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SHORT COMMUNICATION

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Letter to the Editor: The male to female ratio at birth: environmental versus social factors

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ABSTRACT

A series of recent publications discussed an increase in the male-to-female (M/F) ratio at birth supposedly under the impact of radiation from nuclear tests and accidents. However, social factors have not been sufficiently analyzed. Additional doses due to the radioactive contamination have usually been negligible compared to the natural background radiation. Bias is not excluded in epidemiological studies of low-dose radiation: surveillance and recall bias, dose-dependent selection, and self-selection. Among others, ideological bias is aimed at a strangulation of nuclear energy production. One of the main causes of the elevation of M/F ratio at birth in certain regions is the son preference and sex-selective abortions after a prenatal ultrasonic gender testing. Migrations contribute to a global M/F shift. A relatively high M/F ratio prior to the introduction of the ultrasonic testing is an indication to other perinatal sex selection methods, e.g., female neonaticide and abandonment of newborn girls. Besides, reduced M/F ratio has been associated with an older age at childbearing. In conclusion, the hypothesis that anthropogenic elevation of the radiation background contributed to the skewing of M/F ratio toward males is unproven. Dose–response relationships at low radiation doses should be studied in large-scale animal experiments applying dose rates comparable to those in humans.

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Introduction

This letter comments on a recent publication series. An increase in the male-to-female (M/F) ratio at birth supposedly under the impact of radiation from nuclear testing (worldwide) and Chernobyl fallout (in Europe) has been investigated by Victor Grech and Hagen Scherb with co-workers [1–20]. A conclusion was that "birth rates are greatly reduced and the M/T (male live births divided by total live births) ratio is skewed upward significantly with population exposure to ionizing radiation, even at great distances from major nuclear events" [1]. The significance of supposedly radiation-related shifts of sex ratios [2,15] has been questioned [21–23]. A review concluded that "there is little consistent evidence that ionizing radiation affects the sex ratio" [24]. In particular, the natural background radiation and social factors that could have influenced M/F and M/T ratios have been left out of consideration.

Natural background radiation

The annual individual doses from the natural background radiation (NBR) are generally expected to be in the range of 1–10 mSv (millisievert), with 2.4 mSv being the estimated global average [25]. Some national averages are over 10 mSv [26]. In Europe, mean annual individual doses from NBR are around 5–7 mSv in several countries [27,28]. There are populated areas where the dose rate from NBR is 10–100 times higher than the average, e.g., 260 mGy/a (milligray/year) in Ramsar, Iran, or 70 mGy/a at certain locations in Kerala, India; yet, there are no reliable data on shifts of sex ratios at birth in such areas [29,30]. A study based on over 150,000 consecutive live singleton newborns in Kerala did not indicate any impact of the elevated NBR on the sex ratio [31]. For comparison, the maximum annual dose from the global fallout due to

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the nuclear testing was estimated to be 0.14 mSv in 1963, having decreased by almost an order of magnitude by 1979 [25]. Annual individual doses in the vicinity of reactors have been in the range 0.001–0.5 mSv [25], so that the above dose comparisons pertain also to the reported shift of sex ratios at birth among people residing near nuclear facilities [13,14,16,19]. In this connection, a role of bias and confounding factors cannot be excluded [32], discussed below.

In regard to the Chernobyl accident, "as far as whole body doses are concerned, the six million residents of the areas of the former Soviet Union (SU) deemed contaminated received average effective doses for the period 1986–2005 of about 9 mSv, whereas for the 98 million people considered in the three republics, the average effective dose was 1.3 mSv, a third of which was received in 1986. This represents an insignificant increase over the dose due to NBR over the same period (around 50 mSv)" [33]. Outside the former SU, individual doses in addition to NBR were lower: the first year doses after the Chernobyl accident reached 1 mSv only at several places in Europe; all country averages were below 1 mSv/a [28,34]. For comparison, a single computed tomographic (CT) examination produces a dose 2–20 mSv, while the doses from interventional diagnostic procedures usually range from 5 to 70 mSv [35]. Health risks have never been proven for the above-mentioned dose levels [36,37].

Epidemiological studies

A study performed in the 1950s revealed changes in the M/F ratio of children born to survivors of the atomic bombing of Hiroshima and Nagasaki [38]. Later on, additional complexities in the problem were recognized and the effect of exposure on the M/F ratio was not confirmed [39]. Male radiologists tended to father a lower proportion of boys compared to the control group [40]. The results of human studies of paternal pre-conceptional exposures are summarized by a table in [41], whereas both increased and decreased M/F ratios in the offspring were reported, most of the differences being statistically insignificant. The most significant result ($p < 0.001$) was a *decrease* of the M/F ratio in the offspring of fathers exposed to a pelvic irradiation (1,394 exposed *vs.* 1,926 controls) with estimated testicular doses 20–200 mSv [41,42]. Reduced sex ratio (deficit of boys) was found also in the offspring of irradiated women with an ovarian dose about 200 mGy [43].

Bias is not excluded in epidemiological studies of low-dose radiation effects: surveillance basis, dose-dependent selection and self-selection, higher participation of cases (e.g., cancer patients) compared to the controls. Other bias and confounders have been discussed [30,36,37,44]. Better recollection by cases of the facts related to radiation exposures (recall bias) may contribute to the overestimation of doses in the cases. The recall bias was noticed in some studies of CT and other radiological procedures, whereby patients are more likely to recall medical exposures than unaffected controls [45]. The selection and self-selection bias is a problem for epidemiological research; it is known also from studies of radiofrequency magnetic fields, where, analogously to low-dose ionizing radiation, there is some association with cancer but no supporting experimental evidence [46]. In populations exposed to ionizing radiation, the self-selection bias must be stronger than for radiofrequency electromagnetic fields because carcinogenicity of the former is known to the broad public. It can be reasonably assumed that people informed on their higher doses would visit medical institutions more often being averagely given more attention.

Other kinds of bias are not excluded in the epidemiological research; for example, men employed at Sellafield nuclear plant fathered a greater than expected proportion of boys, a possible explanation being the younger paternal age. It is known that fathers aged 20–29 years produce more boys than others, while there was an excess of Sellafield fathers in this age range [41]. By analogy, a bias might have been operative also in other research of sex ratios in the vicinity of nuclear facilities [13,19]. Addressing the issue of occupational exposure, a study performed on 621 radiation workers could not find a link between parents' exposure and the gender ratio of their children [29]. In the author's opinion, the reported relationships of low-dose exposures with the sex ratio at birth and other non-cancer endpoints, being devoid of physiological plausibility, witness against cause-effect relationships of the same doses with cancer, assumed on the basis of the epidemiological research.

Experimental data

The diversity of results and potential bias in the epidemiological research indicate that the question can be reliably solved by means of wide-scale animal experiments. The following studies should be

referred to in this connection. Experiments using 18 generations of exposed mice with the daily dose about 0.29 mGy suggested that low-dose low-rate exposures do not affect the sex ratio in mouse litters [47]. No sex ratio changes in the offspring of exposed mice were found by other researchers [48–52]. Note that the doses applied in animal experiments are much higher than average doses to residents of the contaminated territories after the Chernobyl accident. These latter doses are generally within the window for the maximum adaptive response protection. According to experimental data, this window occurs at doses between 0 and 100–700 mGy from low dose rate, low linear energy transfer radiation exposures, where the risk is expected to be below the spontaneous level of the cancer risk [53].

Social factors

The important statements by Victor Grech: "… All of the above are overshadowed by femicide, the selective destruction of female fetuses in societies (primarily Asian) which prize males more than females" and "Gendercide and femineglect (the deliberate neglect of females vis-à-vis health, education, etc.) is rampant" [4,5] have been commented previously [54]. Except for the Baltic States, all the regions of the former SU showed a significant increase in M/T ratio at birth from 1986 on [1]. The highest M/F ratios were reported from the South Caucasus (Azerbaijan, Armenia, and Georgia) [1], being explained by the son preference and sex-selective abortions [55]. The same is probably true for the North Caucasus, where the birthrate has been the highest in Russian Federation. The elevation of the M/T and M/F ratios at birth in the former SU coincided with the increasing availability of the prenatal ultrasonic gender testing in the late 1980s [1,55]. A relatively high M/T ratio at the time of the generally unavailable prenatal gender testing (1981–1985) in Caucasus [1] is an indication to the female neonaticide—the ancient family planning tool [55,56–58].

Migrations further contribute to the gender imbalance: shortage of men as a result of the emigration creates additional stimuli for sex-selective abortions in their native areas. A considerable gender imbalance is observed in Russia among immigrants from the Caucasus and Middle Asia. According to a census (2015), the M/F ratio in Crimea among ethnic Russians was 0.85, Tatars—0.98, Armenians—1.3, Karaites—1.3, Krymchaks—1.4 [59]. Evaluating statistics, it should be taken into account that gender imbalance is masked by a relatively low life duration of males. Obviously, the social significance of a gender imbalance is decreasing with age. Official statistics based on censes tends to underestimate the gender imbalance as predominantly males are involved in migrations, some of them remaining uncounted by censes. Presumably, prohibitive measures against sex-selective abortions will not be sufficiently effective. Such prohibitions would stimulate "traditional" methods of demographic regulation such as the female neonaticide and neglect of newborn girls [60,61]. Apart from traditions, a mechanism maintaining the higher birth rate and son preference is an insufficient social security. Ageing people depend on their children for support, while sons and their families are more likely than daughters to be caregivers, e.g., in China [62]. An improvement of the social security in developing countries must positively influence the demographic processes.

Gender imbalance due to the son preference and sex-selective abortions is known to occur in China, India, and some neighboring countries, in the Caucasus and among immigrants from Asia to Europe and the United States [58,63,64]. On one hand, there are many immigrants from the Caucasus in the former SU (except for the Baltic States discussed above); on the other hand, similar tendencies of the son preference probably exist also in some other groups of the ex-Soviet population. Insufficient security coupled with the tolerant attitude toward violations of laws and regulations might have motivated some families to have sons: for more safety and economical success. The dynamics of M/T ratio in Europe [1] must have been influenced by the ongoing immigration from countries with the son preference and gender imbalance [64].

Discussion

The author is grateful to the colleagues for their responses [6,8,17] to [65,66]. The following citations from the responses by Hagen Scherb should be further commented: "A social factor that may skew the birth sex ratio is gender selective abortion, a practice reported from parts of Asia and parts of North Africa [67]. However, this method requires advanced techniques for prenatal gender ascertainment that were not available at the time

of the Windscale fire in 1957 and during the era of the major atmospheric nuclear weapons testing prior to 1963" [8]. Apart from sex-selective abortions, requiring prenatal gender testing, there has always been some percentage of female neonaticide and neglect of newborn girls in certain cultures [56–58]. The death of unwanted babies was largely inevitable in cultures, where birth control was insufficiently understood [68]. Moreover, since olden times, there have been methods of attempted prenatal gender prediction and selection, possibly successful in some percentage of cases [69,70]. Finally, a reduced M/F ratio has been linked to the older age at childbearing [71]. The age of mothers at childbirth is averagely higher in more developed countries, generally tending to increase [72]. The continuously higher M/F ratios at birth in Europe compared to the US, illustrated by graphs [8], have an explanation unrelated to radiation: the ongoing immigration to Europe from Asia and Africa, including the regions with the son preference. The immigration to the US occurs largely from Latin America, where prenatal sex-selection is not a part of the culture, females are valued relatively high, the son preference considered to be "fairly mild" [73]. Immigrants bring their reproductive stereotypes with them; the dynamics of the sex ratio at birth may be partially determined by the immigration.

Furthermore, "…we found a significant dose-response association of Chernobyl fallout with subsequent sex ratio increases at the district level in Germany" [8]. The increase in the male proportion at birth with an odds ratio of 1.009 in 1987 in the data subset from Bavaria, former GDR, and West Berlin [9] was deemed "extremely small" [24] and may be a spontaneous fluctuation. Of note, the average additional individual dose received during the first year after the Chernobyl accident in the former GDR was around 0.21 mSv, and in the former Federal Republic of Germany (FRG)—0.16 mSv [28], which is a small addition to the national average from NBR—around 3.6 mSv/a [27,28]. The slight increase of the perinatal mortality in the Eastern part of Germany after 1986 was discussed in support of the radiation role after the Chernobyl accident [10,11,74]. The ratios perinatal deaths/total births in GDR plus West Berlin were as follows: 1986–2,183/242,068 = 9.02 per 1,000 total births; 1987—2,281/246,704 = 9.24 per 1,000 [10]. This slight increase might have been caused by social factors (decline of the communist regime) and emigration of some medical personnel from the former GDR to the West. No comparable increase in the perinatal death rate was noticed in the former FRG as per statistics from [11]. In general, oscillations of the perinatal mortality in the former Eastern Bloc after the Chernobyl accident [10,75] could have been caused by political and economical perturbations of that time accompanied in some places by a decline in the quality and availability of some medical services and products, foodstuffs, infant food etc.

With regard to the Fukushima Daiichi accident, it was commented: "Our data clearly show that in highly tsunami-impacted regions there is indeed a more than 50% increase in perinatal mortality, but this is confined to March and April 2011 only. From May through December 2011, nowhere in Japan perinatal mortality remained elevated. Moreover, the perinatal mortality increase in Chiba, Saitama, and Tokyo 10 months after the natural and technical catastrophes cannot be explained by 'derangements of perinatal care' as the general infrastructure had not been compromised at all in these three prefectures" [17]. It should be commented that the radiophobia causes misappropriation of resources to accommodate pseudo-dangers [76]. Overtreatment of thyroid and urinary bladder lesions favored by the radiophobia has been discussed previously [77,78]. It is known by the example of Chernobyl accident that evacuations of people, psychological stress and anxiety favored by exaggerated radiation-related risks are noxious factors per se that would be less potent after a catastrophe without radioactive contamination. In particular, exposures to stress after a nuclear accident may have detrimental effects on pregnant women [79,80]. Expectant mothers with anxiety and post-traumatic stress were reported to be at a higher risk of preterm birth [81]. The proportion of male births declines with the increasing gestation, the male excess tending to be maximal in spontaneous preterm births [82]. The exaggeration of risks from low-dose exposures, resonated by mass media and rumors, contributed to anxiety. A presumed risk of fetal abnormalities, illustrated, e.g., by newspaper images reproduced in the scientific report [83], seen on the Internet, could move families to a decision to make abortion. There was an increase in the induced abortion rate in several countries after the Chernobyl accident, while wanted pregnancies were interrupted [84–86]. It was reasonably assumed that "the public debate and anxiety among the pregnant women and their husbands 'caused' more fetal deaths… than the accident" [87]. Biased information "repeatedly created a situation of panic, like a posttraumatic stress

disorder" [88]. After the Chernobyl accident, "conflicting information and false rumors spread considerable alarm among the public in general and among pregnant women in particular" [89]. Biased publications in professional journals may prevent physicians from giving adequate advice to patients inquiring about a possible abortion. Radiophobia with psychosomatic manifestations developed in many exposed people [90], being probably more prevalent in more contaminated areas thus contributing to dose-effect correlations. Reiterations of the perinatal mortality "jump" [18,20,91] after the Fukushima accident can contribute to anxiety and elevation of the abortion rate, reportedly increased in the Fukushima Prefecture after the accident from 17,61 to 18,5/100 pregnancies [92]. Moreover, it cannot be excluded that radiophobia led to illegal abortions during the last trimester of pregnancy possibly influencing perinatal mortality figures. Considering that a certain percentage of abortions after a prenatal ultrasonic gender testing would be sex-selective, the enhanced abortion rate may contribute to an increased M/F ratio at birth.

"The doubling of the background radiation level, say, from 1 mSv/a to 2 mSv/a, represents a doubling of an important physical environmental parameter relevant for the development of life on the earth, and cannot as such be considered a 'low dose' and of no effect" [8]. A local increase from 1 to 2 mSv/a is of minor significance as the doses would remain under the global average of NBR. Considering the possibility of radiation hormesis [36], the doubling of "background radiation level… from 1 mSv/a to 2 mSv/a" [8] can be even beneficial, by analogy with a doubling of exposure to the sunlight, e.g., of prison inmates. An elevation of the mean value from 2.4 to 4.8 mSv/a can be regarded as a doubling although the twofold value would remain below many national averages of the NBR. Among arguments is also that "the dose (Gray or Sievert) in the radiation sciences is a surprisingly old and crude concept" [8,17]. Some refinement of the biological weighting factors for different types of radiation can be indeed awaited from further research [93] but hardly any gross revision of the scale of values.

"Furthermore, the letter to the editor [65] implies that low doses of radiation are innocuous. This flies in the face of the linear no-threshold (LNT) hypothesis that states that even at low doses, there is a linear relationship between dose and risk, particularly vis-a-vis, the probability of cancer induction, all the way down to zero exposure" [8]. The concept of LNT may be "pragmatic or prudent for radiation protection purposes" [94] but it is not the same as the scientific validity. The LNT postulates that linear dose-effect correlations, proven to some extent for higher doses, can be extrapolated down to minimal doses. However, the DNA damage and repair are permanent processes in a dynamic equilibrium. By analogy with other environmental factors, an evolutionary adaptation to a natural background radiation can be reasonably assumed. Living organisms have been adapting to the NBR in a similar way as to other environmental factors: chemical substances and elements, products of water radiolysis, ultraviolet light, etc. Natural selection is slow; adaptation to a changing environmental factor would correspond to some average from the past. The NBR has been decreasing during the time of life existence on the Earth [95]. The conservative nature of the DNA repair suggests that cells and organisms may have retained some capability to repair damage from higher radiation levels than the today's radiation background [95]. The statements that the LNT hypothesis is unfalsifiable are unfounded: to reject the LNT, it would suffice to prove radiation hormesis [96]. There is some experimental evidence in favor of radiation hormesis and adaptive responses [25,97–104]. Evidence against the LNT and/or in favor of hormesis has been observed also in some human studies [102,105]. Admittedly, the data on adaptive responses in cells or animals were judged by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) to be insufficiently well developed for the purposes of biological modeling thus remaining a source of debate [25]. Summarizing the above, it can be reasonably assumed that with the dose rates tending to a wide range NBR level, radiation-related risks would tend to zero, and can even fall below zero within some dose range according to the concept of hormesis. It is not surprising that a task group of the Society of Nuclear Medicine and Molecular Imaging recently concluded that the LNT hypothesis is invalid for the low-dose dose-rate region [106].

Last but not the least, the ideological bias aimed at the strangulation of nuclear energy should be pointed out [107]. Nuclear power has returned to the agenda because of the concerns about increasing global energy demand, declining fossil fuel reserves and climate changes. Health burdens were reported to be the greatest for power stations based on lignite, coal, and oil. The burdens are smaller for natural gas and still lower for the nuclear power. This ranking also applies for the greenhouse gas emissions [108]. The global development of nuclear

energy must be managed by a powerful international executive based in the most developed parts of the world. It would prevent a dissemination of nuclear technologies to unstable regions, where conflicts and terrorism are not excluded. It would enable the construction of nuclear power plants in optimally suitable places, disregarding national borders, considering all socio-political, geological and other preconditions, quality of working by local professionals, etc. [37]. In this way, nuclear accidents like in Fukushima, caused by the earthquake and tsunami, or in Chernobyl, favored by a disregard for written instructions [109,110], would be prevented.

Conclusion

It is known that the ionizing radiation can damage the developing embryo or fetus, cause congenital malformations and injuries of the nervous system, which can enhance the prenatal mortality. Mainly on the basis of animal studies and observations following exposures of pregnant women, the International Commission on Radiological Protection and UNSCEAR considered that there is a threshold for these effects at about 100 mGy [111,112], which is much higher than average doses discussed above for nuclear tests, accidents, and residents in the vicinity of nuclear facilities.

The proposition that "the M/T ratio is skewed upward significantly with population exposure to ionizing radiation, even at great distances from major nuclear events" [1] is not sufficiently corroborated. The statement that "the global correlation of health and socioeconomic indicators with M/T suggests that M/T may be a useful sentinel health indicator" [7] can hardly be agreed with as the M/T and M/F ratios depend on many known and unknown factors. In particular, social factors have not been taken into account in [1–20]. Among social factors contributing to the elevation of M/F ratio at birth in certain regions is the son preference and sex-selective abortions after a prenatal ultrasonic gender testing. A relatively high M/F ratio in some areas prior to the introduction of the ultrasonic testing is an indication to other perinatal sex selection methods, e.g., female neonaticide and abandonment of newborn girls. Apart from traditions, a mechanism maintaining the higher birth rate and son preference is an insufficient social security. Ageing people depend on their children for support. Insufficient security coupled with the tolerant attitude towards violations of the law motivated some families to have sons: for more safety and economical success. Migrations further contribute to the gender imbalance: shortage of men due to the emigration creates additional stimuli for sex-selective abortions in their native areas. The dynamics of M/T ratio in countries receiving immigrants is influenced by the ongoing immigration from regions with the son preference and gender imbalance: the immigrants bring their reproductive stereotypes with them. An improvement of the social security in the developing countries would counteract the population growth and gender imbalance.

In conclusion, the role of radiation from the nuclear testing, nuclear facilities, and Chernobyl fallout as a factor modifying the sex ratio at birth is unproven and theoretically implausible. Dose–response relationships at low radiation doses should be studied in large-scale animal experiments [113] involving different mammal species, using doses and dose rates comparable to human exposures in question, shielded from bias and conflicts of interest.

Conflict of interest

The author declares that he has no conflict of interest.

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