fragment of the

[3]These analysis were performed in Heidelberg University the laboratory of Sanitary Chemistry (Germany) under the leadership of Professor L. Erdinger.

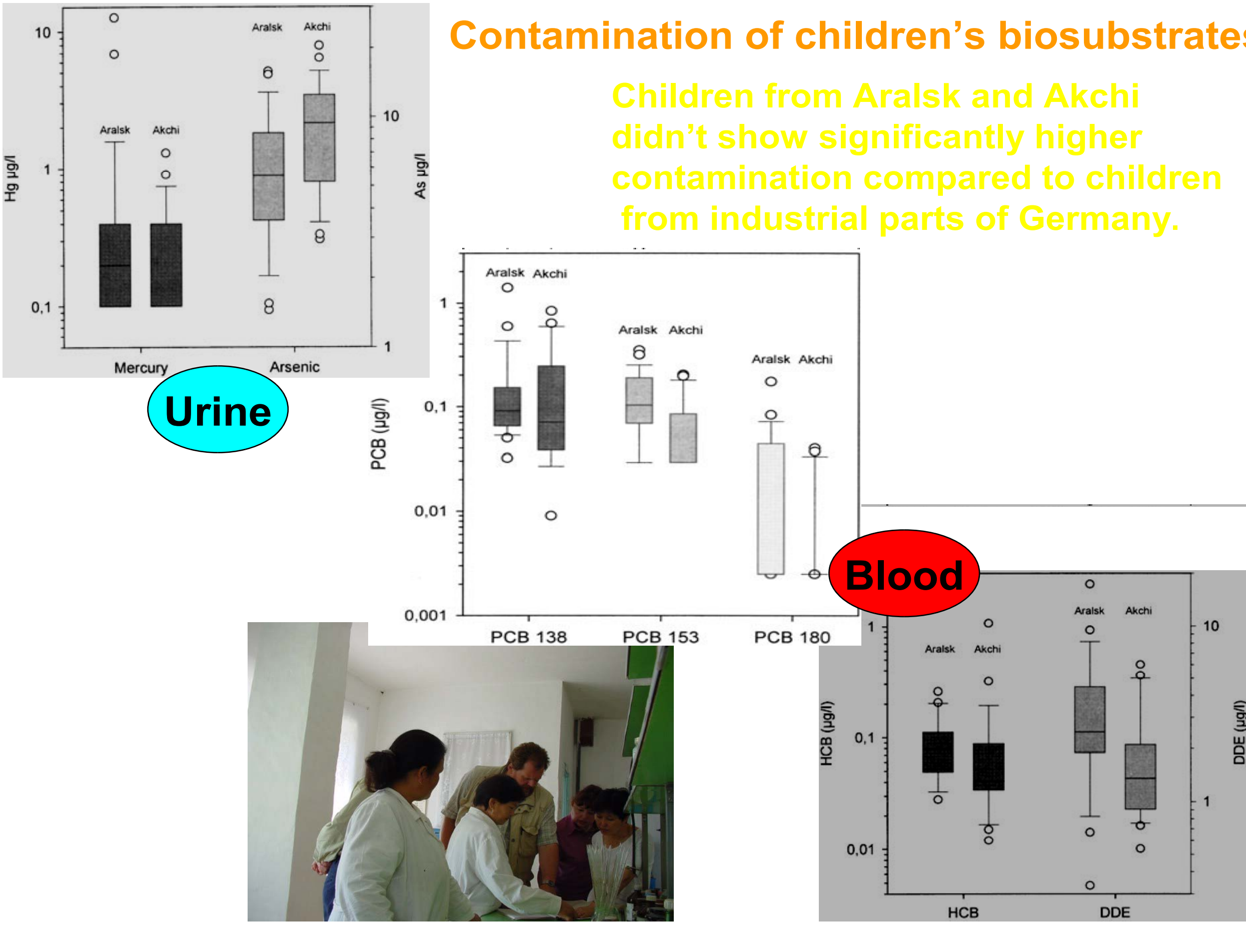

Figure 7. Levels of contamination of biosubstrates of children from Aralsk and Akchi.

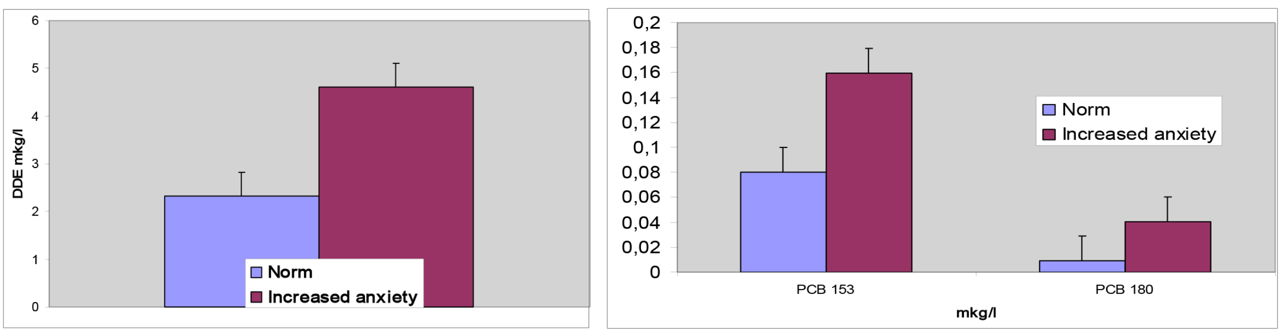

Figure 8. The differences between PCBs' contents in blood of children with different levels of anxiety. Left: DDE, Right – PCBs.

study was to analyze whether family can impact to level of genomic instability of young children.

For this we carried out multidisciplinary studies, in which families with children of 5 - 8 years old took part. This investigation was conducted in 2 Russian industrial towns—Magnitogorsk (South Ural Region, 440 000 of citizens, in the city one of the biggest Russian Metallurgical combine is located) and Koryazhma (Archangelsk Region, 42 000 citizens, the greatest in Europe Pulp-and-Paper industrial complex is located).

In Magnitogorsk all of surveyed children were selected by randomization among 1364 healthy boys and girls, visited municipal kindergartens (with common meal 3 times per day and 5 days per week, and common day regimen). These kindergartens were located near children's houses in 2 areas of the city. After randomization 85 families with children, lived around metallurgical combine (MC) on the Left Bank of Ural River were selected[4], and 81 ones, lived in the other area of the city on the Right Bank took part in the study. Selected areas were practically at equal distance from MP and had practically equal levels of exposure to chemicals, presented in air [15]. All selected children had not chronic diseases, were healthy during 2 months before the study and had normal level of alarm.

In Koryazhma 105 families with healthy boys and girls of 7 - 8 years old from 7 municipal primary schools (all working in the town, with common meal two part per day and 5 days per week and common day regimen) took part in the study. These families were selected from 348 ones with second-form school children by children's health. Koryazhma is little town, and differences in air pollution—by the results of previous study—were not detected.

Both studies had common design, included 3 main parts:

1) Cytogenetic analysis of children's peripheral blood in micronucleus test with Cytochalasin B for estimation: a) Spontaneous levels of genomic instability. In total, 33 indexes of genetic damage (micronuclei and nucleoplasmic bridges, **Figure 4**), cellular proliferation, mitotic activity and apoptosis were evaluated by standard procedure [16] and by our own extended protocol [15]. For each child was analyzed about 1500 - 3000 cells.

2) Psychological testing for determination of the levels of emotional stress expression: **for** children was used M.Luscher's 8-coloured test for determination of alarm expression; for their parents—the complex of 4 standard psychological questionnaires, detected an expression of psychological depression, alarm, overfatigue and quality of interpersonal relations with members of family, friends, colleagues etc. In Koryazhma the Subjective Well-being Scale [18] has been used for adults in addition.

3) Family's social status was evaluated by questioning parents with of especially elaborated worksheet concerning parent's social positions, economic state and confounding factors.

For more correct comparison between different data all of social and psychological data, obtained in points in accordance to recommendation of tests procedure, than were translated into categories from 1 to 5, where 1 is the best quality of the situation, 5—the worst.

4) Statistical analysis. For analysis of correlation the Spearmen criterion was used, for evaluation of differences between cohorts—Mann-Whitney U Test was used.

Our results shown:

[4]Ural River crosses the town.

In Magnitogorsk families from 2 areas of the city did not differ by the main social indices: family's matrimonial status, number of family members, monthly income per 1 person, conditions of residing, parent's smoking and alcohol drinking (some data are present in **Table 1**). But levels of parent's education and social status were slightly lower among families living around MP on the Left Bank of the Ural River.

Differences between Magnitogorsk and Koryazhma by social indices were not detected (**Table 1**).

Because earlier we have shown children's health correlated with quality of interpersonal relation in their families [14], the aim of the next fragment of the study was to analyze whether family can impact to level of genomic instability of young children.

For this we carried out multidisciplinary studies, in which families with children of 5 - 8 years old took part. This investigation was conducted in 2 Russian industrial towns—Magnitogorsk (South Ural Region, 440,000 of citizens, in the city one of the biggest Russian Metallurgical combine is located) and Koryazhma (Archangelsk Region, 42,000 citizens, the greatest in Europe Pulp-and-Paper industrial complex is located).

In Magnitogorsk all of surveyed children were selected by randomization among 1364 healthy boys and girls, visited municipal kindergartens (with common meal 3 times per day and 5 days per week, and common day regimen). These kindergartens were located near children's houses in 2 areas of the city. After randomization 85 families with children, lived around metallurgical combine (MC) on the Left Bank of Ural River were selected[5], and 81 ones, lived in the other area of the city on the Right Bank took part in the study. Selected areas were practically at equal distance from MP and had practically equal levels of exposure to chemicals, presented in air [15]. All selected children had not chronic diseases, were healthy during 2 months before the study and had normal level of alarm.

In Koryazhma 105 families with healthy boys and girls of 7 - 8 years old from 7 municipal primary schools (all working in the town, with common meal two part per day and 5 days per week and common day regimen) took part in the

Table 1. Comparison of the cohorts of families from Magnitogorsk and Koryazhma by the main social indices (in categories).

City/Area		Income, category ± SD	Matri-monial status, category ± SD	Dwelling category ± SD	Education Category ± SD		Social status Category ± SD	
					Mother	Father	Mother	Father
Magnito-gorsk	Right Bank	2.9 ± 1.0	1.4 ± 1.0	2.7 ± 1.8	3.0 ± 0.6	3.3 ± 0.7	3.6 ± 0.7	3,8±0,8
	Left Bank	2.66 ± 1.2	1.4 ± 1.0	2.3 ± 1.6	2.6 ± 0.6*	2.6 ± 0.7*	3.6 ± 0.9	3,3±1,0*
Koryazhma[1]		2.71 ± 0.9	0.49 ± 0.5	2.09 ± 1.3	2.5 ± 1.0	2.50 ± 1.0	3.30 ± 1.0	3.1 ± 1.3

*)differences between the two areas in Magnitogorsk are significant, p ≤ 0.05; 1) differences between Magnitogorsk and Koryazhma are not significant.

[5]Ural River crosses the town.

study. These families were selected from 348 ones with second-form school children by children's health. Koryazhma is little town, and differences in air pollution—by the results of previous study—were not detected.

Both studies had common design, included 3 main parts:

1) Cytogenetic analysis of children's peripheral blood in micronucleus test with Cytochalasin B for estimation: a) Spontaneous levels of genomic instability. In total, 33 indexes of genetic damage (micronuclei and nucleoplasmic bridges, **Figure 4**), cellular proliferation, mitotic activity and apoptosis were evaluated by standard procedure [16] and by our own extended protocol [15]. For each child was analyzed about 1500 - 3000 cells.

2) Psychological testing for determination of the levels of emotional stress expression: **for** children was used M.Luscher's 8-coloured test for determination of alarm expression; for their parents—the complex of 4 standard psychological questionnaires, detected an expression of psychological depression, alarm, overfatigue and quality of interpersonal relations with members of family, friends, colleagues etc. In Koryazhma the Subjective Well-being Scale [18] has been used for adults in addition.

3) Family's social status was evaluated by questioning parents with of especially elaborated worksheet concerning parent's social positions, economic state and confounding factors.

For more correct comparison between different data all of social and psychological data, obtained in points in accordance to recommendation of tests procedure, than were translated into categories from 1 to 5, where 1 is the best quality of the situation, 5—the worst.

4) Statistical analysis. For analysis of correlation the Spearmen criterion was used, for evaluation of differences between cohorts—Mann-Whitney U Test was used.

Our results shown:

In Magnitogorsk families from 2 areas of the city did not differ by the main social indices: family's matrimonial status, number of family members, monthly income per 1 person, conditions of residing, parent's smoking and alcohol drinking (some data are present in **Table 1**). But levels of parent's education and social status were slightly lower among families living around MP on the Left Bank of the Ural River.

Differences between Magnitogorsk and Koryazhma by social indices were not detected (**Table 1**).

Children's alarm expression in the two areas of Magnitogorsk didn't differ: 3.0 ± 4.5 points on the Left Bank and 3.45 ± 2.6 points on the Right Bank. Children from Koryazhma had practically the same average level of alarm expression (3.22 ± 2.48 points).

In Magnitogorsk the percentage of complete families didn't differ between cohorts from 2 areas: 92.6% on the Left bank and 90.6%—on the Right one, but in Koryazhma the part of incomplete families was significantly higher (39.4%; X^2

= 29.24; $p < 0.001$). In Magnitogorsk the average levels of mother's emotional stress expression detected by the sum of categories of all tests had been used were 7.06 ± 2.50 on the Left Bank and −7.00 ± 2.30 on the Right Bank. For fathers that indices were 6.35 ± 2.79 and 6.13 ± 3.50, consequently. In Koryazhma the levels of mother's stress expression didn't differ from the once in Magnitogorsk (7.37 ± 3.37), but fathers' indices of stress expression were significantly higher then in Magnitogorsk (13.37 ± 6.03; U = 408,00; Z = 7.60; p = 0.000000).

Children's genomic instability detected in micronuclei test didn't differ between the two Magnitogorsk areas (**Table 2**), but in Koryazhma it was significantly higher.

So, the average characteristics of surveyed cohorts of families with children from Magnitogorsk and from Koryazhma were practically identical.

The next reasoning demand to analyze separately the correlation between parents and their children in each town (**Figure 9**).

1) In Magnitogorsk it was important, that the reasons of parents' emotional stress overexpression differed qualitatively between cohorts from different areas of the town:

a) families, living around MP on the left Bank of Ural River, were stressed by income and residing conditions (material prosperity);

b) families from the Right Bank of Ural River were stressed by quality of intrafamily relationships and levels of education.

At the same time, only in families, oriented to material prosperity (Left Bank), income was one of the reasons of genomic instability in blood lymphocytes cultures of their children (**Figure 9**, left). And, on the contrary, only in families, oriented to more spiritual values and cultural wealth, the reasons of genomic instability in children's blood was quantity of members of family (**Figure 9**, right).

So, the parents' relationship to main vital values (material and cultural) as well as possession these values in many respects, has defined levels and type of genomic instability in blood lymphocytes of their children.

In Koryazhma we saw that the levels of genomic instability in children's blood were higher, than in Magnitogorsk (**Figure 10**, right) and didn't differ between schools. Speed of division of cultivated blood cells was higher in Koryazhma, too (**Figure 10**, left), what demonstrates more expressed tendency to early ageing of

Table 2. Some main indices of genomic instability in cultured children's blood lymphocytes in Magnitogorsk and Koryazhma (micronuclear test with Cytochalasin B).

Town	Area	Binuclear cells with MN per 1000 cells ± SD	Mitosis per 500 cells ± SD	Apoptosis per 500 cell ± SD	Proliferative pool (%) ± SD
Magnitogorsk	Right Bank	8.21 ± 7.03	17.32 ± 3.51	5.34 ± 2.76	63.7 ± 9.2
	Left Bank	9.10 ± 8.42	20.40 ± 4.84	5.48 ± 3.01	69.9 ± 7.0
Koryazhma		3.77 ± 3.72*	15.37± 5.69	7.48 ± 6.94**	65.7 ± 8.96

*) $\chi^2 = 34.5$; $p < 0.0001$; **) $\chi^2 = 51.85$; $p < 0.0001$.

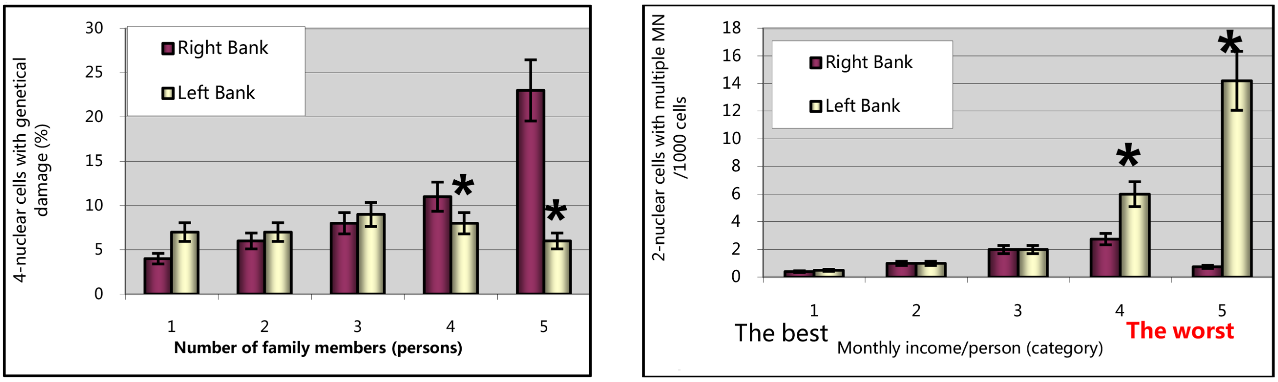

Figure 9. The association between parent's problems and genomic instability in blood lymphocytes of their children's in Magnitogorsk. *) differences between children's cohorts from the two areas are significant (Mann-Whitney U-test, $p \le 0.05 \div 0.001$).

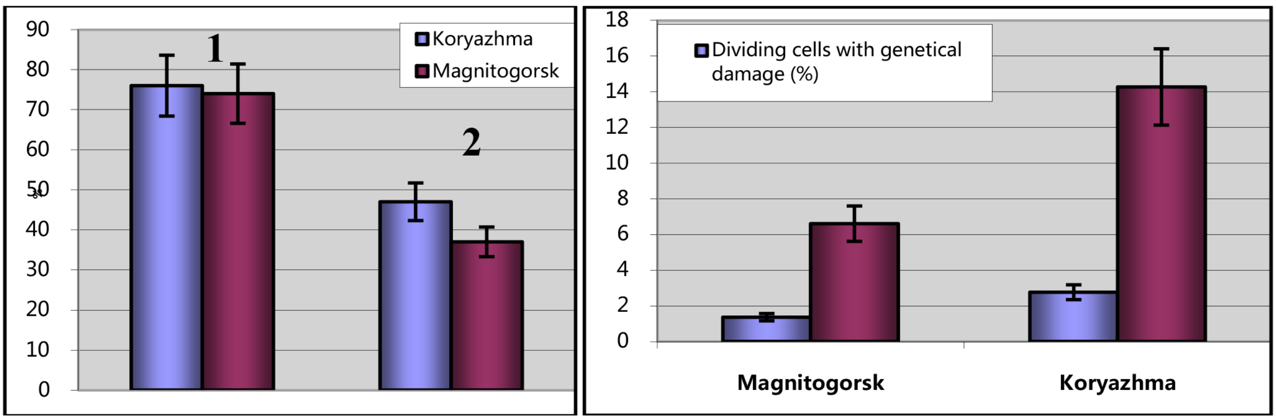

Figure 10. Comparison of genomic instability of children's blood cultures in Magnitogorsk and Koryazhma. The left picture: 1. cellular proliferation; 2. frequency of rapidly divided cells among divided (right); The right picture: characteristic of genomic instability.

children's organism. Lower level of programmed cellular death (apoptosis), detected in Koryazhma, in complex with high level of genetic damage, allow supposing fastening of these damages into generations of dividing cells.

In total, negative tendencies in children's genomic instability were more expressed in Koryazhma than in Magnitogorsk and these our data qualitatively correlated with frequencies of cancer cases, detected in studied towns.

Social conditions of life in Koryazhma were close to ones existed in Magnitogorsk. Analysis of correlations demonstrated the same regularities as in Magnitogorsk—increasing of genomic instability in children's blood lymphocytes with decrease of income, deterioration of residing conditions, etc.

In addition to 4 standard psychological scales, what had been used in both cities, in Koryazhma we analyzed parents' quality of life. Some results of these analysis (**Figure 11**) are the next: the more negatively father evaluated his quality of life, the higher frequency of rapidly dividing cells were detected in blood of his child (what give negative prognosis for children's early ageing) and the more frequently were detected lymphocytes with genetic damage in children's blood. Moreover, father's dissatisfaction of his quality of life correlated with decreasing

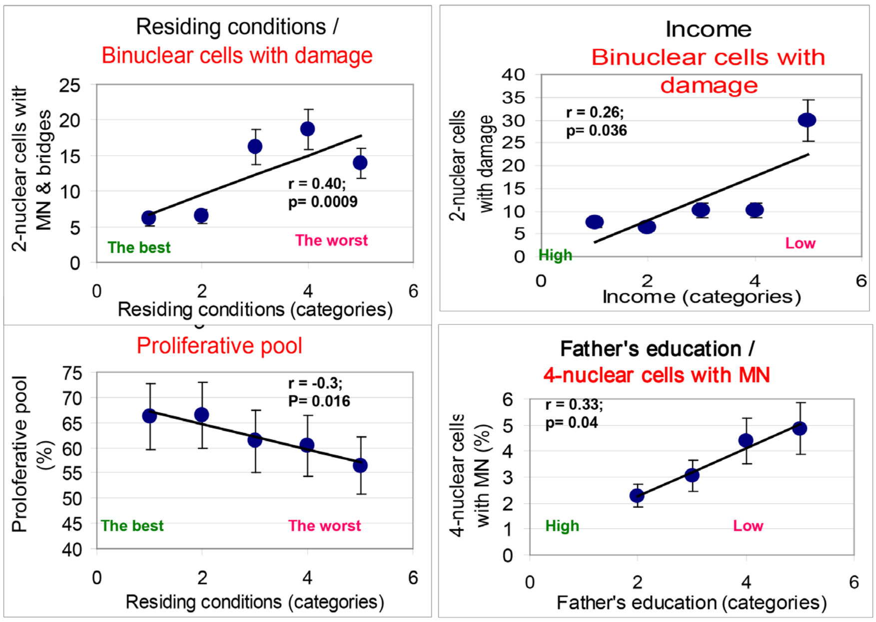

Figure 11. Some results of the analysis of intrafamily correlations in Magnitogorsk and Koryazhma.

of apoptosis in children's blood lymphocyte, what in complex with high frequency of damaged cells give negative prognosis to tumor development.

Both in Magnitogorsk and Koryazhma, children's level of alarm correlated with degree of their father's overfatigue ($r = 0.79$; $p \le 0.001$), mother's emotional stress expression ($r = 0.51$; $p \le 0.02$), her dependence on social environment ($r = 0.40$; $p \le 0.0003$) and with other indicators of emotional climate of family.

In all cities the most of important role in biochemical regulation of children organism and in balance between the departments of their autonomous nerve system, responsible for contacts of an organism with an environment, plays family integrity and parent's drinking alcohol.

Thus, our data, obtained in 2 independent multi-disciplinary studies, testifies that not severity of social load in each family (level of income, for instance), but namely parents' relation to these situation, what characterizes their quality of life, significantly influences on degree of genomic instability of their children. That is, only those social factors, which create problems for parents, did increase genomic instability of their children. That is, our results have shown that parent's responsibility for health of their children is much more significant than we thought before, because genetic damage in blood lymphocytes are the nonspecific indicators of many future diseases, including cancer, hormonal disruption and deficiency of immune system.

So, we would note that ethical characteristic of family—quality of life as"…perception of individuals their positions in life in context of culture and systems of values in which they live, according to their purposes, expectations, standards and cares" [9], lifestyle and emotional climate are potential source of children's genomic instability and modifier of genotoxic effects, induced by environmental pollution. From the other hand, good quality of life in the family, lifestyle and emotional climate is wonderful instrument for preservation of health of our children and of future generations.

Therefore, now exists the acute necessity in creation of new paradigm for upbringing and education our children as future parents. Next, it is the necessity to change preschool and school educational system in direction of more ethical and psychological comfort and spirituality both for children and teachers.

Researches, which results are presented in this publication, are unique, first of all, by the complex of very important problems which authors seek to understand. The data had been obtained are so important, too, because they for the first time show that genetic health of young children (preschool and primary school children) in many respects is defined by the relation of parents to that complex of problems which exist in each family. We believe that the obtained data will be useful not only for parents who care about health of the children, but also for family doctors, teachers and psychologists. Unfortunately the received results can't be discussed in comparison to the data of other researches because other such researches don't exist yet. But we hope that our work opened the way to the new scientific direction of researches directed to complex analysis of the reasons of human genetic instability.

2.3. Genetic Predisposition to Expression of Human Stress

Because environmental pollution rise risk of increase stress expression, we supposed that genetic predisposition to stress expression could be exists. And this predisposition we tried to look for among family of genes, encoding enzymes of detoxification.

Table 3. Number of persons with different stress expression among men with minor allelic variants of GSTM1 and PON 54 genes.

Gene (allele)	Number of people with allelic variants	Number of people with different stress expression					
		Alarm		Overfatigue		Psychological depression.	
		Alarm	Norm	Overfatigue	Norm	Depression	Norm
PON 54 (L/M or M/M)	29	**23**	6	**21**	8	12	17
GSTM1 (0/0)	30	**22**	8	**21**	9	14	16

Table 4. Number of people with different types of nonadaptive stress expression and frequency of GSTM, GSTT1 and PON 54 allelic variants among them.

Psychological test	Number of people in nonadaptive stress	Number of people with different allelic variants							
		PON 54		**GSTM1**		**GSTT1**		Totally for 3 genes	
		L/M + M/M	L/L norm	0/0	Norm	0/0	Norm	Mutant allels	Norm allels
Psychological depression	15	**9**	**6**	**11**	**4**	7	8	**13** (86.7%)	2
Alarm	36	**22**	**14**	**21**	**15**	6	30	**29** (80.5%)	5
Overfatigue	16	**10**	**6**	**9**	**7**	3	13	**13** (81.3%)	3
Interpersonnel relations	20	9	11	9	11	5	15	**16** (80%)	4
Totally in state of nonadaptive stress	22	**15**	**7**	**14**	**8**	4	18	**18** (81.8%)	4

For this among workers of chemical plants and control populations (totally 54 men of 43 ± 3 years old) we studied gene polymorphism of the GST super-gene family (GSTM1+/+ or GSTM10/0 and (GSTT1+/+ or GSTT10/0) and PON 54 (L/L, L/M or M/M). In parallel among the same persons we evaluated levels of emotional stress by standard psychological questionnaires, detected expression of psychological depression, alarm, overfatigue and quality of interpersonal relations. Both GSTM1 and GSTT1genes ensure the synthesis of the relevant products that belong to the Phase II detoxification enzyme system, responsible for biotransformation and degradation of certain electrophilic compounds. PON 54 gene takes part in the Phase I of detoxification enzyme system. GSTM1, GSTT1 and PON 54 genes polymorphism analysis was carried out in blood samples as described elsewhere[6]. Results are present in the **Table 3** and **Table 4**.

In addition, the correlation between non-adaptive stress expression and frequency of GSTM1 0/0 in population ($P \leq 0.05$) was detected. Presence of the minor alleles of genes, encoding enzymes of detoxification, bind with decreasing of detoxificative functions of their products. So, real toxic load to the organism, holding these alleles, increases, what lead to non-adaptive stress development.

References

[1] Smith, L.E., Nagar, S., Kim, G.J. and Morgan, W.F. (2003) Radiation-Induced Genomic Instability: Radiation Quality and Dose Response. *Health Phys.*, **85**, 23-29. https://doi.org/10.1097/00004032-200307000-00006

[2] Druliner, B.R., Ruan, X., Sicotte, H., O'Brien, D., Liu, H., Kocher, J.A. and Boardman, L. (2018) Early Genetic Aberrations in Patients with Sporadic Colorectal Cancer. *Mol Carcinog*, **57**, 114-124. https://doi.org/10.1002/mc.22738

[3] El-Zein, R.A., Abdel-Rahman, S., Santee, K.J., Yu, R. and Shete, S. (2017) Identification of Small and Non-Small Cell Lung Cancer Markers in Peripheral Blood Using Cytokinesis-Blocked Micronucleus and Spectral Karyotyping Assays. *Cytogenet Genome Res.*, **152**, 122-131. https://doi.org/10.1159/000479809

[4] WHO Media Center. Cancer, Fact Sheet N°297, Updated February 2014. http://www.who.int/mediacentre/factsheets/fs297/en

[5] WHO EUROPE. Social determinants of health. URL 21.04.2018 http://apps.who.int/iris/bitstream/handle/10665/108082/e59555.pdf?sequence=1&ua=1

[6] Taché, J. and Selye, H. (1985) On Stress and Coping Mechanisms. *Issues Ment Health Nurs.*, **7**, 3-24. https://doi.org/10.3109/01612848509009447

[7] Selye, H. (1985) The Nature of Stress. *Basal Facts.*, **7**, 3-11.

[8] Smith, M.J. and Selye, H. (1979) Stress: Reducing the Negative Effects of Stress. *Am J Nurs.*, **79**, 1953-1955. https://doi.org/10.1097/00000446-197911000-00016

[9] Selye, H. (1979) Correlating Stress and Cancer. *Am J Proctol Gastroenterol Colon Rectal Surg.*, **30**, 18-20.

[10] Ingel, F.I. (2005) Quality of Life and Human Individual Genomic Susceptibility. Whether There Is an Exit from a Vicious Circle? Ecologicheskaa genetica [Russian]. Vol. III, 38-46.

[6] This fragment of the study WAS performed by I. E. Sidorova.

[11] Ingel, F., Platonova, V. and Katosova, L. (2001) Human Emotional Stress, Dioxin Blood Content and Genetic Damage in Chapaevsk Town. *Chemosphere*, **43**, 989-998. https://doi.org/10.1016/S0045-6535(00)00460-4

[12] Neri, M., Bonassi, S., Knudsen, L.E., Sram, R.J., Holland, N., Ugolini, D. and Merlo, D.F. (2006) Children's Exposure to Environmental Pollutants and Biomarkers of Genetic Damage. I. Overview and Critical Issues. *Mutat Res.*, **612**, 1-13. https://doi.org/10.1016/j.mrrev.2005.04.001

[13] Neri, M., Ugolini, D., Bonassi, S., Fucic, A., Holland, N., Knudsen, L.E., Srám, R.J., Ceppi, M., Bocchini, V. and Merlo, D.F. (2006) Children's Exposure to Environmental Pollutants and Biomarkers of Genetic Damage. II. Results of a Comprehensive Literature Search and Meta-Analysis. *Mutat Res.*, **612**, 14-39. https://doi.org/10.1016/j.mrrev.2005.04.003

[14] Khussainova, Sh., Ingel, F., Eckl, P.M., Sherjazdanova, Kh., Kosdauletova, G., Kozhanov, V., Petrova, I., Leschenko, G., Karsybekova, L., Gubinsky, A. and Erdinger. L. (2009) The Aral Sea Basin Assessment of the Quality of Life and the Health of Children. *Central European Journal of Occupational and Environmental Medicine*, **15**, 53-64. http://www.omfi.hu/cejoem/Volume15/Vol15No1-2/CE09_1-2-04.html

[15] Ingel, F., Erdinger, L., Eckl, P., Khussainova, Sh. and Krivtsova. E. (2010) Genomic Instability, Radiosensitivity and Adaptive Response of Blood Lymphocytes from Children Living in the Aral Sea Region. *Correlation with Emotional Stress and Blood Contamination Central European Journal of Occupational and Environmental Medicine*, **16**, 31-45.

http://www.omfi.hu/cejoem/Volume16/Vol16No1-2/CE10_1-2-04.html

[16] Milne, E., Greenop, K.R., Ramankutty, P., Miller, M., de Klerk, N.H., Armstrong, B.K., Almond, T., O'Callaghan, N.J. and Fenech, M. (2015) Blood Micronutrients and DNA Damage in Children. *Mol Nutr Food Res.*, **59**, 2057-2065. https://doi.org/10.1002/mnfr.201500110

[17] Serebrianyĭ, A.M., Antoshchina, M.M., Aleshchenko, A.V., Riabchenko, N.I. and Pelevina, I.I. (2008) The Mechanisms of Adaptive Response. Estimation of Capacity of Human Blood Lymphocytes to Radiation Adaptive Response Using Different Criteria. *Tsitologiia*, **50**, 462-466 [Russian].

[18] Pavot, W. and Diener, E. (2008) The Satisfaction with Life Scale and the Emerging Construct of Life Satisfaction. *Journal of Positive Psychology*, **3**, 137-152. https://doi.org/10.1080/17439760701756946