Cytogenetic Effects of the Action of Ionizing Radiations on Human Populations

Vladimir A. SHEVCHENKO[1], Galina P. SNIGIRYOVA[2]

[1] N. I. Vavilov Institute of General Genetics, Russian Academy of Sciences, Moscow
[2] Moscow Research Institute of Diagnostics and Surgery, Ministry of Health and Medical Industry of the Russian Federation

Introduction

The methodology for assessing the genetic risk from the action of ionizing radiations on human populations has been elaborated by the United Nations Scientific Committee on the Effects of Atomic Radiation (1-3). On the basis of over 30-year international experience of investigation of genetic effects of ionizing radiations in experimental objects (microorganisms, plants, animals) as well as relatively rare investigations of genetic effects in man, UNSCEAR made an estimate of expected genetic effects of radiation in future generations per dose unit - 1 Sv.

The main source of information on absorbed doses has been accepted to be physical dosimetry. This method makes it possible to obtain evidence on the type of ionizing radiation, dose rate, duration of exposure and dose distribution in space. However, evidence on genetically important doses based on physical dosimetric measurements in the case of wide-scale accidents, such as in Chernobyl, is most often very limited.

A promising method for estimating absorbed doses is biological dosimetry, namely cytogenetic analysis (4). Radiation can induce two types of chromosome aberrations: unstable - dicentrics, centric rings, acentric fragments; and stable - reciprocal translocations and other types of translocations.

Most often absorbed doses are assessed on the basis of the frequency of unstable aberrations (dicentrics) (5). Centric rings can also be used for this purpose, but the frequency of their occurrence makes up only 5-10% as compared to the rate of dicentric chromosomes (6). By comparing the rate of dicentric chromosomes with a standard dose-effect curve obtained in an experiment in vitro, it is possible to determine a radiation dose. This method has been recommended for practical use by the documents of WHO, IAEA and UNSCEAR (1, 4, 7). Dicentric chromosomes are easily recognized without using special staining techniques. However, the use of dicentrics as well as other aberrations of the unstable type for the purposes of biological dosimetry is not always possible since the frequency of cells containing such chromosomes declines in time post exposure (8, 9). In this connection, the retrospective assessment of absorbed doses (this primarily concerns cases of emergency and accidents) by the frequency of dicentrics without additional investigations is practically unfeasible, if years have passed since the exposure occurred. More promising for the purpose of biological dosimetry is the analysis of stable aberrations (translocations) the frequency of which remains constant for a long time after exposure to radiation (months, years). The probability of occurrence of stable (translocations) and unstable (dicentrics) aberrations after exposure is the same (10, 11). However, translocations are not subjected to selection during cell proliferation, in contrast to dicentrics. In some works, the data for exposed individuals undergoing radiotherapeutic treatment and for Hiroshima survivors confirm this fact (9, 12).

The use of biological dosimetry, and, in particular, cytogenetic analysis, makes it possible to fill in the gap in the knowledge about absorbed doses in people exposed as a result of large nuclear catastrophes, which was repeatedly demonstrated in studies of the impacts of the accidents at the Chernobyl nuclear power plant in 1986 (13-19), in Goiania (Brazil) in 1987 (20) and other radiation situations (21, 22). In their turn, the data on absorbed doses refined with the help of cytogenetic methods permit assessing the genetic risk from radiation for future generations.

The objective of the present work is the analysis of available materials on practical application of the cytogenetic method for dose assessment in people participating in the post-accidental rescue and clean-up operations in Chernobyl (so-called “liquidators”). These materials will be compared with the results of cytogenetic investigations performed in other regions of Russia exposed to radiation (the village Muslyumovo in the Chelyabinsk region, several localities of the Altai Territory in the vicinity of the Semipalatinsk nuclear test site) as well as with the results of cytogenetic monitoring in the population living around the Three Mile Island (TMI) nuclear power plant (Pennsylvania, USA) where a nuclear accident occurred in 1979. The work presents the results of cytogenetic investigations obtained by the traditional method of analysis of the frequency of unstable chromosome aberrations and by the FISH

Table 1 Cytogenetic results obtained in 1986 in the liquidators of the Chernobyl Nuclear Power accident

[(M ± SEM) $\times 10^{-3}$]

Group	Number of persons	Number of cells scored	Number of chromosome aberrations	Dicentrics + centric rings	Absorbed whole body dose ** mGy ± SEM 1	2
Chernobyl Nuclear Power Plant staff	83	6015	23.7 ± 2.0*	5.8 ± 1.0*	474 ± 315	303 ± 199
Physicians	37	2590	13.1 ± 2.3*	2.7 ± 1.0*	198 ± 212	125 ± 123
Dosimetrists	23	1641	31.1 ± 4.3*	4.8 ± 1.7*	381 ± 345	243 ± 214
Drivers	60	5300	14.7 ± 1.7*	3.2 ± 0.8*	264 ± 211	168 ± 124
Builders of the “Sarcophagus”	71	4937	32.4 ± 2.5*	4.4 ± 0.9*	347 ± 260	221 ± 159
Pripyat population	35	2593	14.3 ± 2.4*	1.9 ± 0.8*	131 ± 168	81 ± 92
Control	19	3605	1.9 ± 0.7*	0	-	-

Level of significance * - $p< 0.05$; SEM, standard error of the mean;
** - dose estimations on the basis of: 1 - reference 15, 2 - reference 23, on the basis of the sum of dicentrics and centric rings (0.011 and 0.018 dicentrics per 1 Gy per 1 cell).

method based on the frequency of stable chromosome aberrations.

Cytogenetic examination of the victims of nuclear accidents

A. *Cytogenetic examination of the liquidators working in Chernobyl*

Cytogenetic examination of the liquidators working in Chernobyl was started in 1986 in the laboratory organized by the N. I. Vavilov Institute of General Genetics of the Russian Academy of Sciences directly in Chernobyl in accordance to the resolution of the Governmental Commission on the liquidation of the consequences of the accident (13, 14, 15).

All examined people working in the zone of the accident in 1986 were grouped as follows:

employeers from the Chernobyl nuclear power plant (CNPP) who participated in the liquidation of the consequences of the accident and in decontamination of the territory in 1986-1987; physicians of the medical station in Pripyat who examined the workers of the Chernobyl nuclear power plant before the accident and participated in the evacuation of the population of Pripyat and the personnel of unit ¹4 and later in medical examination of the liquidators working in the 30 km control zone; a group of dosimetrists who participated in the dosimetric control on the CNPP territory during decontamination works; drivers who transported concrete and other materials for constructing the "sarcophagus" around unit 4;

builders of the "sarcophagus" who directly participated in its construction;

part of the population of Pripyat evacuated after the accident but remaining in the 30 km zone and participating in the liquidation works (members of the local administration, militiamen, workers of consumer's co-operatives, etc.).

Blood samples were collected within several days (groups 1, 3, 4, 5) and within 1-3 months (groups 2, 6) after the evacuation of people from the 30 km zone. The results of cytogenetic examination are presented in Table 1. They demonstrate that the frequency of chromosome aberrations in the examined liquidators significantly exceeds (up to 17-fold) the control level. The highest frequency of cytogenetic injuries was recorded in the builders of the sarcophagus, CNPP personnel and in the dosimetrists. The greatest spread in the frequency of chromosome aberrations between individuals was observed among the sarcophagus builders (up to 16%). A more homogeneous distribution was noted in the group of inhabitants from Pripyat (from 1 to 6%) and in the CNPP personnel (from 0 to 10%).

Absorbed doses were assessed by the frequency of dicentrics and centric rings using a calibration dose-effect curve generated in vivo (analysis of dosimetric data for the liquidators whose absorbed dose was precisely measured by the physical method) (15) and linear coefficients of calibration dose-effect curves obtained in vitro for acute exposure in the low dose range (23). Table 1 presents the values of average absorbed doses calculated on the basis of cytogenetic data. These values are from 81 to 474 mGy in the groups of people exposed to radiation in 1986. The highest level of absorbed doses was recorded for the CNPP personnel, dosimetrists and sarcophagus builders.

It should be noted that the results of dose assessment obtained from the dose-effect curve in vivo (15) completely agree with the real dose situation in Chernobyl while the dose estimate by the calibration curve of Lloyd et al. (23) generated under high dose rate conditions needs correction in view of the peculiarities of dose formation in Chernobyl. The correction factor is apparently equal to the ratio of α coefficients in corresponding regression equations: 0.018 (15) and 0.011 (23) dicentrics per 1 Gy per cell. This ratio in the given case is 1.6. It should also be stressed that according to the data presented in the report of UNSCEAR 1982 (1) the accepted coefficients for different genetic effects are 2.0 upon transition from acute exposure conditions to prolonged exposure and 3.0 upon transition from acute exposure to chronic exposure.

Beginning in 1990, the cytogenetic examination of the liquidators was continued in the Moscow Research Institute of Diagnostics and Surgery of the Ministry of Health and Medical Industry of the Russian Federation (16, 24-26). Over 400 individuals involved in reconstruction works in 1986-1987 have been examined. As a rule, the dose officially recorded in the documents did not exceed 250 mSv. For a significant part of the liquidators (about 30%) information on absorbed doses was lacking. Particular attention was given to the formation of a control group. This group consisting of 82 persons included those who had never had contact with ionizing radiation and had never been subjected to therapeutic and serious diagnostic irradiation. The frequency of dicentrics and centric rings in the control group made up 0.2 ± 0.1 per 1,000 cells (26,849 metaphases analyzed). Cytogenetic examination involved analysis of the frequency of unstable aberrations (dicentrics and centric rings) by the conventional method and analysis of the frequency of stable translocations by the FISH method.

Table 2 gives the main results of cytogenetic examination obtained using the conventional method. Throughout the whole follow-up period, beginning from 1990, the level of cells with unstable aberrations - dicentrics and centric rings - significantly differed from the control. Only in 1995 the frequency of cells with dicentrics and centric rings was at the control level (group 6).

Thus, despite a long period of time after the exposure, a high level of cells with unstable aberrations was preserved in peripheral blood of the examined people.

Analysis of the frequency of stable translocations with the FISH method was carried out in 53 liquidators who worked in Chernobyl in 1986 and in 12 persons from the control group. The cytogenetic study was performed in 1994-1995, i.e. 8-9 years after the accident. The data of this study are presented in Table 3. In the group of liquidators, the frequency of cells with translocations exceeds that in the control group nearly 4-fold. On this basis of the data obtained, an absorbed dose was assessed using the calibration dose-effect curve for acute radiation exposure generated after ^{137}Cs gamma-irradiation of whole blood in the range of 0 to 3 Gy (33). This dose made up 200 mGy. 32 out of 53 examined liquidators had official data on absorbed doses, but no dependence of the frequency of cells with translocations on the radiation dose value was revealed (r=0.143, p=0.44).

Table 4 demonstrates the results of cytogenetic examination with the FISH method for a group of liquidators who had dosimetric data and for liquidators for whom such information was not

Table 2 Results of cytogenetic analysis of lymphocytes in the liquidators and the control group

[(Mean ± SEM) $\times 10^{-3}$]

Group (year of sampling)	Number of persons	Number of cells scored	Number of cells with aberrations	Cdr	a c e
I (1990)	23	4268	14.9 ± 1.9*	1.0 ± 0.5*	5.3 ± 1.1
II (1991)	110	20077	19.7 ± 1.0*	0.9 ± 0.2*	6.8 ± 0.6*
III (1992)	136	32000	31.8 ± 1.0*	1.4 ± 0.2*	9.0 ± 0.5*
IV (1993)	75	18581	34.8 ± 1.4*	0.9 ± 0.2*	11.9 ± 0.8*
V (1994)	60	18179	31.8 ± 1.3*	1.8 ± 0.3*	10.3 ± 0.8*
VI (1995)	41	12160	18.8 ± 1.2*	0.4 ± 0.2	7.3 ± 0.8*
Control	82	26849	10.5 ± 0.6	0.2 ± 0.1	3.9 ± 0.4

Level of significance * - $p< 0.05$; SEM, standard error of the mean;
Cdr, cells containing dicentrics and/or centric rings; ace, acentrics.

Table 3 Frequency of symmetrical translocations in a group of liquidators (pooled data) and in the control group

Group	Number of persons	Number of cells scored	Number ofstable translocations	($F_P \pm$ SEM) $\times 10^{-2}$	($F_G \pm$ SEM) $\times 10^{-2}$	Estimated dose(mGy)
Liquidators	53	45007	166	0.37 ± 0.03*	1.17 ± 0.05	200 (100,300)
Control	12	13586	13	0.10 ± 0.03	0.32 ± 0.05	-

Level of significance * - $p< 0.05$; SEM, standard error of the mean;
F_P, translocations/cell; F_G, genomic translocation frequency.

available. A higher level of cells with translocations was established in the second group including liquidators whose absorbed doses were not officially documented.

Table 5 presents the data of individual cytogenetic analysis with the FISH method for 10 liquidators in whom the frequency of cells with translocations significantly differed from the control level. For these patients, the absorbed radiation doses were estimated in the range from 300 to 1,000 mGy.

It is important that all the above estimates of absorbed doses based on the FISH method were made without corrections for prolonged and chronic exposures.

Thus, the liquidators examined immediately after the exposure to radiation displayed a high level of unstable chromosome aberrations which permitted us to estimate average absorbed doses depending on the character of their work in the range of 81-474 mGy. It was revealed that the level of cells with unstable chromosome aberrations - dicentrics and ring chromosomes - decreases in time but over 8 years after the exposure it exceeded the control level. The use of unstable aberrations for the purposes of biological dosimetry in case years have passed since the exposure occurred requires an experimental determination of a temporal parameter characterizing the dynamics of reduction of the level of such aberrations.

Analysis of the frequency of stable translocations with the FISH method is more promising for biological dosimetry since it permits estimating absorbed doses irrespective of the time post exposure. The cytocenetic examination (analysis of stable translocations) of the liquidators working in Chernobyl demonstrates the possibility of assessing absorbed doses within 8-9 years after the action of ionizing radiations. It should be pointed out that the individual doses were not always in agreement with the dosimetric data presented in the official documents of these people. The scatter in the dose values in the group of examined liquidators

Table 4 requency of symmetrical translocations in two groups of liquidators (with and without official doses)

Group	Official dose	Number of persons	Number of cells scored	Number of stable translocations	($F_P \pm$ SEM) $\times 10^{-2}$	($F_G \pm$ SEM) $\times 10^{-2}$	Estimated dose(mGy)
I	YES	32	26947	84	0.31 ± 0.03	0.98 ± 0.06	100 (0,200)
II	NO	21	18060	82	0.45 ± 0.05	1.43 ± 0.09	300 (200,400)

F_P, translocations/cell; F_G, genomic translocation frequency.
SEM, standard error of the mean.

Table 5 Frequency of translocations (detected by FISH), dicentrics and rings (obtained with conventional scoring) and individual dose estimates (95% CL)

Pat-ient No	Docum -ented dose (mGy)	FIS H m e t h o d					Conventional method		
		cells scored	translo cations	F_P±SEM $\times 10^{-2}$	F_G±SEM$\times 10^{-2}$	Estimated dose(mGy)	cells scored	Dic+ Rc	(dic+Rc) /cell±SEM$\times 10^{-2}$
1	-	583	6	1.03 ±0.42	3.27 ±0.75	600 (400,800)	250	0	0
2	-	1016	15	1.48 ±0.38	4.70 ±0.68	700 (600,800)	1000	8	0.80 ±0.28
5	145	1297	8	0.62 ±0.22	1.97 ±0.39	400 (300,500)	300	0	0
6	170	1314	10	0.76 ±0.24	2.42 ±0.43	400 (300,500)	300	0	0
9	-	473	11	2.33 ±0.69	7.40 ±1.25	1000 (800,1200)	300	3	1.00 ±0.58
12	-	1161	9	0.77 ±0.25	2.44 ±0.46	400 (300,500)	300	2	0.67 ±0.47
34	-	1157	6	0.52 ±0.21	1.65 ±0.38	300 (200,400)	300	0	0
35	-	1209	7	0.58 ±0.22	1.84 ±0.39	300 (200,400)	300	0	0
44	800	1688	11*	0.59 ±0.19	1.87 ±0.33	300 (200,400)	300	0	0
45	293	857	6	0.70 ±0.29	2.22 ±0.51	400 (300,500)	300	0	0

*;10 cells.

Table 6 Frequency of unstable chromosome aberrations in blood lymphocytes in the Altai population

[(M ± SEM) $\times 10^{-3}$]

Group	No of per-sons	No of cells	Cells with aberr-ations	Total number of aberrations	dic + R_c	a c e	C_{dr}	Chromatid aberra-tions
Tyumentsevo (control)	30	7831	10.2 ±1.1	10.7 ±1.2	0.3 ±0.2	5.7 ±0.9	0.3 ±0.2	4.7 ±0.8
Ugly	15	1958	7.8 ±2.0	16.8 ±2.9	3.7 ±1.4*	9.2 ±2.2	1.0 ±0.7	3.1 ±13
Ozernoye-Kuznetsovo	12	1523	12.0 ±2.8	12.0 ±2.8	0.7 ±0.7	6.0 ±1.9	0.7 ±0.7	5.4 ±1.9
Zelenaya Dubrava	24	2749	31.6 ±3.4*	32.0 ±3.4*	1.1 ±0.6*	8.1 ±1.7	1.1 ±0.6*	22.1 ±2.8*
Laptev Log	84	22195	14.4 ±0.8*	16.5 ±0.9*	3.1 ±0.4*	5.3 ±0.5	1.9 ±0.3*	7.6 ±0.6*
Naumovka	26	4275	16.8 ±2.0*	17.5 ±1.9*	2.6 ±0.7*	6.2 ±1.3	2.6 ±0.7*	8.8 ±1.4*
Belenkoye	35	9069	13.6 ±1.2*	16.9 ±1.4*	1.3 ±0.4*	7.3 ±0.9	1.2 ±0.4*	7.5 ±0.9*
Topolnoye	30	6530	20.4 ±1.8*	20.5 ±1.8*	1.7 ±0.5*	6.2 ±1.0	1.7 ±0.5*	12.3 ±1.4*

Level of significance * - $p<0.05$; SEM, standard error of the mean;
dic, dicentrics; R_c, ring chromosomes; ace, acentrics; C_{dr}, cells containing dic+R_c.

constituted up to 1 Gy. However these values may appear to be underestimated as the calculations were made without corrections for prolonged and chronic exposures.

B. Cytogenetic examination of the Altai population exposed to ionizing radiations as a result of nuclear explosions on the Semipalatinsk nuclear test site

As a result of nuclear tests in the air on the Semipalatinsk nuclear test site in 1949-1962, a number of regions of the Altai Territory were exposed to the action of high doses of ionizing radiations capable of inducing serious genetic effects. According to the data of the Semipalatinsk nuclear test site (27), radioactive products from more than 50 explosions made in the air and on the earth for a period from 1949 till 1962 spread in the direction of the Altai Territory. A collective effective dose from the first nuclear explosion in 1949 made up 32,000 man-Sv. A total dose for the Altai population from all subsequent explosions is estimated at 10,000 man-Sv. Thus, the contribution from the explosion in 1949 constitutes about 80% of the total collective effective dose received by the Altai population as a result of nuclear tests on the Semipalatinsk test site (27).

The dotted line indicates the rates of cells with chromosome aberrations in a group of Moscow citizens. Absciss - dose, Sv; ordinate - the number of cells with dicentrics and rings per 1,000 cells.The study of genetic impacts from nuclear explosions for the Altai population was started only when several decades had passed since the radiation exposure. This fact creates a unique situation in estimating genetic effects in the exposed part of the population - it is necessary to choose approaches enabling the study of genetic effects within such a long time after the exposure.

In this section, we present the materials of cytogenetic examination of people from 7 settlements of the Altai region (226 individuals) that suffered most greatly from the explosion in 1949 (21, 22, 28).

In 1992, blood samples were collected in the following settlements: Uglovskoye (average dose - about 0.1 Sv), Ozernoye-Kuznetsovo (about 0.1 Sv), Laptev Log (0.97 Sv) and Topolnoye (2.43 Sv). Later on, in 1993 and in 1994, cytogenetic examinations were continued in the villages Zelyonaya Dubrava (0.18 Sv), Belenkoye (1.87 Sv) and Naumovka (1.86 Sv). The village Tyumentsevo was chosen as a control (0.05 Sv). The social-economic and climatic-geographic conditions were analogous for all examined groups.

The results of these cytogenetic studies are presented in Table 6. In addition to chromatid aberrations (mainly single fragments), the spectrum of aberrations included chromosome aberrations: acentric fragments, centric rings, dicentric and even tricentric chromosomes. Atypical monocentric chromosomes resulting from translocations were also detected. In some exposed individuals cells with multiple chromosome aberrations were found.

In the populations of Zelyonaya Dubrava, Laptev Log, Naumovka, Belenkoye and Topolnoye the frequency of aberrant metaphases significantly

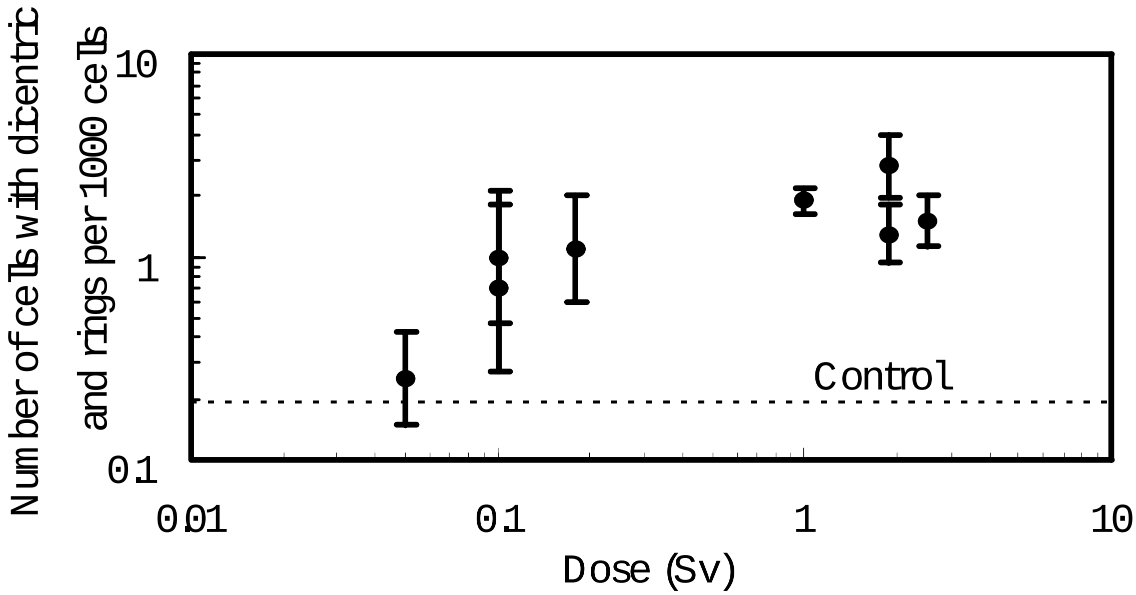

Fig. 1. The frequency of cells with dicentrics and centric ring chromosomes in the examined groups of the Altai population depending on the effective dose of irradiation caused by the nuclear explosion on the Semipalatinsk nuclear test site in 1949.

exceeds the control level. In the same populations, a statistically significant excess over the control level by the frequency of chromatid aberrations was observed. No differences were found by the frequency of acentric fragments (non-associated with dicentrics and centric rings), except an increased frequency of acentric fragments in the inhabitants of the village Belenkoye ($p<0.05$).

Most informative in respect of biological dosimetry are dicentrics and centric ring chromosomes as recognized markers of radiation effects (5). For all examined populations, except the village Ozernoye-Kuznetsovo, the average rate of cells with dicentrics and centric rings (C_{dr}) significantly exceeds the control level. The frequency of these chromosomes in the examined groups of people from the villages Uglovskoye, Naumovka, Laptev Log, Topolnoye, Belenkoye and Zelyonaya Dubrava exceeds the control level 12-fold, 9-fold, 6-fold, 6-fold, 4-fold and 3.5-fold, respectively.

Fig. 1 shows the frequency of cells with dicentrics and centric rings in the inhabitants of several settlements of the Altai region depending on the values of effective doses presumably absorbed by them. These doses were estimated on the basis of experimental measurements and with the help of mathematical simulation performed by the Central Physical-Technical Institute of the Ministry of Defence of the Russian Federation (29).

Statistical analysis of the results presented in Fig. 1 was performed on the basis of linear dose-effect relationship. Approximating equation coefficients were determined by the method of maximum likelihood assuming Poisson distribution. The following linear regression equation was derived:

$$y = (0.8 \pm 0.2)\times 10^{-3} + (0.6 \pm 0.2)\times 10^{-3} \times Sv^{-1} D,$$

where y is the frequency of cells containing dicentrics and centric rings (C_{dr}), D - dose. The level of significance of the linear regression coefficient is $p<0.05$. The results of the study clearly demonstrate that despite a long post-exposure time (several decades) an increased number of cells with unstable chromosome aberrations, the level of which depends on the effective dose value, is observed in peripheral blood of the examined people. It can be inferred that the source of such cells carrying dicentrics and centric ring chromosomes are radiation-injured stem cells of blood-forming tissue.

Among 40,777 cells analyzed in the examined groups of the Altai population 10 cells were found to have multiple chromosome aberrations. The distribution of multiaberrant cells among these groups and their characteristics are shown in Table 7. One multiaberrant cell containing five acentric fragments was found in peripheral blood of the examined persons from Tyumentsevo (control group). Multiaberrant blood cells, including dicentrics, tricentrics and centric rings, were discovered in the examined inhabitants from the settlements exposed to ionizing radiations. The frequency of multiaberrant cells in them is higher than in the control group.

The nature of such multiaberrant cells is not completely understood yet (30, 31). Probably they are induced by chemical or biological mutagenic factors. One of possible explanations of the nature of such cells is the action of densely-ionizing radiations, and first of all, of alpha-particles of various radionuclides, assuming their high concentration in the human body. Since ^{239}Pu, a source of alpha-particles, is a component of the mixture of products of the nuclear explosion that affected the Altai population, it can be inferred that the entry of plutonium into the human organism caused the appearance of multiaberrant cells. This hypothesis is confirmed by the data of A. M. Marenny et al. (32) who detected hot particles (a source of alpha-radiation) in the lungs and in the lymph nodes of ten patients from the radionuclide-contaminated regions of Altai who were operated from lung cancer.

Thus, within 43-45 years after the first nuclear explosion on the Semipalatinsk nuclear test site in 1949, the inhabitants of all examined settlements revealed an increased frequency of unstable

Table 7 Frequency of multiple cells in blood lymphocytes of people from different radionuclide-contaminated areas

Group	Patients *	Age (Year of birth)	Sex	Description of multiple cells
Muslyumovo (116 persons)	1	1949	f	tric-2; dic-3
	2	1975	m	tric-2
	3	1950	f	dic-8; ace-4
	4	1980	m	dic-2
	5	1915	f	tet-1; tric-1; dic-1
	6	1958	f	dic-2
Altai (178 persons)	1	1947	m	dic-2
	2	1945	m	ace-9; SF-1
	3	1930	m	tric-5;dic-5;Rc-1;t-2
	4	1941	m	dic-3; ace-1
	5	1956	m	dic-1; ace-2;
	6	1949	f	dic-2;tric-2; ace-11
	7	1935	m	tric-2;dic-2;t-1;ace-5
	8	1949	f	dic-2; ace-7
	9	1961	m	dic-2
	10	1946	m	dic-1; ace-2
Control (30 persons)	1	1962	f	ace-5

dic, dicentric; tric, tricentric; tet, tetracentric; R_C, centric ring;
ace, acentric (double fragment); SF, single fragment; t-translocation;
* people with multiple aberrations

Table 8 Frequency of symmetrical translocations (FISH method) in blood lymphocytes in the Altai population

Group	No of persons	No of cells scored	No of translo-cations	$(F_P \pm SEM)\times10^{-2}$	$(F_G \pm SEM)\times10^{-2}$
Laptev Log	14	7026	29	0.41 ±0,08*	1.29 ±0,11
Belenkoye	6	3213	18	0.56 ±0,13*	1.76 ±0,19
Topolnoye	4	2762	11	0.40 ±0,12*	1,26 ±0,17
Altai region (Total)	24	13001	58	0.45 ±0.06*	1.42 ±0.10
Control	12	13586	13	0.10 ± 0,03	0.32 ±0,05

Level of significance * - $p<0.05$; SEM, standard error of the mean; F_P, translocation/cell; F_G, genomic translocation frequency; m, standard error of the mean.

Table 9 Frequency of symmetrical translocations (FISH method) in blood lymphocytes in the Laptev Log (Altai region) population

Group	No. of persons	No.of cells scored	No. of translocations	$(F_p \pm SEM)\times10^{-2}$	$(F_G \pm SEM)\times10^{-2}$
I (born before 1949)	8	4271	25	0.58 ± 0.12*	1.82 ±0.17
II (born after 1949ã)	6	2755	4	0.14 ± 0.01	0.44 ± 0.10
Control	12	13586	13	0.10 ±0.03	0.32 ±0.05

Level of significance * - $p<0.05$; SEM, standard error of the mean;

chromosome aberrations, mainly dicentrics and centric rings. The frequency of cells with such chromosome aberrations was linearly related to effective doses presumably accumulated by the populations of the examined settlements. At present, it is hard to say anything about the initial level of dicentrics and centric rings immediately after the explosion since the dynamics of these chromosome aberrations for a period of several decades is unknown. This hinders the use of the presented data for the reconstruction of absorbed doses in the Altai population.

The results of cytogenetic examination of the Altai population with the FISH method are presented in Table 8. The average levels of translocations for the populations of Laptev Log, Belenkoye and Topolnoye are 0.41 per 100 cells, 0.56 per 100 cells and 0.40 per 100 cells, respectively. These values significantly exceed our control level and therefore it is safe to assume the presence of radiation-induced changes in the cell chromosome apparatus in the examined persons. As noted above, about 80% of the external radiation dose falls on the explosion made in 1949; therefore people born before 1949 received the highest doses. In connection with this, the results of examination of this group of the population should be analyzed separately. For example, the group of examined persons from the village Laptev Log included those born before and after 1949. As seen in Table 9, the average level of stable translocations for 8 individuals born before 1949 is 0.58 per 100 cells and for 6 individuals born after 1949 it is 0.14 per 100 cells. In the first group, the frequency of stable translocations is more than 5 times higher than in the control, and in the second group the frequency of stable translocations does not differ from the control level. The data obtained are far from being sufficient to make any final conclusions, however even these results confirm the fact that the most affected part of the population are people born before 1949 and that they must be, in the first turn, in the focus of attention when undertaking medical and preventive measures.

The absorbed dose value estimated by the frequency of stable translocations for three villages, Laptev Log, Belenkoye and Topolnoye, is about 300 mGy. It should be mentioned that this value was obtained using the linear-quadratic dose-effect model for acute exposure (33). The situation observed in the Altai region due to surface nuclear explosions is much more complicated in terms of dosimetry than that could be assessed with the use of this model. It is important to take into account the long-term chronic irradiation from external and internal radiation sources (29). A true estimate of effective doses based on the frequency of stable aberrations can be obtained only given clear-cut data on the dynamics of irradiation of the population both during the nuclear test period and after it. A correction factor 3 is usually used for assessing chronic irradiation doses (1). Hence it follows that in the case of the exposure that took place in the Altai region the linear-quadratic model yields underestimated dose values. In view of the above-stated, the average dose for the examined groups of the population calculated on the basis of cytogenetic analysis makes up about 1 Gy.

It is obvious that the values of absorbed doses for the part of the Altai population exposed to ionizing radiations from nuclear explosions on the Semipalatinsk nuclear test site will be corrected with accumulation of cytogenetic data obtained by the FISH method.

C. Cytogenetic examination of the population of Muslyumovo located on the banks of the radionuclide-contaminated Techa river

In 1949-1951, the plutonium-producing plant ("Mayak") in the Chelyabinsk region discharged radioactive waste products (a total of 2.76 mln Ci) into the open hydrosystem of the rivers Techa, Iset, Tobol (34). 124,000 people, including 28,100 of those living on the Techa banks, were exposed to radiation. The doses of exposure were rather high - a collective dose made up about 6,000 man-Sv. Nearly 7,500 individuals evacuated from 20 settlements received, according to official data, average effective equivalent doses from 3.5 to 170 cSv (34). The highest radiation doses were recorded for the evacuated population of the village Metlino (170 cSv, 1,200 people). Among non-evacuated settlements, the most serious radiation situation remains in Muslyumovo (30 km from the Mayak plant). In 1949, the population of this settlement was 4,000 people, and at present it is about 2,500 people. The level of exposure here is critical - an average bone marrow dose is 0.25 Gy. In nearly 5% of the population an average bone marrow dose is 1 Gy (35). The first medical examinations were organized within 2 years after the discharge of radioactive waste products into the Techa river only for the population of one settlement in the upper reaches of the river - Metlino. In other settlements the medical examination was started only after 3-6 years. The register of exposed people living along the river was initiated only in 1968. These facts in combination with a high migration of the exposed population has created a situation in which the assessment of remote radiation effects becomes rather difficult.

At the same time, even the first studies showed that the exposure of people in the upper reaches of the Techa river had led to the development of chronic radiation sickness (particularly in Metlino where this disease was diagnosed in 1956 in 64.7% of the adult population and in 63.15% of examined children) (36). Chronic radiation sickness was revealed in a total of 935 people. An increase in the incidence of leukoses in the examined population was established. For a period of 33 years, 52 cases of hemoblastoses were recorded, including 37 leukosis patients among 17,200 people examined since 1950, which is by 15 cases more than expected without irradiation.

Besides chronic radiation sickness, a decrease in immunologic reactivity, depression of hemopoiesis, an increase in cases of vegetovascular dystonia, hypertensive disease, pathologic pregnancy and labor, and increased infantile mortality were recorded in the inhabitants of the riverside settlements. As shown in the work by M. M. Kosenko and M. O. Degteva (36), the mortality from cancer increased in 1950-1982 as compared to a group of people living in non-contaminated areas with similar social-economic conditions.

Cytogenetic examinations of the population of Muslyumovo were performed in 1993-1994. The examination was carried out on a total of 116 persons. The data of the cytogenetic analysis were compared with the results of examination of the control group (30 individuals, 7,831 metaphases analyzed) formed of the inhabitants from a non-contaminated region of the Altai. In view of the tasks of the examination, all people were divided in several groups. The first group included all examined people. The second group united inhabitants of Muslyumovo born before 1949 (beginning of the contamination of the Techa river) and living there permanently. The third group was composed of people born from 1949 till 1956 (this time is characterized by the highest level of contamination of the Techa river). The fourth group consisted of people born after 1957, and the fifth group was formed of migrants, i.e. people who came to Muslyumovo at different times, including those evacuated from villages exposed to radioactive contamination.

Table 10 presents the results of cytogenetic examination by the conventional method (analysis of unstable chromosome aberrations). In all groups, the frequency of chromosome aberrations exceeded the control level. It is worth noticing that the value of this frequency was higher in the second and third groups. In all examined groups exchange aberrations (dicentrics and centric rings) were revealed, and their frequency significantly exceeded (5-10-fold) that in the control group. The highest frequency of dicentrics and centric rings, as well as cells containing such aberrations, was noted in the second and third groups. These results are presented in Fig. 2. The frequency of acentric fragments did not differ significantly in the groups of examined people from Muslyumovo and in the control group. In all examined groups an excess over the control level by the frequency of chromatid aberrations was observed.

Cells with multiple chromosome aberrations were found in the examined persons from Muslyumovo (Table 7). On the whole, 6 multiaberrant cells were discovered among 32,203 analyzed metaphases, including tricentric and tetracentric cells which are not practically found normally.

It can be assumed that the appearance of cells with multiple aberrations is the result of the action of alpha-radiation from plutonium and its fission products (30, 31, 37). According to A. V. Trapeznikov et al. (38), the Techa river contains about 8 Gbq $^{239, 240}$Pu. This estimate was made within the river section from 50 km to 240 km from the Mayak plant, i.e. up to the place of confluence with the Iset river.

Thus, the cytogenetic study carried out in Muslyumovo revealed an increased level of

Table 10 Cytogenetic results obtained in a human population continually exposed to low doses of radiation in the South Urals, Chelyabinsk area, Muslyumovo

(M ± SEM) x 10^{-3}]

Group	No of persons	No of cells	Cells with aberrations	Total number of aberrations	dic + R_c	a c e	C_{dr}	Chromatid aberrations
1	116	32203	14.4 ±0.7*	15.3 ±0.7*	2.2 ±0.3*	5.4 ±0.4	1.4 ±0.2*	7.6 ±0.5*
2	23	6730	19.3 ±1.7*	19.4 ±1.7*	2.7 ±0.6*	6.6 ±1.0	1.9 ±0.5*	9.8 ±1.2*
3	46	5730	15.8 ±1.7*	17.2 ±1.7*	3.2 ±0.7*	7.6 ±1.1	2.1 ±0.6*	6.3 ±1.1*
4	49	14052	11.9 ±0.9	12.4 ±0.9	1.5 ±0.3*	3.3 ±0.5	1.1 ±0.3*	7.6 ±0.7*
5	21	5691	13.3 ±1.5	15.4 ±1.6*	2.2 ±0.6*	6.7 ±1.1	0.9 ±0.4	6.4 ±1.1
Cont-rol	30	7831	10.2 ±1.1	10.7 ±1.2	0.3 ±0.2	5.7 ±0.8	0.3 ±0.2	4.7 ±0.8

1, total; 2, born before 1949; 3, born in 1949-1956; 4, born in 1957-1988; 5, migrants.
Level of significance * - $p<0.05$; SEM, standard error of the mean;

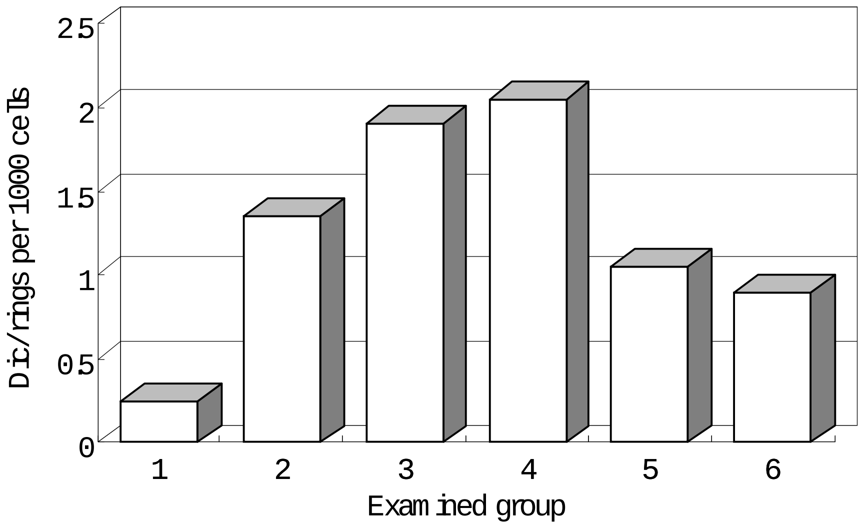

Fig. 2. The frequency of cells with dicentrics and centric ring chromosomes in the examined groups of the population of Muslyumovo (Chelyabinsk region).
1 - control group; 2 - all examined individuals; 3 - born before 1949;4 - born in the period from 1949 to 1956; 5 - born in the period from 1957 to 1988; 6 - evacuated from other settlements.

chromosome aberrations of the exchange type - dicentrics and centric rings - which are characteristic of ionizing radiation exposures. The highest level of such aberrations (9-10 times exceeding the control) was detected in the people born before 1949 or in the period of the most significant contamination of the Techa river with radionuclides. Cells with multiple chromosome aberrations detected in the blood of the examined inhabitants of Muslyumovo seem to be the result of organism exposure to densely-ionizing alpha-radiation from plutonium and its radioactive products.

D. Cytogenetic examination of the population from the neighborhood of the Three Mile Island nuclear power plant in USA

In 1979, an accident occurred at the Three Mile Island (TMI) Nuclear power plant (unit ^{1}2) located within several miles from the capital of Pennsylvania, Harrisbugr (USA). The extent and consequences of this accident have not been uniquely assessed yet. According to the official data stated in the NUREG report in 1980 (39), no impact from this accident on the population, flora and fauna is expected. At the same time, the discovery of radioactive iodine in the air, calculations of experts concerning the extent of possible discharges of radioactive inert gases, publications of scientists on radiation effects in trees and animals observed after the accident prompt the public and scientists to perform new studies for assessing the impacts from this nuclear incident (40).

In 1994-1995, cytogenetic examinations of the population living in the neighborhood of the TMI nuclear power plant were carried out. The aim of this study was to analyze the level of unstable and stable chromosome aberrations in people assumed to be exposed to ionizing radiations due to the TMI accident. The basis for such assumption were the signs of radiation damages in people (skin reddening, peculiar metallic smack in the mouth, irritation of mucous membranes, vestigo, vomiting, diarrhea, etc.) at the moment of the accident and also a number of diseases that occurred some time later.

The cytogenetic study was carried out in July-August, 1994 and in January-February, 1995. In selecting a group of patients, their possible diagnostic and therapeutic irradiation as well as a number of additional factors that might influence the results of cytogenetic analysis were taken into account. The results of the study are presented in Table 11 and in Fig. 3. Given a relatively normal general level of chromosome aberrations, a significant increase in the frequency of cells containing chromosome aberrations, namely dicentrics, was recorded. In the group of examined people from the TMI region this rate exceeded 10-fold the control level (0.2×10^{-3} dicentrics per 1,000 cells). Dicentrics were found in 20 persons, i.e. in 70% of cases. The rate of cells containing exchange aberrations (dicentrics) varied from 0.2 to 0.8% and exceeded the control level 10-40-fold, respectively. In one patient, a cell with tricentric was discovered.

The obtained results suggest that the group of examined individuals from the TMI neighborhood presumably exposed to the action of ionizing radiations as a result of the accident at the nuclear

Table 11 Frequency of unstable chromosome aberrations in blood lymphocytes from persons living in the neighborhood of TMI

[(M ± SEM) × 10^{-3}]

Groups	Number of persons	Number of cells scored	Total number of aberrations	Cdr	ace	Chromatid aberrations
Population	29	14854	14.0±1.0*	2.0±0.4*	4.0±0.5	7.0±1.0
Control	82	26849	10.9±0.6	0.2±0.1	3.9±0.4	6.6±0.5

Level of significance * - $p<0.05$; SEM, standard error of the mean;
Cdr, cells containing dicentrics and/or centric rings.

Table 12 Frequency of symmetrical translocations detected by FISH and results of conventional cytogenetic examination of persons living in the neighborhood of TMI.

Groups	FISH method				Conventional scoring		
	Cells svored	Translo cations	(F_P±SEM) × 10^{-2}	(F_G±SEM) × 10^{-2}	Cells scored	Cdr	(Cdr ± SEM) × 10^{-2}
Population	3468	17	0.49±0.12*	1.55±0.21	3024	14	0.46±0.12
Control	13586	13	0.10±0.03	0.32±0.05	26849	5	0.02±0.01

F_P, translocations/cells; F_G, genomic translocation; Level of significance * $p<0.05$; SEM, standard error of the mean; C_{dr}, cells containing dicentric and/or centric rings.

power plant is characterized by an increased frequency of chromosome exchange aberrations - dicentrics.

In 6 persons from the examined group the rate of stable translocations was analyzed with the FISH method. Cells with translocations were found in peripheral blood of all examined people, and the level of these cells exceeded the control; in 3 persons these differences were statistically significant. Table 12 demonstrates the data on the frequency of translocations in the group of examined people from the TMI neighborhood. It is seen that its value exceeds 5-fold the control level. Here the frequency of translocations per genome (F_G) and the results of traditional cytogenetic analysis (analysis of unstable aberrations) are also presented.

The ratio of stable and unstable aberrations is assumed to be 1:1 (10, 11). The prevalence of cells with translocations indicates that for a period of 15 years after the accident the level of cells with unstable chromosome aberrations decreased due to their elimination from the blood channel. Despite a rather high level of cells with dicentrics, the retrospective dose assessment in this case is hardly feasible.

The frequency of cells with translocations in peripheral blood of the examined individuals living in the neighborhood of TMI is 0.49±0.06 per 100 cells. This value is close to the level of cells with translocations observed in the Altai population (see Table 8). This fact permits the comparison of these groups with respect to absorbed radiation doses. In view of a limited amount of data (the number of examined persons, the number of metaphases analyzed), an average absorbed dose was determined for the whole examined group of people. On the basis of the obtained cytogenetic data and using calibration dose-effect curves (33) a dose estimate of 0.30±0.10 Gy was obtained. This dose is consistent with the situation of acute radiation exposure. In the case of prolonged and chronic exposure, which is more real for the situation observed after the TMI accident, the dose assessment should involve the use of correction factors 2-3. In this case an estimated dose for the exposed group of people is 0.6-0.9 Gy.

Thus, the cytogenetic examination of people living in the vicinity of the TMI nuclear power plant and presumably exposed to radiation as a result of the accident that took place in 1979 revealed in them an increased level of stable and unstable chromosome aberrations. This finding undoubtedly indicates that the examined group of people was affected by ionizing radiation. The preliminary data on the frequency of translocations obtained with the FISH method made it possible to estimate an average absorbed dose for the given group of examined persons. This value is 0.6-0.9 taking into account the prolonged or chronic character of the exposure.

Conclusion

The presented cytogenetic data obtained from the examination of different groups of people exposed to ionizing radiations permit us to make the following conclusions.

The use of the cytogenetic method for examining people exposed to radiation as a result of the Chernobyl accident, nuclear explosions on the Semipalatinsk nuclear test site, radioactive contamination of the Techa river (Chelyabinsk region) and as a result of the accident at the TMI nuclear power plant (USA) revealed increased levels of unstable and stable chromosome aberrations as compared to the control.

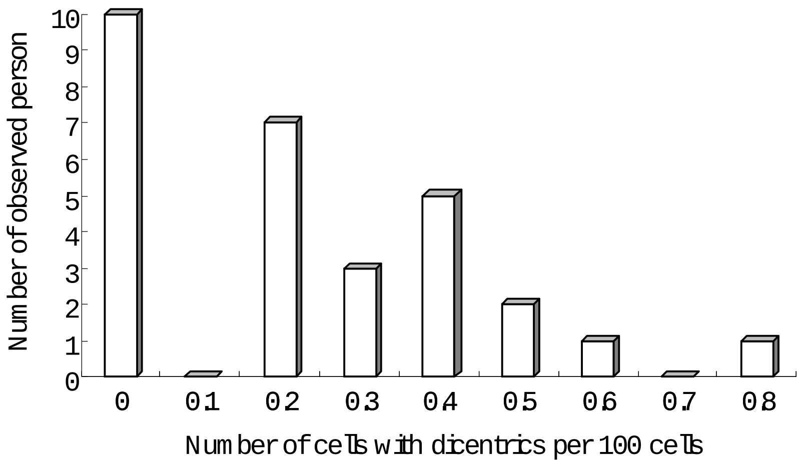

Fig. 3. The distribution of the inhabitants from the TMI region depending on the number of cells with dicentrics.

Dose estimations in the liquidators working in Chernobyl made on the basis of the frequency of unstable chromosome aberrations (dicentrics and centric rings) using the materials of examinations carried out in 1986 yielded values from 81 to 474 mGy.

The level of cells with unstable chromosome aberrations was found to decline in time. At the same time, during 8 years after the accident in Chernobyl this level in the examined people exceeded the control level.

The examination of the populations living in the Techa river region (Muslyumovo), in the Altai region and in the neighborhood of the TMI nuclear power plant (USA) revealed high levels of cells with dicentrics and centric rings significantly exceeding the control values. The detection of such chromosome aberrations within 15-45 years after the action of ionizing radiations suggests the preservation of a certain portion of cells with unstable chromosome aberrations in people with rather high doses. Multiaberrant cells found in the Altai population and in the population of Muslyumovo apparently suggest their exposure to densely-ionizing alpha-radiation from plutonium and its fission products.

As has already been noted, the most widely accepted and sufficiently accessible method of biological dosimetry based on the analysis of the frequency of unstable chromosome aberrations (dicentrics and centric rings) cannot be effectively employed for retrospective assessment of absorbed doses without clear-cut knowledge about the character and rate of temporal elimination of cells containing such chromosome aberrations. Only when there is a possibility of reconstructing the picture of an exposure (dose range, exposure conditions, post-exposure time) using mathematical simulation one can try to make dose estimates by the frequency of cells with dicentrics and centric rings. Otherwise, particularly upon exposure to low doses, when much time has passed since the exposure occurred, the use of this method of biological dosimetry is of low efficiency and practically unfeasible in most cases.

Analysis of stable translocations is presently the most promising method in retrospective assessment of irradiation doses. The efficiency of this method particularly increased after the development of the technology for scoring stable translocations - fluorescence in situ hybridization (FISH) - which permits the cytogenetic analysis to be performed rather easily (41, 42).

The presented results of cytogenetic examination of the liquidators in Chernobyl demonstrate the possibility of dose assessment within 8-9 years after the accident. The range of absorbed doses in the group of examined people appeared to be up to 1 Gy from the background level.

Retrospective assessment of individual doses, particularly in the low dose range, based on the FISH method is impeded by the fact that in order to obtain reliable results it is necessary to analyze a rather large number of cells, which is impossible for several reasons. This task is simplified when we deal with retrospective assessment of a dose for a definite group of people. The obtained cytogenetic data are a good illustration of that. The absorbed dose estimated with the FISH method, taking into account the character of exposure for the populations of three villages of the Altai region, is about 1 Gy and for the population of the TMI region (USA) it varies from 0.6 to 0.9 Gy.

It should be noted in conclusion that the importance of analysis of stable translocations for retrospective dose assessment by no means minimizes the role of cytogenetic examination with the use of the conventional method (analysis of unstable chromosome aberrations) that remains to be decisive in the case of long-term monitoring in human populations from regions with an unfavorable ecological situation.

References

1. United Nations. Ionizing radiation. Sources and biological effects. UNSCEAR 1982, report to the General Assembly with annexes. United Nations sales publication. E.82. 1982, United Nations, New York, 1982.
2. United Nations. Genetic and Somatic Effects of Ionizing Radiation.United Nations Scientific Committee on the Effects of Atomic Radiation, 1986, Report to the General Assembly, with annexes. United Nations sales publication E.86.IX.9. United Nations, New York, 1986.
3. United Nations. Sources, Effects and Risk of Ionizing Radiation. United Nations Scientific Committee on the Effects of Atomic Radiation, 1988, Report to the General Assembly, with annexes. United Nations, New York, 1988
4. Biological dosimetry: chromosomal aberration analysis for dose assessment. Technical Reports series N260. International Atomic Energy Agency (IAEA), Viena, 1986, pp.1-69.
5. Bender M.A., Awa A., Brooks A.L. et al.// Mutat. Res. 1988. V. 196. P.103-159.
6. Bauchinger M.// Mutat.Res. 1995. V.339. P.177-189.
7. Method of human chromosome aberration analysis. Edit. by K.Backton, H.Evans. WHO, Geneva, 1976, 64p.
8. Bauchinger M.// Strahlentherapie. 1968. V. 135. P. 553-564.
9. Awa A., Sofuni T., Honda T. et al.// J. of Rad. Res. 1978. V. 19. P. 126-140.
10. Buckton K.E. // Int.J. of Rad. Biol. 1976. V.29. P.475-488,
11. Tucker J.D., Ramsey M.J., Lee D.A., Minkler J.L.// Int.J. of Radiat. Biol. 1993. V. 64. ¹ 1. P. 27-37.
12. Lucas I.N., Awa A., Straume T. et all. // Int. J. Radiat. Biol.. 1992. V. 62. ¹ 1. P. 53-63.
13. Shevchenko V.A., Akayeva E.A., Yeliseyeva I.M., Yelisova T.V. Safety problems in cases of emergency. M.: VINITI, 1990, V.12, 69-90 (in Russ.).
14. Shevchenko V.A., Semov A.B., Akayeva E.A., Yelisova T.V. Rad. biologiya. Rad. ecologiya. 1995, V.35, ¹5, 646-654 (in Russ.).
15. Semov A.B., Iofa E.L., Akayeva E.A., Shevchenko V.A. Rad. biologiya. Rad. ecologiya. 1994, V.34, ¹6, 865-871 (in Russ.).
16. Chernobyl catastrophe: causes and consequences. Part 2. Minsk, SENMURV, 1993, 85-137 (in Russ.).
17. S hevchenko V.A., Snigiryova G.P. // SCOPE-RADTEST III Workshop on " Methodologies of Dose Reconstruction, Epidemiology, and Sub-surface Transport", March, 27-31. Brussels-Liege, Belgium. 1995. RL.08.95. P.10.
18. Pyatkin E.K., Nugis V.Yu., Chirkov A.A. Med. Radiol. 1989, V.34, ¹6, 52-56 (in Russ.).
19. Bauchinger M. // Stem Sells. 1995. V.13. P.182-190
20. RamalhoA.T., A.C.H.Nascimeo and A.T.Natarajan.// Radiat. Protect. Dosimetry. 1988. V. 25. P. 97-100.
21. Shevchenko V.A., Snigiryova G.P., Suskov I.I., Akayeva E.A. et al. Rad. biologiya. Rad. ecologiya. 1995, V.35, ¹5, 588-596 (in Russ.).
22. Shevchenko V.A., Suskov I.I., Snigiryova G.P. et al. Vestnik nauchnoy programmy “Semipalatinsky poligon Altai”. 1994, ¹3, 5-33 (in Russ.).
23. Lloyd D.C., Purrot R.J., Reder E.J. // Mutat. Res. 1980. V. 72. P. 523-532.
24. Snigiryova G.P., Lyubchenko P.N., Shevchenko V.A., Novitskaya N.N. et al. Hematologiya. Transfusiologiya. 1994, V.39, ¹3, 19-21 (in Russ.).
25. Snigiryova G.P., Shevchenko V.A., Novitskaya N.N. Rad. Biologiya. Rad. Ecologiya, 1995, V.35, ¹5, 654-661 (in Russ.).
26. Snigiryova G.P., Shevchenko V.A., Novitskaja N.N., Hazins E.D. // Int. Workshop on Determination of Radiation Doses among Critical Groups of the Population in the FSU after Chernobyl, Munchen, 1994.
27. Kisilev U.I., Lobarev V.M., Shoikhet Ya. N. Vestnik nauchnoy programmy “Semipalatinsky poligon Altai”. 1994, ¹1, 1-9 (in Russ.).
28. Snigiryova G.P., Shevchenko V.A. // SCOPE-RADTEST III Workshop on "Methodologies of Dose Reconstraction, Epidemiology, and Sub-surface Transport", March, 27-31, Brussels-Liege, Belgium, 1995. RL.07.95. P.10.
29. Lobarev V.M., Sudakov V.V., Zelenov V.I. et al. Vestnik nauchnoy programmy “Semipalatinsky poligon Altai”. 1994, ¹1, 27-56 (in Russ.).
30. Bochkov N.P. and Katosova L.D.// Mut.Res. 1994. V. 323. P. 7-10.
31. Neel J.V., Awa A.A., Kodama Y. et al. // Radiation Effects Research Foundation. CR 3-92. P. 1-14.
32. Marenny A.M., Kovalev E.E., Shoikhet Ya. N. et al. Vestnik nauchnoy programmy “Semipalatinsky poligon Altai”. 1994, ¹4, 73-78 (in Russ.).
33. Braselmann H., Schmid E., Bauchinger M. // Mut.Res. 1994. V. 306. P. 197-202.
34. Nazarov A.G., Burlakova E.B., Osanov D.P. et al. Resonance. Conclusions of theUnified Scientific Group on the Enviromental Protection. Penyagin AN, Editor. Chelyabinsk South-Ural Publishing House, 1991, 55p.
35. Degteva M.O., Kozheurov V.P., Vorobiova M.I. // The Science of the Total Environment. 1994. V.142. P.49-61.
36. Kossenko M.M, Degteva M.O. // The Science of the Total Environment. 1994. V.142. P.73-89.
37. Sevan’kaev A.V., Tsyb A.F., Lloyd D.C. et al. // Int. J. Radiat. Biol. 1993. V. 63. N.3. P.361-367.
38. Trapeznikov L.V., Pozolotina V.N., Chebotina M.Y. et al. // Health Phys. 1993. V.65. N.5. P.481-488.
39. Nakao H. Three Mile Island. Kyoto, Japan. 1980. 280 P.
40. Investigations of Reported Plant and Animal Health Effects in the Three Mile Island Area. NUREG-0738 EPA 600/4-80-049, Washington. 1980. 33 P.
41. Pincel D., Straume T. and Gray J.//Proc. of the Nat.Acad.of Sciences (USA). 1986. V. 83. P. 2934-2938.
42. Lucas I.N., Tenjin T., Straume T. et al. // Int. J. of Radiat. Biol. 1989. V.56. N. 1. P. 35-44.