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FREQUENCY CHANGES OF INHERITED ANOMALIES IN THE REPUBLIC OF BELARUS AFTER THE CHERNOBYL ACCIDENT

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Abstract — Complex cytogenetic, embryologic and clinical studies of possible genetic consequences of the Chernobyl nuclear accident for the population of Belarus have been carried out. They showed that groups of the population (pregnant women, fetuses, school children) had received biologically significant doses of radiation, as assessed by the registration of ring and dicentric chromosomes in blood lymphocytes. The study of more than 22,000 embryos and fetuses, and of 4090 neonates with compulsory registered congenital malformations, showed a considerable increase of anomalies of intrauterine origin since 1987. They correlated with the level of ^{137}Cs contamination in the areas, but did not correlate with the preconception dose to the mother from the same radionuclide. Teratogenic effects of the Chernobyl pollution have not been conclusively identifed. The increase of embryonal anomalies was mainly due to the group of multifactorial defects, and to the anomalies with a large contribution from dominant mutations. The Down's syndrome incidence showed no increase.

INTRODUCTION

Among numerous negative consequences of the Chernobyl accident, the possibility of genetic effects has been of special concern. The main radionuclides ^{137}Cs and ^{90}Sr released from the reactor can damage the genetic structures of cells (a mutagenic effect) and/or disturb a normal organ formation (a teratogenic effect). At least 120,000 people of reproductive age and children have been exposed to biologically significant doses by the contamination. These are people still living in regions with ^{137}Cs contamination $\geq$555 kBq.m^{-2} (15 Ci.km^{-2}), the so-called liquidators (personnel engaged in the clean-up after the accident), and people living in the areas with less contamination but with a high transfer coefficient of long-lived radionuclides from the soil into the plants. During the first post-accident years the measures to protect the population were less thorough in the areas with a contamination level less than 555 kBq.m^{-2}, and the boundaries of these areas were not clearly defined.

The literature on genetic effects of low-dose radiation on children is inconclusive. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), which continuously studies the problem, applies a doubling dose of 1 Sv per generation. They estimate the rate of abnormal births due to gene and chromosome mutations to be 1700 cases per 1,000,000

Table 1. The incidence of dicentric and ring chromosomes in different groups of the Belarus population.

Region	Year of examination	Persons from contaminated areas		Dicentrics and rings (%)
		Number	Contingent	
Gomel	1986	18	1 group of women*	0.37 ± 0.09
Gomel	1986	18	Neonates	0.38 ± 0.10
Gomel	1987	25	2 groups of women**	0.21 ± 0.05
Mogilev	1988	8	3 groups of women***	0.57 ± 0.16
Mogilev	1988	22	Neonates	0.42 ± 0.07
Brest	1992	15	Schoolchildren	0.36 ± 0.08
		Persons from control areas		
Novopolotzk	1986	16	Women	0.04 ± 0.03
Grodno city	1987	21	Neonates	0.15 ± 0.05
Grodno city	1989	21	Neonates	0.13 ± 0.05
Minsk city	1990–1991	30	Women	0.12 ± 0.04
Minsk city	1990–1991	30	Neonates	0.04 ± 0.02
Minsk city	1993	20	Schoolchildren	0.16 ± 0.06

*Pregnant women evacuated from the most contaminated zones of Gomel region during May, 1986.
**Pregnant women who lived for a year in a zone contaminated with ^{137}Cs at >15 Ci.km^{-2}.
***Pregnant women who lived for 2 or more years in a zone contaminated with ^{137}Cs at >15 Ci.km^{-2}.

live births in the first generation[1-4]. From this estimate, noting that the natural incidence of congenital anomalies is 3.6 to 4.6 per 100 live births, that the doses received by the residents of Belarus are much lower than 1 Sv, and with a birth rate of about 140,000 a year, direct methods of medical registration should be considered unsuitable for determination of whether the additional radiation exposure from the Chernobyl accident would cause any increase in congenital anomalies in the region. Bochkov *et al*[5] state that according to official statistics, the anomaly incidence varies so greatly that it will be nearly impossible to detect a small increase in the incidence due to ionising radiation or any chemical substance. Moreover, the technical report of the Consulting Committee on the Radiological Effects of the Chernobyl Nuclear Accident[6] states that "there are not yet any epidemiological data that would indicate a relation between the exposure to any radiation dose and severe congenital anomalies in humans". Meanwhile, Rose[7] and Strigini *et al*[8], summarising epidemiological studies, reported an increase in Down's syndrome births for parental pre-conception radiation doses less than 0.1 Gy, that is, for doses comparable with those in the areas of Belarus with a contamination level of $\geq$555 kBq.m^{-2}, and especially with the doses received by the liquidators.

Various aspects of teratology, mutagenesis, and human genetics have been studied in Belarus for many years. By the time of the Chernobyl accident the National Congenital Malformation Monitoring System (since 1979), Abnormal Embryo and Early Fetal Morphogenesis Monitoring System (since 1980), and Multiple Congenital Malformation Syndrome Monitoring (since 1983) were in operation. Abnormal developments in spontaneous abortuses were monitored from 1968 to 1987[9].

CYTOGENETIC EFFECTS

Cytogenetic effects were studied in the most important groups of the population, pregnant women, neonates and school children living in the southern areas of Gomel, Mogilev and Brest regions, and in the liquidators. Lymphocytes from peripheral blood were cultured and chromosome aberrations recorded using conventional techniques[1]. From each subject 300 metaphases were usually examined. Summarised data are presented in Table 1, showing that evacuated pregnant women (group 1) and their newborn infants, and the individuals living in the contaminated areas for a long time (groups 2 and 3) received biologically significant radiation doses manifested as an increased amount of dicentric and ring chromosomes. In the women who had lived in the areas of strict radiological control for two years (group 3), more mutagenic effects were found than in women evacuated from the areas. Cytogenetic examination of schoolchildren from Luninets and Stolin districts (Brest region) with a ^{137}Cs contamination of 1–5 Ci.km^{-2} actually showed the same frequency of dicentric and ring chromosomes (0.36 $\pm$ 0.08%) as women from Gomel region evacuated in May 1986, but higher than that registered in pregnant women from Gomel region who had lived in the radionuclide contaminated areas for about a year. Similar results have been obtained by other researchers[10-13].

MALFORMATIONS IN LEGAL MEDICAL ABORTUSES*

Estimation of the teratogenic and mutagenic effects of the Chernobyl accident has benefited from the experience in registration of embryonal anomalies in our Institute. By the time of the accident the Institute had obtained morphological data on over 10,000 legal abortuses in Minsk, at the ovulatory age of 5–12 weeks. During 1986 to 1991, 1176 abortuses from the most contaminated areas of Gomel and Mogilev regions were examined. Most embryos from both groups (Minsk and outside Minsk) were damaged at curettage, and not all organs were always suitable for examination. Therefore, malformation frequency was determined not for the whole number of the embryos examined with a binocular microscope, but only for those where a particular organ could be examined and whose age exceeded the age of physiological persistence of embryonal structures for a particular anomaly.

As has been stated earlier[14], the analysis of more than 21,000 abortuses showed no change in malformation frequency registered in the city of Minsk, nor in the city of Gomel, and its total for 1980 to 1991 was found to be 4.93%. In the contaminated areas of Gomel and Mogilev regions, however, the malformation frequency reached 7.97%, which significantly exceeded the controls from Minsk ($p < 0.05$).

Analysis of the frequency changes of particular nosologic categories of the anomalies showed that all anomalies had increased in frequency in the contaminated areas. The increase was highest for cleft lip and palate, double kidneys and ureters, polydactyly and neural tube defects. These defects are of heterogeneous aetiology. Dominant mutations contribute much to polydactyly causation, whereas raphe defects (both of the face and of the neural tube) are mainly of multifactorial origin, and the contribution from genetic factors has not been determined. No increase was found of monosomies or trisomies in medical abortuses, neither were any direct teratogenic effects found resulting from the death of organ-initiating cells, which is a characteristic radiobiological response of the embryo. All these factors prevent unambiguous estimation of a potential contribution

*The term 'legal medical abortus' means a conception product obtained through pregnancy termination at a medical institution at the woman's request.

by ionising radiation to the increased congenital malformation frequency found in the abortuses from the contaminated areas.

CONGENITAL MALFORMATION FREQUENCY IN NEONATES

Congenital malformation registration is used all over the world to monitor harmful environmental effects on human reproduction, particularly effects on genetic structures and on the developing embryo.

The malformations registered and the registration methods of the Belarus National Genetic Monitoring System are comparable with European (EUROCAT) and International (International Clearinghouse) monitoring systems. The Belarus National Genetic Monitoring System registers congenital malformations unambiguously diagnosed, irrespective of the level of a physician's education, or of the facilities of the medical institution. The list of mandatory registered congenital malformations (MRCM) is presented in Table 2. In total, MRCMs constitute about 44% to 50% of all congenital malformations registered in the maternity hospitals in Belarus. In each case of congenital malformation, the diagnosing physican fills in a special registration form, which is sent by mail or E-mail to the Minsk Genetic Centre. The scientists of the Belarus Institute for Hereditary Diseases verify the record completeness and diagnosis during regular trips to the districts, or during family consultations at the Centre. The complete register is updated every six months.

Table 2 shows the frequencies of MRCMs in three areas during the four years preceding the accident compared to seven post-accident years. The frequency of MRCMs increased in all three areas, with the increase being especially significant in the areas with ≥ 15 Ci.km^{-2} contamination with ^{137}Cs. Elevation of MRCM frequency in control regions could be connected with general ecological disturbances in the Republic.

Apart from the study of congenital malformation frequencies under the National Monitoring Programme, all manifest congenital malformations diagnosed in neonates from the strict control areas (SCA) were subjected to additional analysis. The trends were similar to those for MRCMs: no change in nosological distribution, nor any unusual defects of embryonic development have been found.

Attempts to analyse the monitoring system data and

Table 2. Incidence of obligatory registered malformations in Belarus for 1982 to 1993 (per 1000 neonates).

Malformation	Areas contaminated with ^{137}Cs				Control (30 regions)	
	>15 Ci.km^{-2} (17 regions)		>1 Ci.km^{-2} (54 regions)			
	1982–1985	1987–1993	1982–1985	1987–1993	1982–1985	1987–1993
Anencephaly	0.28	0.35	0.24	0.54*	0.35	0.37
	11	17	48	154	23	39
Spina bifida	0.58	0.76	0.67	0.83*	0.64	0.84
	23	37	132	238	42	87
Cleft lip and/or palate	0.63	0.99	0.70	0.90*	0.50	0.91*
	25	48	137	259	33	95
Polydactyly	0.10	1.01*	0.30	0.60*	0.26	0.47*
	4	49	60	172	17	49
Limb reduction defects	0.15	0.43*	0.18	0.32*	0.20	0.19
	6	21	36	91	13	20
Oesophageal atresia	0.08	0.10	0.12	0.16	0.11	0.12
	3	5	23	46	7	13
Anorectal atresia	0.05	0.08	0.08	0.09	0.03	0.07
	2	4	16	26	2	7
Down's syndrome	0.91	0.82	0.86	1.02	0.63	0.98*
	36	40	170	293	41	102
Multiple malformations	1.04	2.40*	1.41	2.10*	1.18	1.47
	41	117	277	603	77	153
Total	3.87	6.94*	4.57	6.56*	3.90	5.43*
	151	338	899	1882	255	565
Per cent increase after Chernobyl	79		44		39	

*Significant difference (p = 0.95) between the values for 1982–1985 and those for 1987–1993.

unambiguously trace teratogenic effects of the additional Chernobyl ionising radiation exposure on pregnant women have been unsuccessful. Information on 4986 children could be obtained only from the strictly controlled areas and the 30 km exclusion zone around the reactor, born in December 1986, and in January and February 1987, i.e. of children whose critical intrauterine period coincided with the first post-accident months. These children showed 15 various MRCMs only, which is insufficient for statistical analysis. The study of abortuses is not suitable for this purpose, since gamete mutation can not be excluded.

In order to trace a possible relation between a frequency increase of congenital malformations and the increased level of gamete mutations, the particular nosologic types of anomalies, in which the mutation component is known to contribute greatly to the origin, were analysed. The largest increase was seen in polydactyly and multiple congenital malformation groups (Table 2). A smaller increase was recorded in the group of limb reduction defects. The contribution of dominant *de novo* mutations is most significant for these three MRCM groups. However, the incidence of trisomy 21, the most common chromosomal disease due to *de novo* mutation, did not increase in the strict controlled areas. Fluctuations of Down's syndrome frequency were within the pre-Chernobyl limits. The start incidence in the control zone was unusually low, which could be connected with incomplete registration.

Thus, we have no convincing data on mutation origin of the increased frequencies of MRCMs in the strict control areas. However, a statistically significant increase of easily diagnosed polydactyly, both in abortuses and neonates, and a marked increase of multiple congenital malformations, does not exclude the effect of an additional mutagenic factor on parental gametes.

To determine a possible relation between the increased congenital malformation frequency and the additional human radiation exposure, congenital malformation frequencies were also correlated with the average maternal preconception dose. No correlation between the congenital malformation freuency and the preconception dose was found[14].

CONCLUSION

The general conclusion can be drawn that in the post-accident period, the number of malformed newborns increased greatly in Belarus. It exceeded considerably the predicted increase for the anomalies induced by ionising radiation according to common risk estimates. The higher the radionuclide contamination density, the more intensive was the increase. The absence of correlation between anomaly frequency and maternal dose, and the increase of multifactorial anomalies, is evidence of a set of negative factors, not radiation only, contributing to the malformation frequency increase.

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