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Dynamics of the Level of Chromosomal Aberrations in Residents of Industrial Cities under the Conditions of Changing Atmospheric Pollution

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Abstract—The level and range of chromosomal aberrations in residents of Kemerovo, a large industrial center of Western Siberia, was studied in two periods of time: from 1986 to 2000 and from 2001 to 2012. Cytogenetic studies were performed on 668 persons (333 persons in the first period and 335 persons in the second period). The frequency of aberrations among residents in Kemerovo was lower in 2001–2012 than in 1986–2000, which is consistent with the reduced emission of pollutants into the air in Kemerovo. The new background level of chromosomal aberrations in Kemerovo's residents, who do not come into contact with industrial genotoxicants, was established at 1.48 ± 0.08% and can be used in further genetic and ecological studies.

Keywords: chromosomal aberrations, environmental pollution, industrial cities

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INTRODUCTION

Investigation of the genomic reactions to mutagenic agents of the environment is one of the most important tasks in modern ecology. The analysis of DNA damage is commonly based on studying chromosomal aberrations (CAs), sister chromatidal exchanges, micronuclei, aneuploidy, and stable chromosomal aberrations using the FISH method; at the level of the organism, congenital morphogenetic variants and disorders are studied (Sycheva, 2013). CAs in blood lymphocytes are the best known indicator.

CAs are structural chromosomal damage that occurs spontaneously or as a result of an exogenous (chemical, physical, and biological) influence (Russell, 2002). Structural CAs in peripheral blood lymphocytes have been investigated for more than 40 years as the biomarkers reflecting the early effects of the genotoxic carcinogens (Bochkov et al., 2001; Hagmar et al., 2004). The frequency of CAs in residents of territories with various degrees of the anthropogenic load has been measured by many researchers (Druzhinin, 2003; Pilinskaya et al., 2011; Minina, 2013). CAs in peripheral blood lymphocytes have been proved to be useful for predicting the risk of oncological diseases in residents of urban territories (Bonassi et al., 2000; Minina, 2011). The increased level of CAs in residents of cities with well-developed industries has been established (Valinurov et al., 1998; Volkov et al., 2001; Ingel and Prikhozhan, 2002; Druzhinin, 2003).

In Kuzbass, a constantly revised data base of CAs in the residents of Kemerovo oblast, including the city of Kemerovo, has been created. The quantitative characteristics of this database were first published more than 10 years ago (Druzhinin, 2003). It has been considerably enlarged in recent years, which required the revision and verification of the previous estimates.

Kemerovo is a large industrial, administrative, and cultural center of Kuzbass in the southeast of Western Siberia in the middle of the Kuznetsk Depression on both banks of the Tom River. The high concentration of coal processing, chemical, and CHP plants, as well as intensive traffic, unfavorable meteorological conditions with frequent windless days and temperature inversions, have affected the ecological situation in the city. A correlation is shown between the dynamics of CAs in residents and changes in the concentration of separate genotoxic pollutants in the air (Volkov et al., 2001).

In the 2000s, significant transformations occurred in the state of the environment. They were caused by changes in the social and economic situation in the region. The gross emissions of polluting substances from the basic industries (coal production, metallurgy, and heat power engineering) decreased and the degree

Table 1. Gender–age composition of Kemerovo's residents involved in the investigation

Group	Period of observations, years	Investigated, in total	Age, years		Gender	
			min–max	mean ± st.err	m	f
Children and adolescents	1992	26	14–17	15.0 ± 0.2	9	17
	1993	81	10–17	13.4 ± 0.2	40	41
	1994	67	11–17	14.2 ± 0.2	37	30
	1995	23	9–17	15.5 ± 0.5	20	3
	1996	40	11–16	14.5 ± 0.1	20	20
Adults	1986	56	19–34	22.9 ± 0.6	33	23
	1995	9	18–59	30.9 ± 4.5	1	8
	1998	31	19–60	28.9 ± 1.9	17	14
	2005	79	21–59	45.2 ± 0.9	24	55
	2008	62	24–62	42.5 ± 1.1	14	48
	2010	20	18–63	43.4 ± 1.1	8	12
	2012	174	19–67	42.7 ± 0.5	165	9

Mean ± st.err are the average values ± standard error; min–max are the minimum and maximum values.

of their ecological threat changed (Mun et al., 2011). However, the carcinogenic risk for residents, which is associated with the presence of powerful carcinogens in the air of cities and particular districts of Kuzbass, is still high (Larin et al., 2004; Glushkov et al., 2006; Mun et al., 2006).

Thus, the aim of this study was to carry out a comparative analysis of the genotoxic effects (the level and spectrum of CAs) in Kemerovo's residents in 1986–2000 and 2001–2012.

MATERIALS AND METHODS

The environment of Kemerovo was analyzed based on the data from the Reports on the State of the Environment in Kemerovo oblast (1998–2013) and the Hygienic and Epidemiological Center of Kemerovo oblast.

The material to analyze the dynamics of the clastogenic effects were the results of the cytogenetic studies carried out from 1986 to 2012 at the Department of Genetics of the Kemerovo State University and the Laboratory of Cytogenetics of the Institute of Human Ecology, Siberian Branch, Russian Academy of Sciences. The data obtained on 668 residents of Kemerovo, who do not come into contact with industrial genotoxicants, were analyzed. The analyzed group included school children and adults (lecturers and students of the Kemerovo State University (1986, 1995, and 1998), the staff of the Energetik health center (2005 and 2008), and healthy blood donors of the blood transfusion station of Kemerovo oblast (2010 and 2012). On the whole, the cytogenic analysis was performed on 431 adults (aged 40.4 years on average) and 237 children and adolescents (14.5 years on average). Among them, 388 were males and 280 females. Before 2000 (in the 1990s), 333 persons were examined. In 2005–2012, their number comprised 335 persons. The gender and age characterization of the studied groups is given in Table 1.

The material to study CAs was the whole peripheral blood of Kemerovo's residents taken from their ulnar veins in aseptic conditions. The blood cells were cultivated according to the standard protocol in 48 h cultures of the peripheral blood lymphocytes (Hungerford, 1965; Druzhinin, 2003). The nutrient mixture was prepared based on a RPMI-1640 medium (4.5 mL), fetal calf serum (1 mL), and phytohemagglutinin (0.1 mL) (PanEko). The mixture was kept in sterile cultural flasks at 37°C for 48 h. Colchicine (0.5 μg/mL) was introduced into the cultures 2 h prior to fixation. After the hypotonic treatment and the fixation of cells, the suspension was pipetted on cooled and clean microscopic slides and dried. The preparations were stained with a 1% Giemsa stain (Merk) and analyzed using an Axio Scope 2 plus microscope (Carl Zeiss).

The metaphases for the analysis and the criteria for the registration of cytogenetic defects were consistent with the generally accepted recommendations (Bochkov et al., 1971). From 100 to 200 metaphases per person were analyzed. The proportion of aberrant metaphases was determined as the ratio of the number of cells with chromosomal aberrations to the total number of studied cells. Two types of aberrations were considered: chromatidal abberations (individual fragments and interchromatidal exchanges); and chromosomal abberations (paired fragments; dicentric chromosomes with and without fragments, circular chromosomes, atypical monocentrics). Achromatic gaps were not involved.

Mathematical processing of the results was performed using the program STATISTICA for

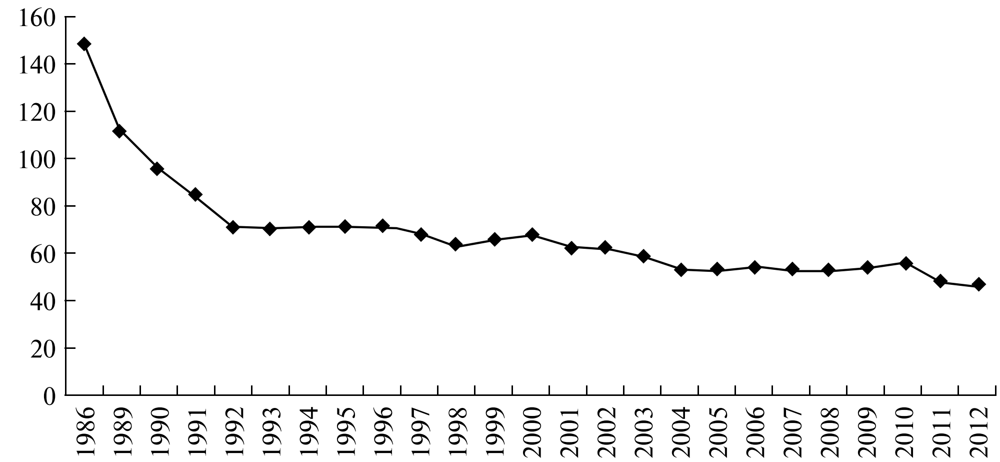

Fig. 1. The dynamics of the gross emissions of pollutants from stationary sources in Kemerovo. *X* axis—year of observations. *Y* axis—total emissions of pollutants, thousand tons/year.

WINDOWS v.8.0. The normality of the distribution was verified using Shapiro–Wilk's W test. It was found that the analyzed distributions were different from normal ($p < 0.05$). Therefore, further analysis was performed by nonparametric methods. When analyzing the differences between several independent samples, the Kruskal–Wallis test was used. Differences between two independent samples were evaluated with the Mann–Whitney U-test. For studying the relations between air pollution and CA, correlation (Spearman's rank correlation coefficient) and regression (linear regression coefficients) analyses were used (Glanz, 1999). In order to eliminate the error of the first kind during multiple comparisons, the Bonferroni test was applied (Grjibovski, 2008).

RESULTS AND DISCUSSION

The radiation situation of in the air of Kemerovo was evaluated according to the data obtained by the Russian Federal Service for Hydrometeorology and Environmental Monitoring. The exposure dose of gamma radiation (EDR) was measured daily at 14 meteorological stations. According to the results of the monitoring, the EDR in all the studied periods of time did not exceed the natural background level, thereby varying from 9 to 14 μR/h (12 μR/h on average). There were no significant changes in the radiation situation of Kemerovo during the period under consideration (1986–2012).

The analysis of the pollution of drinking water in Kemerovo, as well as of the quality of food products (the content of toxic elements, antibiotics, nitrates, pesticides, and mycotoxins), which was performed previously (Volkov et al., 2001), allowed us to establish the absence of any toxic and genetic risks associated with the consumption of drinking water or of substandard food products. In this context, the impact of air pollution was most significant.

As a result of the long-term observations carried out by the Russian Federal Service for Hydrometeorology and Environmental Monitoring, the level of air pollution in Kemerovo was considered high (*Doklad o sostoyanii* ..., 2013). However, if the dynamics of gross emissions in the atmosphere from stationary sources is considered (Fig. 1), a reduction in gross emissions between 1986 and 2012 can be clearly observed. Probably, the observed processes are related to changes in the social-economic situation in Kuzbass, reduction in the production level, introduction of new technologies, and strengthening of the control of environmental emissions from industrial enterprises

The content of the following compounds is regularly monitored at the fixed stations of Kemerovo: ammonia, benzopyrene (BP), formaldehyde, carbon black, suspended matters, sulfur dioxide, nitrogen dioxide, nitrogen oxide, carbon oxide, aniline, dimethylamine, hydrogen cyanide, phenol, hydrogen chloride, and metals.

The largest contribution to the atmospheric pollution of Kemerovo (most significant exceeding of the MAC standards) is made by BP, ormaldehyde, nitrogen dioxide, ammonia, and black carbon. The pollution of the air by chlorine, sulfuric acid, methyl alcohol, toluene, hydrogen chloride, dimethylamine, isopropyl alcohol, aniline, naphthalene, xylene and hydrogen cyanide, and metals does not reach the MAC standards in the average or maximum concentrations. Changes in the contribution of the major pollutants of the air (exceeding the MAC standards) in 1986–2000 and 2001–2012 are given in Fig. 2.

The pronounced, statistically significant changes were observed in the ratio of BP. Its average annual concentration was about 5.2 ng/m^3 in 1986–2000 and 3.4 ng/m^3 in 2001–2012 (the differences are statistically significant, $U = 46.0$; $p = 0.0177$), significantly exceeding the MAC of 1 ng/m^3 in all measurements.

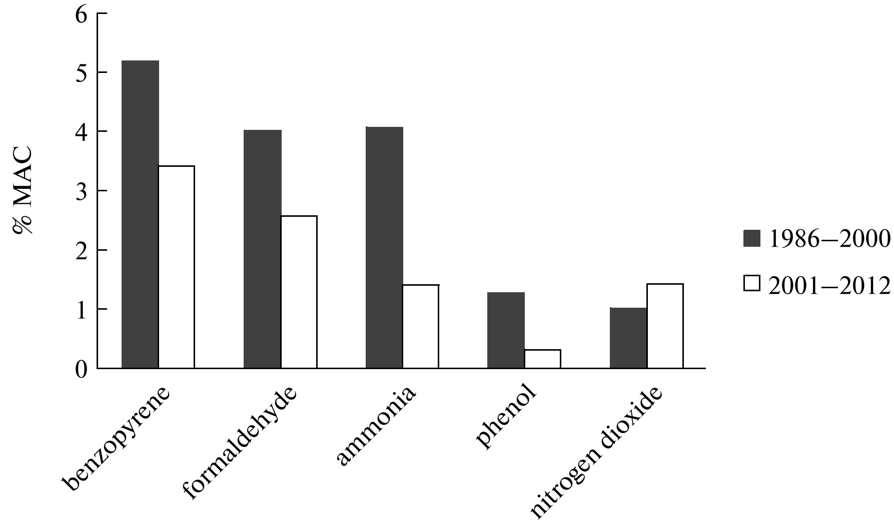

Fig. 2. The average annual concentration of pollutants in Kemerovo during the compared periods of time. *X* axis—pollutant. *Y* axis—average annual concentration of the pollutant, % MAC. $*p < 0.05$, $**p < 0.001$, $***p < 0.01$ (statistically significant differences between the average annual concentrations of pollutants in the compared periods of time are given).

According to the data in the literature, BP is a substance with an obvious mutagenic and carcinogenic effect. Thus, it can be regarded as one of the leading factors of development of CAs in the residents.

Carbon black and dust are significant indicators of air pollution in cities. The average annual concentration of these pollutants in the atmosphere of Kemerovo does not exceed the MAC in any of the periods of observations. However, concentrations above the MAC standards were observed during one-time measurements at individual stations (i.e., an episodic increase was observed). The proportion of samples above the MAC ranged from 1.4 to 14.4%. The maximum one-time concentration of black carbon reached 3.8 MAC. It is known that the presence of dust, black carbon, and suspended matters in the atmosphere can contribute to the development of genotoxic effects of the mutagens in the environment. PAH easy accumulate at the surface of black carbon and other suspended matters. Thus, there are all the necessary conditions for the realization of the mutagenic properties of PAH, in particular BP, in the atmosphere of Kemerovo.

In addition to the considerable reduction in the concentration of BP in the 2000s, there was a statistically significant decrease in the following substances in the atmosphere of Kemerovo: formaldehyde, ammonia, phenol. The concentration of nitrogen dioxide, on the contrary, increased (Fig. 2). Formaldehyde and phenol, as is well known, have pronounced carcinogenic and mutagenic effects on animal and human cells (IARC, 2006; Schmid and Speit, 2007). The clastogenic effects of these substances appear in the increased frequency of CAs in blood cells as a result of long-term contact with them in the working environment (Santovito et al., 2011; Ladeira et al., 2013). The reduced content of formaldehyde and phenol, as well as ammonia (which is often regarded as a weak mutagen) in the atmosphere of Kemerovo during the 2000s can potentially affect the level of CAs in the residents. The problem of the mutagenic activity exhibited by nitrogen dioxide remains controversial. The mutagenic effect of the substance was established by the Ames test, as well as using by tests used to detect DNA breaks and CAs in the lung cells of rats (WHO, 1997), and when studying the cytogenetic damage in peripheral blood lymphocytes of people exposed to high concentrations of the substance in their working area (Jodinger et al., 1998). At the same time, the mutagenic effect of nitrogen dioxide has not been confirmed by the polyorgan micronucleus test on rats (Sycheva et al., 2006).

The first cytogenetic study of residents in Kemerovo was carried out by the Kemerovo State University in 1986. The dynamics of the spontaneous level of chromosomal aberrations in this and subsequent years is shown in Tables 2 and 3.

As a result of the first survey of adults (1986, students and staff of Kemerovo State University), a relatively high frequency of cells with CAs was registered (median 3.0; maximum 13%) (Table 2). In this year, the gross emissions of pollutants in the atmosphere of the city were the highest (Fig. 1). The subsequent investigations of the genotoxic effects produced by the environmental factors of Kemerovo showed a decline in the spontaneous level of chromosomal abnormalities in adults (the differences were statistically significant with the data gathered in 2005–2012). The level of chromosomal disorders registered in Kemerovo's residents in 2005–2012 (median = 1.0) was lower in a statistically significant manner than the regional level of CAs in the adults of Kemerovo oblast (median = 3.0), calculated based on

Table 2. The frequency of cells with chromosomal aberrations in adult residents of Kemerovo in different years and periods, %

No.	Group	*n*	Median	Mode	Lower and upper quartile	Min–Max	Asymmetry	Excess	Mean ± St.err
1	1986	56	3.00	3.00	2.00–6.00	0–13.00	0.92	0.45	4.04 ± 0.42* 4–7
2	1995	9	2.44	m	1.00–4.00	0–6.00	0.72	–1.01	2.44 ± 0.78
3	1998	31	3.00	3.00	2.00–4.00	0–8.00	0.69	–0.14	3.19 ± 0.38* 6, 7
4	2005	79	1.00	m	0–3.00	0 –11.00	1.54	2.79	2.11 ± 0.25* 1, 6
5	2008	62	2.00	3.00	1.00–3.00	0–6.00	0.26	–0.65	1.98 ± 0.19* 1, 6, 7
6	2010	20	0.13	0	0–0.87	0–3.00	2.36	7.04	0.48 ± 0.16* 1, 7
7	2012	174	1.00	1.00	0.50–1.50	0–5.00	1.28	2.52	1.12 ± 0.07* 1, 3, 5, 6
All adults in Kemerovo before 2000 (1986–1998)		96	3.00	3.00	1.50–6.00	0–13.00	1.02	0.95	3.61 ± 0.29
All adults of Kemerovo after 2000 (2005–2012)		335	1.00	1.00	0.50–2.00	0 –11.00	1.97	6.37	1.48 ± 0.08**
Regional background level in adults of Kemerovo oblas		124	3.00	2.00	2.00–4.50	0–12.00	1.31	1.98	3.35 ± 0.22

n is thesample volume; Mean ± St.err is the average ± standard error; Min–Max are the minimum and maximum values, M is multimodality. * Different in a statistically significant manner from the value of that in groups with the designated number (calculated by the Mann–Whitney test, taking into account the Bonferroni correction (0.05/7), differences considered significant at $p < 0.0071$). For example, the value in group no. 1 (1986) is different from that in group nos. 4 (2005), 5 (2008), 6 (2010), and 7 (2012). ** Different from the regional background level of Kemerovo oblast ($U = 9677$, $p = 0.0000001$) and adults in Kemerovo in 1986–1998 ($U = 7936$, $p = 0.0000001$).

Table 3. The frequency of cells with chromosomal aberrations in children from Kemerovo in different years, %

No.	Group	Sample volume (*n*)	Median	Mode	Lower and upper quartile	Min–Max	Asymmetry	Excess	Mean ± St. err
1	1992	26	1.00	0	0–2.00	0–7.00	1.86	3.72	1.27 ± 0.34*[2,3,5]
2	1993	81	3.32	2.00	2.00–5.00	0–8.00	0.25	–0.94	3.32 ± 0.24*[1,5]
3	1994	67	4.00	4.00	1.00–6.00	8.00	0.10	–1.06	3.55 ± 0.28*[1,5]
4	1995	23	3.00	4.00	1.00–4.00	0–7.00	0.22	–0.90	2.97 ± 0.36*[1,5]
5	1996	40	4.00	2.00	2.00–6.00	0–11.00	0.63	–0.23	4.25 ± 0.43*[1,2,3,4]
All children of Kemerovo		237	3.00	2.00	1.00–5.00	0–11.00	0.46	–0.43	3.30 ± 0.15**
Regional background level in children of Kemerovo oblast		267	2.50	2.00	1.50–3.50	0–9.50	0.87	0.99	2.65 ± 0.10

Mean ± St. err—Average ± SEM; Min–Max are the minimum and maximum values; * different in a statistically significant manner from the value of the same parameter in groups with the designated number (calculated by the Mann–Whitney test, taking into account the Bonferroni correction (0.05/5), differences considered significant at $p < 0.01$). For example, the value in the group of 1992 is different from the one in group nos. 2 (1993), 3 (1994), and 5 (1996). ** different from the regional background level in children of Kemerovo oblast ($U = 27{,}046$; $p = 0.0047$).

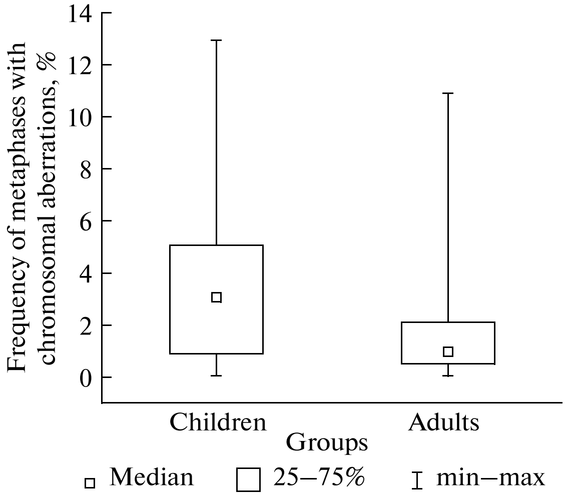

Fig. 3. Chromosomal disorders in children and adults from Kemerovo in 1986–1998

the results of the cytogenetic analysis of rural residents who do not suffer from the genotoxical pressure of the environment (Druzhinin, 2003; Minina, 2013). Therefore, a new background level of chromosomal disorders in Kemerovo's residents, who do not come into contact with industrial genotoxicants, was found in the 2000s. Its value can be used in further genetic and ecological studies (Table 2).

The HA levels (median 3.0%) were significantly higher in children in Kemerovo in 1992–1996 than the regional background levels in children in Kemerovo region (median 2.5%) (Table 3). The highest level of chromosomal aberrations was found in April 1996, when 40 adolescents living in the city of Kemerovo were examined. The reasons for this sharp increase are not clear. The frequency of metaphases with HA have averaged 4.25 ± 0.43%, median 4.0. Such high frequency disturbances were not recorded in any other groups of children or adults. The lowest frequency of CAs in children was registered in 1992 (median 1.0%). In the subsequent years, there were significantly more CAs: the median was 3.3% in 1993, 4.0% in 1994, 3.0% in 1995, and 4.0% in 1996. It is not possible to relate the low (1992) and high (1996) frequency of the CAs to the changes in the emission of the studied pollutants (Fig. 1). Probably, there were some unregistered factors in these years accompanying the mutagenic effects under the conditions of a large industrial city, which require further study. Such factors could be spontaneous emission bursts, which were not included in the official records.

Since the period from 1986 to 1998 was marked by the examinations of both adults and children, it is possible to make comparisons between them. It was found that the indicators of chromosomal mutagenesis (the overall frequency of the aberrations and their individual types) in adults and children living in Kemerovo, were not different in a statistically significantly manner. Thus, for example, the median of the frequency of cells with CAs was 3.00% (n = 237) in children (in total for the period up to 2000) and adults (in total for the same period) (n = 96) (Fig. 3). The correlation analysis also showed the relationship between age and CAs. Thus, we can conclude that the age in the studied sample did not modify the frequency of the chromosomal mutations.

The gender characteristics of the sample also did not have a significant impact on the CAs. There were no differences between males and females in 1986–1998 and 2005–2012 (Fig. 4). However, there were clear distinctions between persons of the same gender, ableit, in different time periods: the frequency of the CAs in both men and women was lower in a statistically significant manner in 2005–2012 than in 1986–1998. This decline is consistent with the dynamics of the gross emissions (Fig. 1) and the changes that took place in the average concentration of the pollutants (BP, formaldehyde, phenol) after 2000 (Fig. 2). Considering the absence of any significant effect of gender and age on the values of the CAs in the sample, the groups of children and adults, as well as men and women, were combined and analyzed together.

The analysis of the quality spectrum of the aberrations demonstrated that the leading type of chromosomal abnormalities among Kemerovo's residents is single and paired fragments. In general, chromatidal aberrations (single fragments) were dominant. It has been found that there was a significant reduction in the frequency of single, paired fragments, and chromatidal exchanges, as well as a slight increase in the frequency of dicentric chromosomes, in the 2000s (Table 4).

The significance of the impact of smoking on the studied cytogenetic indicators was studied. There were no statistically significant differences between smokers and nonsmokers in the period before 2000 and after. For example, the proportion of aberrant metaphases before the 2000s was as follows: median 3.0% in smokers ($n = 62$) and 3.0% in nonsmokers ($n = 271$); while, after 2000 it was as follows: median 1.0% in smokers ($n = 118$) and 1.0% in nonsmokers ($n = 217$).

When analyzing the dependencies between the air pollution and the level of the CAs in Kemerovo's residents, a statistically significant positive correlation between the gross emissions of pollutants into the atmosphere and the level of CAs in the population of Kemerovo was observed (Spearman correlation coefficient rs = 0.68, $p = 0.000001$) (Fig. 5a). In the analysis of the contribution of individual pollutants, statistically significant positive correlation coefficients were revealed by comparing the dynamics of CAs and the concentration of BP (rS = 0.88; p = 0.000001) (Fig. 5b) and formaldehyde (rS = 0.68; $p = 0.000001$) in the air (Fig. 5c). These relations are not surprising and prove the clastogenic effect of these compounds on the human body.

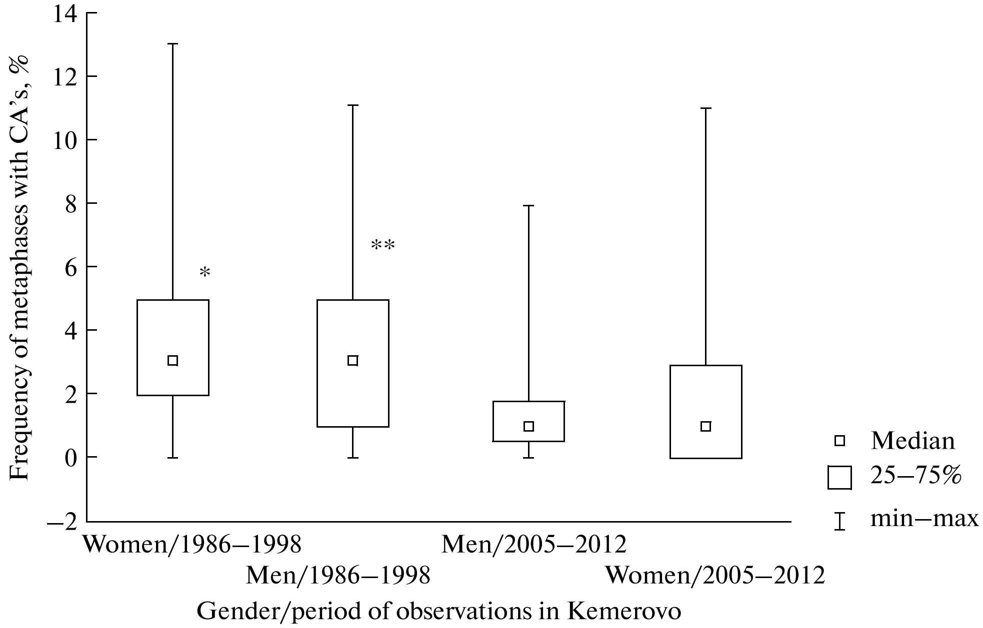

Fig. 4. The level of chromosomal disorders in men and women in two observation periods: 1986–1998 and 2005–2012. $*p = 0.0000001$, statistically significant differences between women in different periods of observation are indicated: 1986–1998 and 2005–2012. $**p = 0.0000001$, statistically significant differences between men are indicated: 1986–1998 and 2005–2012.

CONCLUSIONS

It is obvious that the surrounding environment plays an important role in the formation of the level of cytogenetic instability in residents of large industrial cities. We observed changes in the level of the CAs among residents in Kemerovo over a period of more than 20 years, depending on the dynamics of the concentration of the major pollutants. Direct correlations were found between the content of BP, formaldehyde, and the frequency of blood cells carrying chromosomal damages. A significant reduction in the level of the CAs in a large industrial center of Siberia was found in the 2000s compared to the previous period, which was consistent with the reduction in the emissions in the air. A new background frequency of CAs in Kemerovo's residents was observed (1.48 ± 0.08%), as well as the frequencies of particular types of aberrations (Table 4). It should be noted that the decrease in the level of CAs after 2000 coincides with the reduction in the rates of oncological diseases among Kemerovo's residents. Previously, a statistically significant decrease in oncological diseases was registered in 2000–2009 compared to 1990–1999 (Mun et al., 2013). This can be used as additional evidence of the

Table 4. The qualitative spectrum of chromosomal aberrations (%) in Kemerovo residents during two periods of observations

Types of chromosomal aberrations	1986–1998		2005–2012		$p*$
	median	min–max	median	min–max	
Individual fragments	2.00	0–13.00	1.0	0–10.00	0.000001
Chromatidal exchanges	0	0–1.00	0	0–0.3	0.010313
Paired fragments	1.00	0–6.00	0	0–2.00	0.000001
Dicentrics with fragments	0	0–1.00	0	0–1.00	0.717738
Dicentrics without fragments	0	0–1.00	0	0–1.00	0.004406
Circular chromosomes	0	0–1.00	0	0–1.00	0.691571
Atypical monocentrics	0	0–2.00	0	0–1.00	0.246968

* p value calculated by comparing the values of two periods of observations using the Mann–Whitney U-test.

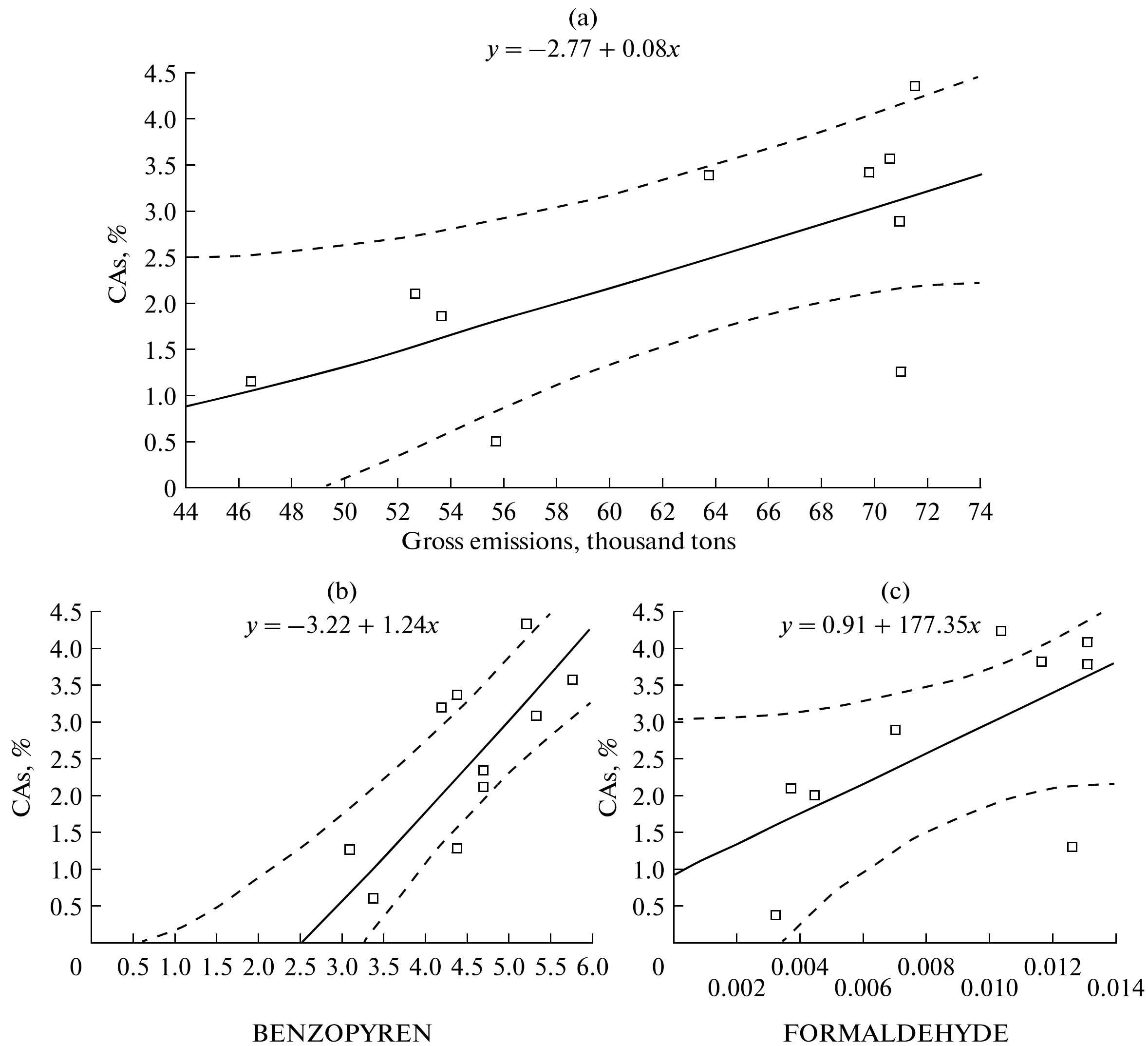

Fig. 5. The dependence of the level of CAs in the peripheral blood lymphocytes of Kemerovo's residents on the concentration of the major pollutants in air. The X axis gives the emission of pollutants. The Y axis gives the level of CAs (the proportion of aberrant metaphases), %. (a) The impact of the emissions of pollutants from stationary sources, thousand tons. (b) The impact of the average annual concentration of BP, ng/m^3; (c) The impact of the average concentration of formaldehyde, mg/m^3.

consistency of the processes of environmental pollution, mutagenesis, and carcinogenesis in residents of industrial cities.

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