Genetic Consequences of the Chernobyl Accident for Belarus Republic

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Introduction Numerous studies have shown that a great number of residents in Belarus, Russia and the Ukraine were exposed to radiation due to radioactive nuclides ejected from the Chernobyl reactor, which increased genetic load, manifested in particular, as chromosome aberrations (Lazjuk G.I. et al., 1990; Pilinskaya M.A. et al., 1994; Sevankaev A.V. et al., 1995). The increase was registered for unstable and stable, chromatid and chromosome types of aberrations (Stepanova E.I., Vanyurikhina E.A. 1993, Vorobtsova I.E., Bogomazova A.N., 1995, Sevankaev A.V. et al., 1995). Proceeding from the findings that the number of dicentric and ring chromosomes (which are the main indicator of radiation mutagenesis at chromosome level) was increasing simultaneously with the increase of other aberrations which are common for chemical mutagenesis (Pilinskaya M.A. et al., 1994; Lazutka J.R., 1996) and from the fact that actual mutation incidences exceeded the calculated figures for the doses obtained (Pilinskaya M.A. et al., 1992, Sevankaev A.V. et al., 1995), one can not exclude the possibility that chromosome aberrations found in the population affected by the Chernobyl disaster are caused not only by ionizing radiation but also by various mutagenes, and the doses based on physical dosimetry could be underestimated.

It is quite obvious that the level of chromosome aberrations can be used as a biological indicator of harmful mutagenic effects on the organism. However, the method is not yet capable of (or only partially suited for) detecting the actual genetic risk even in the cases when aberrations are found in gametes, not in peripheral blood lymphocytes as usually done. The study of the dynamics of genetic losses, as spontaneous abortions and perinatal death due to inherited anomalies, and the study of the dynamics of malformed children births are probably the most reliable methods to determine genetic risk due to any mutagenic factor affecting the population, including ionizing radiation. This is related to the fact that there are a great sequence of events (gamete selection, preimplantation and embryonal death) occurring between gamete mutations (to say nothing about a somatic one) and births of children with congenital diseases. It is nearly impossible to count them and this leads to various uncertainties. Only direct methods, which count the final effect, with all their drawbacks, can provide accurate information on genetic losses. We have estimated possible genetic consequences for the residents of Belarus Republic due to the Chernobyl accident by studying malformations found in legal medical abortuses and by counting congenital anomalies in fetuses and newborns.

Dynamics of anomalies found in legal medial abortuses

The incidence of anomalies has been studied in embryos and fetuses obtained from pregnant women in Minsk-city (control) and in the areas under thorough radiological control (TCA). Contaminated areas in Gomel and Mogilev regions with ^{137}Cs of 15 Ci/km^2 (555 kBq/m^2) and more are placed into the category of thoroughly controlled areas. Five to 12 week abortuses were obtained through curettage and examined by pathoembryologists at Belarus Institute for Hereditary Diseases. The investigation was carried out using dissection under a stereo-microscope. If required, serial histological sections were additionally studied. In all cases the age of embryos or fetuses was determined using the system developed at the Carnegie Institute. Malformation frequency was determined not for the number of examined abortuses, but for the number of examined organs, since after the curettage not all organs were always suitable for the examination. Moreover, since some anomalies are observed by persistence of the structures characteristic of particular stages of embryonic development, when counting particular anomaly, only embryos whose age exceeded the age of corresponding physiological persistence were taken into consideration. All anomalies found at dissection and histological examination have been recorded. In total, 33,376 abortuses, including 2,701 abortuses obtained from TCA, have been studied for the period from 1986 (the second half) to 1996.

The results are partially presented in Table 1. As the table shows, malformation frequency for legal medical abortuses from TCA is considerably higher than that from Minsk-city, which has been observed for both periods of pre-Chernobyl 6 year and post-Chernobyl 11 year. It should be mentioned that the total frequency of 7.21 in TCA during 1986 to 1995 has been found lower than it was in 1992 (9.87) (Lazjuk G.I. et al., 1996).

Significant increase has not been found for

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Table 1 Frequency of Malformations Found in Induced Abortuses in Belarus

Malformations	Regions under study		
	Minsk		TCA
	1980-1985	1986-1996	1986-1995
The number of abortuses examined	10,168	20,507	2,701
Malformation frequency to the number of examined samples (%) *including:*	5.60	4.90	7.21*
CNS anomalies	0.32	0.53	0.54
polydactyly	0.63	0.53	0.79
reduction limb defects	0.07	0.10	0.28

- *significant difference (P<0.05)

anomalies most characteristic for radiation exposure; the central nervous system and anomalies with the greatest contribution of *de novo* mutations (polydactyly and reduction limb defects). However, tendency of their number increase is rather obvious, especially for reduction limb defects.

Dynamics of congenital malformations in newborns

The birth frequency of children with congenital malformations (CM) was studied based on the National Monitoring which has been functioning throughout the whole Republic since 1979. Congenital malformations unambiguously diagnosed in neonatal period are registered irrespective of the level of technical facilities of a medical institution. In each case of congenital malformation, the diagnosing physician fills in a special form registration, which is sent to the Minsk Genetic Center. The scientists of Institute for Hereditary Diseases verify the record completeness and diagnosis during regular trips to the areas, or during consultations with families at the Center. Anencephaly, severe spina bifida cystica, cleft lips and/or palate, polydactyly, reduction limb defects leading to disability, esophageal atresia, anorectal atresias, Down's syndrome and multiple malformations are registered both in stillborns and in fetuses obtained through induced abortion after prenatal diagnostics. The results are presented in Table 2 for the ^{137}Cs contaminated areas and for the control. Thirty regions, where ^{137}Cs contamination density was found to be less than 1.0 Ci/km^2, were taken as the control.

It is clearly seen that the total CM frequency increased both in the control and in the areas contaminated with ^{137}Cs. Moreover, as the level of contamination becomes higher, the greater increase of malformed children birth is seen. While the 50% increase is shown in the control, it is 83 % in the areas with contamination over 15 Ci/km^2. It is quite obvious that the increase of CM in the control can not be caused by ionizing radiation due to the Chernobyl accident. However, dependence on contamination with radioactive Cs can not be excluded for the 1% increase over the control (51-50) recorded in 54 regions and for 33% increase (83-50) in 17 regions.

Such increase can be explained by at least 4 factors.

a) Higher birth frequency of malformed children after the Chernobyl accident is considered to be not a true increase of anomalies in embryos, but only an artifact, the result of more complete registration, in other words, it is the result of closer interest in «disaster areas»,
b) teratogenic effects of embryo exposure to radioactivity from the Chernobyl Nuclear Station,
c) the result of gamete mutations in either parent due to additional exposure on gonads, or
d) the result of a complex of negative factors including the Chernobyl disaster (radiation plus chemical pollutants, poor nutrition, alcoholism).

Artifactual origin of increasing number of CM under the long-term National Monitoring, as it is in Belarus, is virtually excluded, firstly, by counting of only unambiguously diagnosed CM, secondly, by constant control of registration completeness by the researchers from Belarus Institute for Hereditary Diseases, thirdly, by practically equal frequencies before the Accident in various regions and, finally, by the correlation between the increase of CM frequency and the level of contamination.

Teratogenic effect is excluded, since the doses received by intrauterine fetus for a teratogenic terminational (or crucial) period were below threshold. No woman who gave birth to a malformed child, has received over 55 mSv for the period starting from the accident till the end of the 1st trimester. The 1st trimester includes the terminal period of neural tube defects, the most characteristic congenital malformation for radiation teratogenesis. No significant increase of nervous system CM has been found in newborns and abortuses recorded in the National Monitoring (Tables 1 and 2).

Table 2 Incidence of Obligatory Registered Malformations in Belarus for 1982 to 1995 (per 1000 neonates)

Malformation	Areas contaminated with Cs-137				Control (30 regions)	
	>15 Ci/km^2 17 regions		>1 Ci/km^2 54 regions			
	1982-1985	1987-1995	1982-1985	1987-1995	1982-1985	1987-1995
Anencephaly	0.28 11	0.44 26	0.24 48	0.64* 226	0.35 23	0.49 63
Spina bifida	0.58 23	0.89 53	0.67 132	0.95* 335	0.64 42	0.94* 120
Cleft lip and/or palate	0.63 25	0.94 56	0.70 137	0.92* 324	0.50 33	0.95* 121
Polydactyly	0.10 4	1.02* 61	0.30 60	0.66* 232	0.26 17	0.52* 66
Limb reduction defects	0.15 6	0.49* 29	0.18 36	0.35* 123	0.20 13	0.20 26
Esophageal atresia	0.08 3	0.08 5	0.12 23	0.15 53	0.11 7	0.14 18
Anorectal atresia	0.05 2	0.08 5	0.08 16	0.10 35	0.03 2	0.06 8
Down's syndrome	0.91 36	0.84 50	0.86 170	1.03 362	0.63 41	0.92* 117
Multiple malformations	1.04 41	2.30* 137	1.41 277	2.09* 733	1.18 77	1.61* 205
Total	3.87 151	7.07* 422	4.57 899	6.90* 2423	3.90 255	5.84* 744
Percent increase before and after Chernobyl	83		51		50	

*Significant difference (p - 0.05) between the values for 1982-1985 and for 1987-1995.

Thus, the most probable cause leading to the increase of birth of malformed children in Belarus is an increased level of mutations due to chronic additional exposure of the population or a complex of negative factors. This can be indirectly evidenced by;

a) an increased level of mutations in peripheral blood lymphocytes in the population of Belarus, the Ukraine and Russia, who has received additional exposure (Lazjuk G.I. et al., 1995; Pilinskaya M.A. et al., 1992; Vorobtsova E.A., Bogomazova A.N., 1995);

b) the most marked increase of CM frequency in general and CMs with great contribution of *de novo* mutations (polydactyly, reduction limb defects and multiple CM) in the area with ^{137}Cs contamination density of 15 Ci/km^2 and above. At the same time, an increase of malformed children due to trisomies (Down's syndrome is an example), which are *de novo* mutations, has not been found.

To determine a possible relation of increased CM frequency with additional radiation, dependency of CM frequency on additional radiation dose in Gomel and Mogilev regions (excepting large industrial cities) was investigated and compared with the control data in Vitebsk region, which is considered the most safe for radioactive contamination. The values of average cumulative dose were calculated at Institute of Radiation Medicine for individuals of 18 years of age and older in those regions. They represent the combined external and internal exposure since the Chernobyl accident.

Table 3 shows the result of the analysis. Average cumulative doses per each 1% increase of CM in the contaminated regions over the CM increase in the control region are calculated to be 0.31 mSv and 0.20 mSv, for Gomel region and Mogilev region, respectively. Based on these values we can estimate a doubling dose of genetic effects due to radiation exposure to be 0.02 - 0.03 Sv. Our estimate of doubling dose is considerably smaller than the value of 1 Sv adopted by ICRP and UNSCEAR. This suggests that genetic effects of radiation exposure is much higher than it has been usually considered, or the physical dosimetry used to obtain dose values of the population significantly underestimated the real doses.

Conclusions

Table 3 Comparison of CM frequencies with additional radiation doses obtained by rural population of Belarus at the age of 18 years and older

Region under observation	Frequency of CM per 1000 births		Average cumulative dose by Chernobyl (mSv)	Cumulative dose per % Increase of CM (mSv/%)
	1982-85	1987-95	1986-94	
Gomel region	4.06±0.39	7.45±0.24 Increase: 83 %	13.40	0.31
Mogilev region	3.50± 0.53	6.41±0.30 Increase: 83 %	8.82	0.20
Vitebsk region	3.60±0.63	5.04±0.27 Increase: 40 %	0.24	-

Long-term studies have shown the evidence of increased frequency of anomalies in embryos of the residents in Belarus. They are manifested as increased malformation frequencies found in medical abortuses and increased frequencies of CM revealed in newborns. The causes for such increases have not been determined clearly. However, the correlation of anomaly increase found in embryos with the level of contamination density of the areas, and the correlation of CM frequency with group average doses, as well as the increase of CMs with great contribution of dominant *de novo* mutations, evidence a radiation factor playing a certain role in the dynamics of CM.

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