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**RELEVANCE OF THE CHERNOBYL RESEARCH FOR THE EVALUATION OF
GENETIC RADIATION RISKS IN HUMANS**

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Abstract The committee of the United Nations for the evaluation of radiation effects UNSCEAR up to now derives a very low risk for hereditary diseases from experiments in mice. They claim that there are no human data to refer on, and missing effects in the Japanese A-bomb survivors are erroneously generalized for cases of chronic exposures. Vladimir A. Sevchenko criticized their estimates already soon after the Chernobyl accident. He stated that the main contribution of possible effects as many congenital malformations and all polygenic diseases are left out. He also demanded that the estimates must include the following generations until an equilibrium of heritable defects is reached, while the committee considers only the first generation. Sevchenko referred to the rising rates in the Belarussian central registry for congenital anomalies after 1986 and emphasized the importance of biological dosimetry by cytogenetic analysis in order to receive realistic information about the population exposure. We made a compilation of findings about early deaths, congenital malformations, Down's syndrome, cancer and other effects, which were observed in humans after exposure of parents. Few of them are available from occupationally exposed collectives, much information can be drawn from studies in populations exposed by Chernobyl fallout and from the descendants of liquidators. Nearly all types of hereditary defects were found, which are to be expected according to our general knowledge about. It can clearly be shown that the official risk estimates are much too low.

1 Introduction

The most serious effects of ionizing radiation – hereditary defects in the descendants of exposed parents – had been already detected in the 1920s by Herman Joseph Muller. He exposed flies – drosophila – to x-rays and found malformations and other disorders in the following generations. He concluded from his investigations that low dose exposure, and therefore even natural background radiation, is mutagenic. Already in the thirties, the idea arose that cancer is initiated by a single cell transformation, a “somatic” mutation. Likewise, Muller concluded that there is no harmless dose range for cancer induction either. His work was honoured by the Nobel Prize for medicine in 1946.

Muller – as a famous expert for radiation – was designated for a speaker at the Atomic Conference in Geneva in 1955 where the large-scale, so-called peaceful, use of nuclear energy was announced by U.S. President Eisenhower. But then they became aware that he had warned against the deterioration of the human genetic pool by the production of huge amounts of artificial radioactivity, and the invitation was cancelled (his manuscript is still available).

Nevertheless, previously, genetic effects in descendants were thought to be the most significant injuries caused by radiation. From this results the protection of the gonads, if possible, during X-raying for diagnostic purposes.

The International Committee on Radiological Protection ICRP, however, substantially decreased their risk estimate in 2007 (Table 1).

Table 1 ICRP Recommendations 2007

Detriment adjusted nominal risk coefficients for radiation effects in an exposed population

	Present	ICRP 1990
Heritable Effects	0.2 % per Sv	1.3 % per Sv
Cancer deaths	5.5 % per Sv	6.0 % per Sv

The value of 0.2 % per Sv means that, if a population is exposed to a gonadal dose of 1 Sv, 0.2 % of the persons will have a genetic disorder caused by radiation.

The ICRP claims that there is no direct evidence that children of exposed parents will suffer from heritable diseases. They refer to their human reference group, the Japanese survivors of the atomic bomb explosions in Hiroshima and Nagasaki in 1945. The American-Japanese Institute in Hiroshima did not find mutations in the descendants of the survivors. Because of the evidence of such effects in animal studies, they derive their current risk figure from experiments in mice. They consider only dominant mutations in the first generation. Their result corresponds to a doubling dose of about 2 Sv which is similar to the evaluation by the UNSCEAR committee (2001).

There exist a variety of arguments against the Japanese survivors as a suitable reference for common populations, the most relevant in the case of hereditary effects may be the high dose rate by the bomb explosion in comparison to situations of chronic exposure where all stages of sperm development are continuously affected.

Effects in populations exposed by Chernobyl fallout are excluded by the official committees, because they claim that the doses are much too low in order to generate statistically observable increase. This, however, is certainly wrong, because we know from many studies of chromosome aberrations, that the exposures calculated by UNSCEAR are much too low.

Hereditary disorders are classified in 4 groups (see box):

- 1) **Mendelian disorders** due to defective single genes which follow Mendel's laws of inheritance
- 2) **Chromosomal disorders** as e.g. Down's syndrome
- 3) **Polygenic disorders** to be detected in clusters in families
- 4) **Non-chromosomal inheritance** which has nothing to do with genes

The diseases printed in italics in the box were found after low level radiation exposures.

Hereditary disorders (from Uma Devi et al. 2000)

1) Mendelian

Autosomal dominant; examples:

Huntington's chorea, polycystic kidney, multiple polyposis, cerebellar ataxia, myotonic dystrophy

Congenital abnormalities as *syndactyly, brachydactyly, polydactyly*, taste for the chemical PTC (taste is dominant to non-taste), acondroplasia, bilateral aniridia, osteogenesis imperfecta

Autosomal recessive; examples:

Cystic fibrosis, phenylketonuria, lactose intolerance, adrenal hyperplasia

Sex-linked; examples:

X-linked dominant/Duchenne muscular dystrophy, haemophilia A, some forms of colour blindness, fragile-X associated mental retardation, X-linked retinitis pigmentosa

X-linked recessive/birth *deficit of females*

2) Chromosomal

Aneuploidy (numerical chromosomal anomaly); examples:

Down syndrome (trisomy 21), Turner syndrome (X0), Klinefelter syndrome (XXY)

Structural anomalies; examples:

Cri du chat syndrome (deletion in chromosome 5), *preimplantation loss, embryonal death, foetal abortions*

3) Polygenic

Cluster in families; examples:

Congenital abnormalities as *neural tube defects, heart defects, pyloric stenosis, cleft lip with or without cleft palate, undescended testes*

Common disorders of adult life of varying severity. Among the serious conditions are *schizophrenia, multiple sclerosis, epilepsy, acute myocardial infarction*, systemic lupus erythematosus. Moderately serious conditions include *psychoses*, Graves' disease, *diabetes mellitus*, gout, glaucoma, *essential hypertension, asthma*, peptic ulcer, rheumatoid arthritis. The least severe diseases include varicose veins of the lower extremities and allergic rhinitis.

Cancer

4) Non-chromosomal inheritance

Cytoplasmic inheritance, mosaicism, imprinting etc.

2 Findings in children born after the Chernobyl accident and in Kazakhstan

We have formerly made a compilation of findings about foetal deaths, perinatal mortality, and congenital malformations after Chernobyl (Busby et al. 2009). Table 2 shows the results about congenital malformations. They appeared not only in the area of the exploded reactor but also in Turkey, Bulgaria, Croatia, and Germany.

These findings were mainly interpreted as effects induced in utero. Because men and women were both exposed continuously to radioactive fallout, the genetic effects are not always clearly distinguishable from such, which can be generated by exposure of embryos and foetuses in utero.

Table 2 Increase of congenital malformations after exposure by the Chernobyl accident

Country	Effects	Reference
Belarus	Anencephaly, spina bifida, cleft lip and/or palate, polydactyly, limb reduction defects, esophageal atresia, anorectal atresia, multiple malformations	Lazjuk et al. 1997
National Genetic Monitoring Registry		Feshchenko et al. 2002
Highly exposed region of Gomel	Congenital malformations	Bogdanovich 1999; Savchenko 1995; Petrova et al. 1997
Chechersky district, Gomel region	Congenital malformations	Kulakov et al. 1993
Mogilev region	Congenital malformations	Petrova et al. 1997
Brest region	Congenital malformations	Shidlovskii 1992
Ukraine		
Polesky district (Kiev region)	Congenital malformations	Kulakov et al. 1993
Lugyny region	Congenital malformations	Godlevsky, Nasvit 1998
Turkey	Anencephaly, spina bifida	Akar et al. 1988/89; Caglayan et al. 90; Güvenc et al. 93; Mocan 90
Bulgaria , region of Pleven	Malformations of heart and central nervous system, multiple malformations	Moumdjiev et al. 1992
Croatia	Malformations by autopsy of stillborns and cases of early death	Kruslin et al. 1998
Germany		
FRG, Central registry malformations	Cleft lip and/or palate	Ziegłowski, Hemprich 1999
Bavaria	Cleft lip and/or palate	Scherb, Weigelt 2004
	Congenital malformations	Korblein 2004
Ann. Health Rep. W. Berlin 1987	Malformations in stillborns	Government of West Berlin
City of Jena (Registry)	Isolated malformations	Lotz et al. 1996

The authors in Belarus, however, came to another interpretation. A central registry for congenital anomalies had been established there by the Ministry of Health in 1979 for continuous follow-up. The rates of anomalies before and after the Chernobyl accident could be compared. Results in the 17 most contaminated regions are shown in Table 3.

Table 3 Percentage increase in congenital malformations in 17 most contaminated regions of Belarus in the period 1987-1994 in percent (from Lazjuk et al. 1997)

Kind of malformation	Increase
Anencephaly	39 %
Spina bifida	29 %
Cleft lip/palate	60 %
Polydaktyly	910 %*
Limb reduction	240 %*
Esophageal atresia	13 %
Rectal atresia	80 %*
Multiple malformations	128 %*

* significant (p<0,05)

Unfortunately, the data are not continuously published, at least until 2004 there was no decrease (Yablokov et al. 2009). The authors think these effects are genetically induced because it is not plausible that doses in pregnant women rose in the period of decreasing environmental contamination and decreasing food contamination after the accident. The genetic origin is confirmed in those anomalies which are combined with a recognized mutation that is not present in either of the parents (Lazjuk et al. 1999).

The national registry of Belarus was also evaluated in 1995 by a Belarussian-Israeli group of scientists (Lomat et al. 2007). They found the following high rates of diseases – supposedly originated by polygenetic effects - in children of Chernobyl-exposed parents:

- Hematological diseases (6-fold)
- Endocrine diseases (2-fold)
- Diseases of digestive organs (1.7-fold).

Wertelecki et al. (2010; 2014) found increased rates of congenital malformations in the years 2000-2009 – more than 14 years after the accident – in the Ukrainian province (oblast) Rivne, about 200 km west of Chernobyl. Predominantly in the highly contaminated northern part Polissia, there are significant increases in comparison to the southern part, see box:

Congenital malformations in Rivne Oblast, Ukraine

Study of 145,437 live births between 2000-2009

1.6 % congenital anomalies

Neural tube defects

Rivne Non-Polissia 1,6 per 1000 live births (Europe mean 0,94)

Polissia district 2,6 “ “ “ “

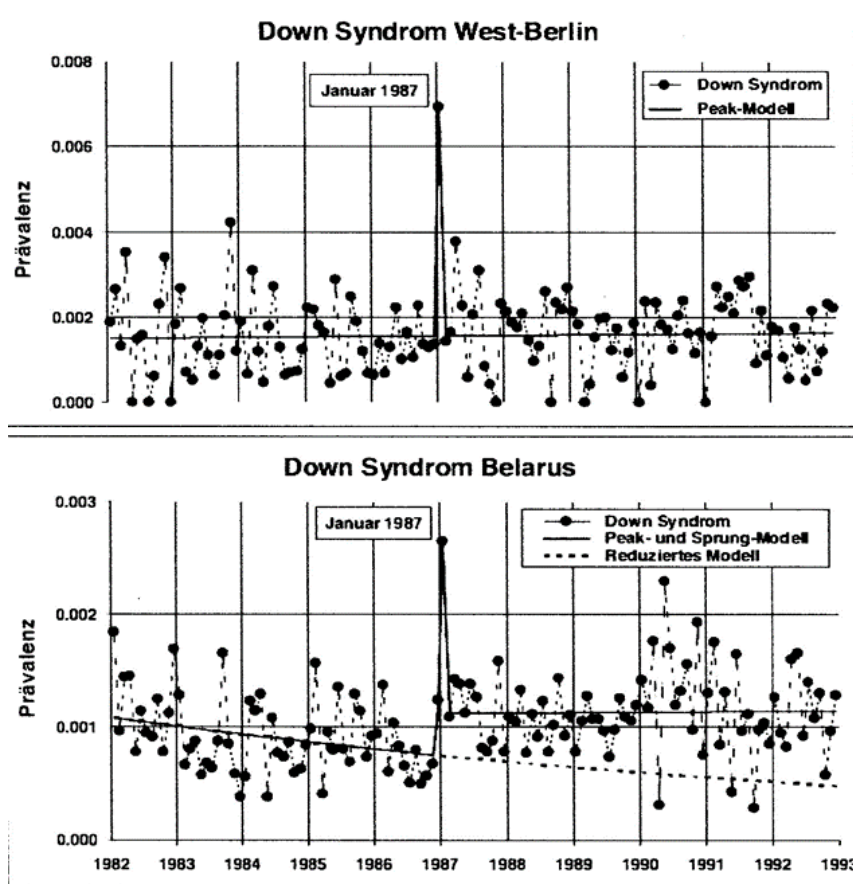
Microcephaly, Mikrophthalmos increased

The authors interpret the effect as induced in utero.

A region where the population has also been exposed to large amounts of radioactivity is near the former Soviet nuclear test site near the town Semipalatinsk (now in Kazakhstan). The tests above ground occurred between 1949-1963. Sviatova and coworkers (2001) studied congenital malformations in three generations of inhabitants, investigating births between 1969-1997. They found significantly increased rates of malformations as a whole, including Down’s syndrome, microcephaly and also multiple malformations in the same individual.

Down’s syndrome as a certain genetic effect increased in several contaminated European countries (Busby et al. 2009; Sperling et al. 2012). Examples are shown in Figure 1. In Berlin West, which was a kind of closed island at that time, the geneticist Sperling registered a sharp and significant increase in cases exactly 9 months after the accident. A very similar situation was observed in Belarus (Zatsepin et al. 2004).

Figure 1 Down's syndrome before and after the Chernobyl accident
(from Scherb and Sperling 2011)



3 Hereditary effects in children of exposed mothers

If a population is exposed, genetic effects will occur in the gonads of fathers as well as of mothers. In Germany, an investigation was done in women who were occupationally exposed to radiation which showed a 3.2-fold significant increase in congenital abnormalities, including malformations, in their offspring (Wiesel et al. 2011). The authors interpret this effect as generated in utero but do not prove such a connection because it appears improbable given the short sensitive phase in pregnancy and the ban on pregnant women working in high risk environments.

Although the study was funded by the Federal Ministry of Environment, Protection of Nature and Nuclear Safety, these alarming results have not resulted in any action. The findings confirm early results in the Department of Medical Genetics of the Montreal Children's Hospital where the genetic effects of diagnostic X-rays were investigated (Cox 1964). The author observed the offspring of mothers who had been treated in childhood for congenital hip dysplasia since 1925 and were X-rayed for several times in the pelvis region. The ovarian dose was estimated to lie between 60–200 mSv. In 201 living births of these women 15 individuals showed severe malformations and other congenital distortions or Down's syndrome, who required hospitalization, and 11 cases occurred with other abnormalities (all congenital abnormalities 12.9 per cent), while the control group showed less than half of this rate. The latter was chosen from a large group of descendants whose parents were unexposed siblings of the study group.

4 Findings in the descendants of occupationally exposed men

Congenital anomalies: Studies in children of exposed men where the mothers were not exposed will show definite hereditary effects. There were only very few of them in occupationally exposed cohorts before 1986, when the accident of Chernobyl occurred. Exposures below the official dose limits were thought to be too low to produce statistically recognizable effects. A compilation of results for congenital malformations is given in Table 4.

Table 4 Congenital anomalies, especially malformations, in descendants (1st generation) of occupationally exposed men

No.	Cohort of fathers	Kind of defect	Dose	References
1	Radiologists U.S.A. 1951	Congenital malformations Increase 20 %		Macht, Lawrence 1955
2	Workers of the Hanford Nuclear facility, U.S.A.	Neural tube defects significantly increased by 100 %	In general < 100 mSv	Sever et al. 1988
3	Radiation workers at Sellafield nuclear reprocessing plant, U.K.	Stillbirths with neural-tube defects significantly increased by 69 % per 100 mSv	Mean 30 mSv	Parker et al. 1999
4	Radiographers in Jordan	Congenital anomalies significantly increased 10-fold		Shakhatreh 2001
5	Liquidators from Obninsk (Russia), 300 children	Congenital anomalies increased 1994-2002	Mainly 10-250 mSv	Tsyb et al. 2004
6	Liquidators from Russia, Bryansk region	Congenital anomalies increased about 4-fold		Matveenko et al. 2005
7	Liquidators from Russia 2379 newborns	Significant increase for: Anencephaly 310 % Spina bifida 316 % Cleft lip/palate 170 % Limb reduction 155% Multiple malformations 19 % All malformations 120 %	5-250 mSv	Lyaginskaja et al. 2009

The findings in Hanford and Sellafield (Nos. 2 and 3 in Table 4) lead to heavy discussions in the scientific community. The registered doses of the workers were very low. The alarming findings did not lead to further studies about hereditary sequels in the American or European populations concerned.

The anomalies seen in the descendants of liquidators also indicate unexpectedly high radiation sensitivity. These studies are most important and should be continued.

Cancer: In 1984, an exceptionally high level of leukaemia cases in children and juveniles was reported in Seascale, a village near the British Nuclear Fuels reprocessing plant in Sellafield in Cumbria, UK. These were then explained by Martin Gardner and co-workers (1990) as a hereditary effect, because the fathers of the patients had worked in the plant. This result has

been discussed in the literature for years and was confirmed or denied in several subsequent studies. The effect, however, had been described in principle already in experimental studies (Nomura 1982; 2006), and has also been found after X-ray diagnostic exposures (Table 5).

Table 5 Cancer in children after preconceptional low-dose exposure of parents

Exposed collective	Malign disease	Gonadal dose/mSv	Relative Risk	Doubling dose/mSv
Sellafield				
Seascale fathers (Gardner et al. 1990)	Leukaemia + lymphoma	200	7	33
all stages of spermatogenesis		10	7	1.7
6 months before conception				
Sellafield workers (Dickinson et al. 2002)	“		1.9	
Further occupational exposure of fathers				
Military jobs (Hicks et al. 1984)	Cancer		2.7	
Regions of U.K. (McKinney et al. 1991)	Leukaemia + lymphoma		3.2	
Preconceptional X-ray diagnostics in				
Fathers (Graham et al. 1966)	Leukaemia		1.3	
Fathers (Shu et al. 1988)			1.4-3.9	
Fathers (Shu et al. 1994)			3.8	
Mothers (Stewart et al. 1958)			1.7	
Mothers (Graham et al. 1966)			1.7	
Mothers (Natarajan, Bross 1973)			1.4	
Mothers (Shiono et al. 1980)			2.6	

McKinney and co-workers found a 3.2-fold increase in leukaemia and lymphomas in children of occupationally exposed men in three British regions in a case-control study (1991). The research of Hicks and co-workers (1984) concerned exposed service men in the air force.

Statistical investigations in Belarus and the other highly contaminated neighbouring states of Chernobyl show increased cancer deaths in children who were born many years after the accident (Yablokov et al. 2006; 2007). Higher rates of leukaemia and other cancers were also observed in children of liquidators (Tsyb et al. 2004).

5 Sex ratio and X-linked lethal factors

Normally, it is not possible to study how many inseminated oocytes (zygotes) will be aborted after irradiation of the gonadal cells, in humans. There is however, one way to prove such an effect. It is observed that men who were exposed before fathering will have fewer daughters than sons as normally, i.e., the male/female sex ratio increases with dose.

Gene mutations may be responsible for the death of the zygote and will also occur in the sex chromosomes where they will predominantly affect the greater X-chromosome. The X-chromosome of the male can only be transmitted to a daughter. A dominant lethal factor will then lead to the death of the female zygote. Recessive lethal factors in the X-chromosome are much more frequent than dominant ones (Vogel et al. 1969). They also affect only female births.

Studies in large exposed populations can show this effect. A very impressive result was obtained in workers of the British nuclear fuel reprocessing plant at Sellafield in West Cumbria (Table 6).

Table 6 Sex ratio for births in Cumbria

(Dickinson et al. 1996)

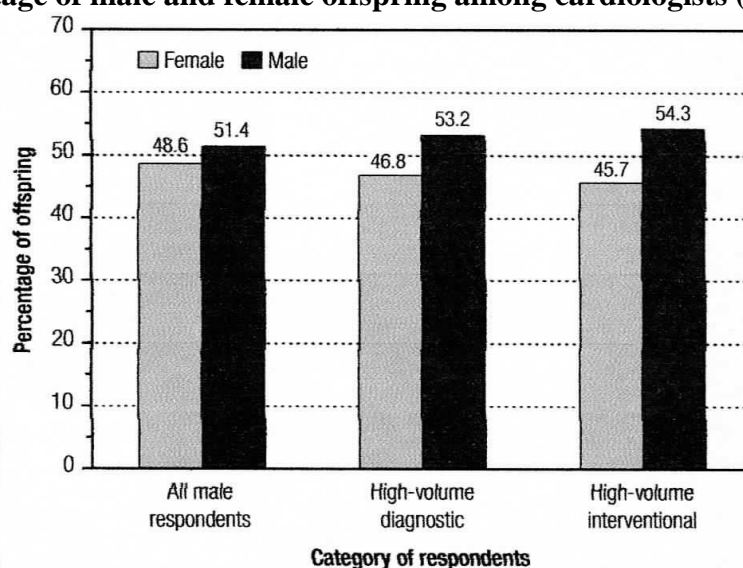
All Cumbrian children	All fathers employed* at Sellafield	Fathers employed at Sellafield > 10 mSv**)
1.055	1.094	1.396

*) employed before conception

**) dose 90 days preconceptional

A similar effect is detected in an investigation of cardiologists, who undertook interventional angiographic procedures in patients, which involve relatively high x-ray exposures at the workplace (Fig.2). The portion of female descendants declines significantly with higher exposures of the father¹.

Fig 2. Percentage of male and female offspring among cardiologists (Choi et al. 2007)



German scientists Hagen Scherb, Kristina Voigt (Helmholtz Center Munich) and co-workers have shown that exposure of both parents in a population may also lead to a decline in female births. They studied different groups of inhabitants in a variety of countries after the Chernobyl accident for hereditary effects and found radiation-induced foetal deaths and early mortality, Down's syndrome and alterations of the sex ratio in newborn children.

The sex ratio was investigated by them as a consequence of:

- Nuclear tests above ground which affected U.S. inhabitants
- Chernobyl emissions in Europe
- Living near German and Swiss nuclear plants

They found significant decreases in the female birth rate in all these conditions (Scherb, Voigt 2007; 2011; Scherb et al. 2012).

Sex ratio is a very relevant parameter. It shows that genetic alterations are induced in the germ cells of men by very low doses, and it proves to be a sensitive indicator for exposures of the population.

¹ The authors wanted to study the reverse, however, if the male births will decline with dose.

6 Summary and discussion

Genetically induced malformations, cancers, and numerous other health effects in the children of populations who were exposed to low doses of ionizing radiation have been proved in scientific investigations.

The question arises as to why the ICRP and UNSCEAR are denying the findings. Their reference population, the A-bomb survivors of Hiroshima and Nagasaki, is not suitable for persons being chronically exposed.

The committees claim that the exposures of the population due to the Chernobyl accident were extremely low. The UNSCEAR committee has done calculations about (1988). Even in the most contaminated regions of the area with more than 37 kBq/m² Cs-137 surface activity the mean dose in people is assumed to be not higher than 10 mSv (effective life time dose). In Turkey and the more distant countries of central Europe the mean dose is estimated at below 1.2 mSv.

Their simple conclusion is then, that such low doses are not able to produce statistically recognizable radiation effects. Many studies, however, of chromosome aberrations in the populations, equivalent to “biological dosimetry” (Schmitz-Feuerhake 2009), show that the exposures are about 100-fold higher.

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