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Abstract

In former times of radiation-research the "genetically significant dose" was regarded as the main measure for protection in diagnostic radiology, because the hereditary effects were considered to be the most dangerous sequelae and also the effects in embryos and fetuses. There was also established the "10 days rule" in order to exclude exposure in the period of possible pregnancy. The International Commission on Radiological Protection (ICRP), however, who is the leading expert board for radiation protection in the developed countries, claims that the genetic radiation risk is nearly negligible, and radiation-induced effects after exposure in utero will not occur below doses of 100 mSv. They refer to reportedly absent effects in the acutely exposed Japanese A-bomb survivors and leave out the conditions in cases of low dose chronical exposure as for example by radioactive contaminations. Congenital malformations were found in a variety of European regions affected by Chernobyl fallout, besides stillbirths and Down's syndrome, showing high radiation risks for the descendants of exposed parents. This is confirmed by two recent studies in Germany in the offspring of exposed military personnel and of female employees in radiation medicine.

Our conclusion is that medical diagnostic radiation exposure in Germany has contributed to the rising rates of congenital malformations in this country. Minimization of gonadal doses must become again a central aim in radiation diagnostics for children and patients in reproductive ages. Current dose limits for occupational exposure and in pregnancy must be lowered considerably.

Keywords: Low Level Effects; Teratogenic Radiation Effects; Radiation Genetics; Chernobyl Effects; Radiation Risk; Radiation-Protection

Abbreviations

Bq: Becquerel Unit of Radioactivity, 1 Bq = 1 decay per second; 1 kBq = 1000 Bq; CT: Computer Tomography, generation of images by multiple X-raying; EUROCAT: European Registration of congenital Anomalies and Twins; ICRP: International Commission on Radiological Protection; Sv: Sievert unit of equivalent and effective dose, 1 Sv = 1000 mSv; UNSCEAR: United Nations Scientific Committee on the Effects of Atomic Radiation

Introduction

In Germany, pediatric physicians are concerned about rising rates of severe malformations in newborn children. Usually discussed risk factors are alcohol, deficiency of folic acid and so-called "life-style". This article wants to draw the attention on a risk factor which is certainly neglected and denied. In former times of radiation research, many scientists were convinced that ionizing radiations will effectively induce birth defects after exposure in utero or in the descendants of exposed parents because they can kill or mutate living cells.

Herman Joseph Muller detected in the 1920s that X-rays are mutagenic. At that time the DNA was not deciphered already, but it was known that chromosomes bear the genetic information and chromosomes could be altered by X-rays and radium. Muller found out that

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X-rays generate morphological and other changes in the descendants of exposed animals. His main study object was the fly Drosophila. He derived from his studies that even low doses will induce mutations as for example from background radiation.

Therefore, for some decades, the "genetically significant dose" was the measure for exposure by diagnostic X-ray applications, that means the dose to the gonads. This is not any more valid now. The dose - if known by the physician - is given by a number in Millisievert (mSv) that will be the so-called "effective dose". This parameter is mainly related to the risk of death by cancer and gives no information about the gonadal dose or any other organ dose.

Many studies were done in rodents in the 1960s and 1970s in which was confirmed that especially malformations of organs and extremities are induced in the descendants after exposure of the gonads or in prenatal development as embryo or fetus [1].

The International Commission on Radiological Protection (ICRP), however, claims that the genetic radiation risk is nearly negligible and radiation-induced effects after exposure in utero will not occur below doses of 100 mSv [2]. An exposure of 100 mSv corresponds to the dose limit for occupationally exposed persons in 5 years. The ICRP is the leading committee to develop standards for radiation protection applied by the majority of all industrial countries of the world. Their evaluation of radiation risks occurs in close cooperation with the United Nation Scientific Committee on the Effects of Atomic Radiation (UNSCEAR).

They refer to reportedly absent effects in the exposed Japanese A-bomb survivors who represent their preferred reference collective. This is assumed having been exposed by a single short irradiation after the explosion of the bomb.

Methodology and Results

Congenital malformations after chernobyl

The Chernobyl reactor accident in September 1986 in Ukraine contaminated large parts of Europe and Turkey. Chromosome aberrations in people as a measure of radiation exposure were found also in great distances until Norway [3]. We have formerly published a compilation of birth defects after Chernobyl [4] which were mainly interpreted as effects induced in utero, and a review about studies about hereditary congenital anomalies in men [5]. Because men and women were both exposed continuously to radioactive fallout in the case of Chernobyl, the effects are not always clearly distinguishable from such induced by exposure to the germ cells.

One distinguishing factor, however, is time. Increases of malformations which last over decades in the affected regions will not be generated in utero because of decreasing exposures. Table 1 shows observations which were done in Belarus. 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. Table 1 shows results [6] (Only severe effects are considered here).

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

Table 1: Percentage increase in congenital malformations in 17 most contaminated regions of Belarus in the period 1987 - 1994 [6].* significant (p < 0,05).

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Unfortunately, the data are not continuously published, at least until 2004 there was no decrease [7]. The authors regard these effects as 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.

Wertelecki., *et al.* found increased rates of congenital malformations in the Ukrainian province (oblast) Rivne, about 200 km west of Chernobyl which are interpreted by them as induced in utero [8,9]. They studied 145, 437 live births between 2000 - 2009 in a period 14 - 23 years after the accident. Results are given in table 2 for the highly contaminated northern part Polissia in comparison to the southern part (Rivne without Polissia) (Table 2).

Kind of malformation	Polissia	Non-Polissia	Polissia/Non-Polissia	Europe mean
All CA	41.0	29.0	1.42	
Neural tube defects	26.1	16.4	1.59	
Microcephaly	6.1	3.1	1.85	0.94
Microphthalmus	2.5	0.8	3.03	

Table 2: Rates of congenital malformations (CA) in Rivne Oblast, Ukraine, 2000-2009, OR in numbers per 1000 births.

All CA in Rivne are among the highest in Europe using the data of the European registry EUROCAT [10]. Neural tube defects are about 2 - 3-fold higher than the mean value registered for Europe. The rate in Polissia is higher for 59% than in the other part of Rivne. Micro-cephaly and microphthalmos are also significantly increased.

High rates of malformations were also found in the descendants of liquidators, e.g. men who were deployed for decontamination tasks after the accident in 1986 [11-13].

Recent observations in Germany

There were only few studies about hereditary and other teratogenic effects after low dose exposures before the Chernobyl event and in occupationally exposed persons. We reported on findings after medical diagnostics [14], medical and nuclear employees showing increased malformations in the descendants [15-18] and also in people affected by atomic bomb testing [19].

In Germany, there is no central registry for birth defects. There had been one in the former GDR (German Democratic Republic, East Germany) which was only locally continued after the reunification in the federal State Saxony-Anhalt. In 1990, a pilot project was started at the university of Mainz observing a local region of about 370, 000 inhabitants. An investigation was done by them in women who were exposed in medical professions. First results were published in 2011 which showed already a considerable effect in the offspring. The following investigation included 27 births of exposed women which resulted in 8 children with severe malformations corresponding to an increase by a factor of 4.8 compared to the control [20].

Although the study was funded by the Federal Ministry of Environment, Protection of Nature and Nuclear Safety, these alarming data did not result in any official reaction or funding enhanced scientific work on the problem. Quite the reverse, at present there are efforts by NGOs to continue the registration because the pilot project was finished in 2019.

In 2018, scientists from Berlin and Bonn proved by whole genome sequencing in parents and children, that malformations in descendants from exposed soldiers were of hereditary origin [21]. These men worked in military radar stations during the Cold War and were irradiated by X-rays which are caused as bremsstrahlung emitted by the high frequency generators, and also by Radium contained in luminous paintings. The authors investigated the genome of 18 descendants of radar soldiers. 10 families had been chosen in which at least one child suffered from a genetically caused anomaly, additionally one case with the father after radiation therapy because of a Non-Hodgkin lymphoma. An exceptional rate of clustered multisite *de novo* (MSDN) mutations was observed originated via the germline of the father. 12 MSDN were found in 18 descendants of the soldiers. While in families without known exposure every fifth child bore a MSDN (20%), the radar families showed two of three cases (67%).

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The suspicion about a radiation effect arose when radar soldiers met to demand for compensation of their health problems and noticed an unusual number of congenital anomalies in their offspring. While the mentioned study was financed by private sponsors, the Ministry of Defence has now approved to finance further research.

Discussion and Conclusion

Genetically induced malformations in the offspring of populations who were exposed to low doses of ionizing radiation have been proved in scientific investigations. The ICRP ignores these findings referring to the A-bomb survivors of Hiroshima and Nagasaki. It is important, however, to consider, that the germ cells are differently sensitive in their stages of development until conception.

The stem cells in men and women are well protected against radiation, so far mutation is considered. The spermiogonia divide and generate many daughter cells with a complete number of chromosomes. These divide to haploid cells and undergo transformation into the mature sperm. It is known that dividing cells are of higher sensitivity against radiation, and it was shown by cytogenetic and experimental investigations, that the haploid stages except the mature stage receive a higher mutation rate than the others. The development of sperm until conception lasts about 87 days, the most sensitive period only 35 days [1].

The egg cells don't carry out mitotic divisions and are in a haploid stage only near the time of conception (first mature division). A continuous exposure may therefore produce higher mutation rates because the sensitive stages are hit continuously.

Therefore, a single high dose-rate exposure of a population and in a catastrophe cannot represent the situation of a continuous exposure as by occupational or environmental contaminations. As expected in former times, stem cell mutations will also occur and there are examples for malformation induction in children of those parents who underwent radiation therapy.

The question arises as to why the ICRP and UNSCEAR are denying the findings after Chernobyl. The committees claim that the exposures of the population due to the Chernobyl accident were extremely low. UNSCEAR has done calculations about [22]. 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 only 9 mSv (effective life time dose for the period 1986 - 2005 except thyroid dose). For the countries near the plant Ukraine, Belarus and Russia this value is estimated to 1.3 mSv, for Western Europe 0.3 mSv.

Their simple conclusion is then that such low doses are not able to produce statistically recognizable radiation effects. Many studies, however, e.g. about chromosome aberrations in the populations, equivalent to "biological dosimetry" [4,23], show that the exposures are about (10-100)-fold higher.

The German local registry for birth defects in Mainz found the far most congenital malformations per 1000 births in Europe registered by EUROCAT in the period 1980 - 2012 [10]. The latter surveys only part of the European population, and data of the Ukraine, Belarus and Russia are not given. The authors of Mainz comment their findings with concern. They state that every 15th birth (6.5%) in that region suffers from a "major" malformation which means that the child needs medical treatment (examples: spina bifida, rectal atresia, cleft lip/ palate, heart defect, brain deformation, limb reduction) [24].

We assume that a great number of the birth defects in Germany results from the extensive use of X-rays by CT-applications in this country. One single CT of the abdomen in adults demands a gonadal exposure of about 20 mSv. Such high organ doses are rare in Germany for exposed workers even after many years of occupation. After official report about 3.5 million CT were done of pelvis, abdomen, and spine in 2014 and a further increasing trend is observed [25]. Our opinion is confirmed by a German study about cancer in children after CTdiagnostics. In these a radiation-induced increase of cancer of 49% was shown - already in childhood [26].

The evidence of congenital malformations by low dose exposures must be noticed by the public and considered by the officials. Diagnostic applications of X-rays and radioactivity should be avoided as far as possible in children and adults of reproductive ages and also in embryos and fetuses. The dose limits for occupationally exposed persons should be lowered significantly.

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Conflict of Interest

There exists no financial interest or any conflict of interests in connection with this report.

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