Letter to the Editor

(*Comment on the Letter to the Editor by Sergei V. Jargin concerning* "*Atomic bomb testing and its effects on global male to female ratios at birth*" *by Victor Grech, The International Journal of Risk and Safety in Medicine 27 (2015), 35–44. DOI: 10.3233/JRS-150641*)

Sir,

In response to findings by Victor Grech of biased global human gender proportions at birth following environmental radiation exposure [1–4], Sergei V. Jargin concludes that '*a significant role of radiation from nuclear testing and Chernobyl fallout as a factor modifying the male to female ratio at birth is improbable*'. Jargin's reasoning mainly builds on two arguments: (1) '*social factors that could have influenced this ratio were not comprehensively analyzed*' and (2) '*the natural radiation background was not mentioned, although additional doses due to the contamination were often negligible compared to doses from the background*'.

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 [5]. 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. Moreover, in western countries prenatal sex-specific selection is not part of the culture where females are valued as much as males. Therefore, the jumps in the secular sex ratio trends after Windscale in Europe [6] and the nearly synchronous jumps after the partial nuclear test ban treaty of 1963 [7] in Western Europe and in the USA can hardly be explained by sex selective abortion. Figure 1 shows an updated version of our synoptic sex ratio trend analysis for Europe and the USA [8] now based on 520 million officially recorded births from 1970 to 2010. In epidemiology, temporality and biological gradient are two indispensable requisites for inferring causality. Temporality means that the presumable cause precedes the observed effect in time, and biological gradient refers to the presence of an exposure-response association. Thus, Fig. 1 yields strong evidence of causality in as much as a clear sex ratio change occurs immediately after Chernobyl in the exposed parts of Europe only, and not in the USA, which remained essentially unaffected by Chernobyl fallout. In other words, Fig. 1 represents a highly significant spatiotemporal dose-response association based on precise and extremely powerful human data. A similar conclusion further highlighting the relative importance of internal versus external radiation exposure can be derived from the synoptic consideration of Russian and Cuban sex ratio trends [9]. In view of these facts, the tacit assumption by Jargin that soft and only gradually changing social factors could have caused abrupt sex ratio changes is implausible, all the more so since we found a significant dose-response association of Chernobyl fallout with subsequent sex ratio increases at the district level in Germany [10]. This is consistent with recent findings form a high background radiation area in India [11, 12] and with a report from a nuclear testing area in Kazakhstan [9, 13].

It is generally accepted that proof of safety is more difficult than proof of hazard [14]. Suggestively, this has been rephrased that '*no evidence of effect is not evidence of no effect*'. Therefore, the negative animal low dose experiment cited by Jargin [15], which is based on only 1053 baby mice distributed
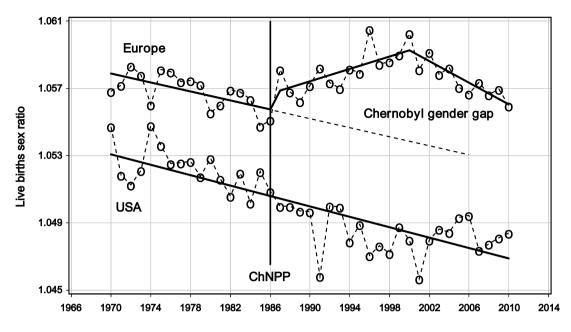
Fig. 1. Secular trends of the live births sex ratio (male/female) in Europe and in the USA, 1970–2010, before and after the Chernobyl nuclear power plant accident (ChNPP).

over 18 generations (i.e. 58.5 mice per generation) is practically meaningless due to its negligible statistical power. Another reportedly negative observation referred to by Jargin concerns the sex ratio shifts among infants born to survivors of the atomic bombings of Hiroshima and Nagasaki [16]. However, scrutiny of these data reveals clear and significant sex ratio jumps after the bombings, not only in Hiroshima and Nagasaki but also in all of Japan [17].

The dose (Gray or Sievert) in the radiation sciences is a surprisingly old and crude concept developed long before the discovery of the molecular structure of the DNA. The basis of this concept is unit energy deposited per unit mass (Joule/kilogram). Therefore, it is clear that dose can only be physically meaningful for energy deposits in volumes of at least a few milliliters, e.g. of water, and not for the interaction of photons, electrons, and α-particles by external or internal emitters with cellular and sub-cellular structures like cells, DNA, and proteins in animate beings. Therefore, comparing the additional radiation exposure of human populations after radiological incidents and accidents with the natural background radiation level is misleading in principle as the specific microbiological consequences of artificial external and internal ionizing irradiation and radionuclides are not taken into account. Jargin's view that the natural annual background radiation dose of 1 mSv/a is trivial and that even multiples of this dose after nuclear accidents were '*often negligible compared to doses from the background*' points to a key dissent in science: 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 earth, and cannot as such be considered a 'low dose' and of 'no effect'. It is hard to imagine any 'environmental parameter' a doubling of which would have no consequences, be it the exposure to the sun, the oxygen and the carbon dioxide contents in the air, or the individual cigarette and alcohol consumption per year. Moreover, Jargin seems not to be aware of or not to acknowledge more recent findings by comprehensive and statistically powerful studies of increased childhood cancers in the vicinity of nuclear power plants [18, 19], in areas of high background radiation [20], and following computerized tomography examinations [21, 22].

In conclusion, the reservation by Sergei V. Jargin towards results of observational epidemiological investigations is certainly warranted in principle in so far as single studies cannot prove causality.

However, the findings presented by Victor Grech must not be considered in isolation, they are rather consistent with early observations after the atomic bombing of Japan, and are clearly in line with our results after Chernobyl and in the vicinity of nuclear facilities [8, 9, 17, 23, 24]. The relief of ionizing radiation as a possible culprit for the sex ratio increases after radiological events offered by Jargin: *social factors* and *negligibility of doses* is not convincing as gradually changing social factors cannot entail abrupt sex ratio changes and a doubling of the background radiation is certainly not trivial. Considering the findings of the last two decades in radiation epidemiology synoptically, evidence continues to show that radiation risks have been systematically underestimated in the past, due to inadequate scientific concepts and underpowered or poorly designed experimental and human studies.

Hagen Scherb
Helmholtz Zentrum München
Institute of Computational Biology
Ingolstädter Landstr. 1
D-85764 Neuherberg, Germany
http://www.helmholtz-muenchen.de/icb/institute/staff/staff/ma/2476/index.html

References

[1] Grech V. Births and male:female birth ratio in Scandinavia and the United Kingdom after the Windscale fire of October 1957. Int J Risk Saf Med. 2014;26(1):45-53.

[2] Grech V. Response to letters to the editor. Int J Risk Saf Med. 2014;26(3):175-6.

[3] Grech V. The chernobyl accident, the male to female ratio at birth and birth rates. Acta Medica (Hradec Kralove). 2014;57(2):62-7.

[4] Grech V. Atomic bomb testing and its effects on global male to female ratios at birth. Int J Risk Saf Med. 2015;27(1):35-44.

[5] Hesketh T, Xing ZW. Abnormal sex ratios in human populations: Causes and consequences. Proc Natl Acad Sci U S A. 2006;103(36):13271-5.

[6] Scherb H, Kusmierz R, Voigt K. Letter to the editor. Int J Risk Saf Med. 2014;26(3):173-4.

[7] Scherb H. Letter to the Editor. Int J Risk Saf Med. 2015;27(2):107-10.

[8] Scherb H, Voigt K. The human sex odds at birth after the atmospheric atomic bomb tests, after Chernobyl, and in the vicinity of nuclear facilities. Environ Sci Pollut Res Int. 2011;18(5):697-707.

[9] Scherb H, Kusmierz R, Voigt K. Increased sex ratio in Russia and Cuba after Chernobyl: A radiological hypothesis. Environ Health. 2013;12:63.

[10] Scherb H, Voigt K. Trends in the human sex odds at birth in Europe and the Chernobyl Nuclear Power Plant accident. Reproductive Toxicology. 2007;23(4):593-9.

[11] Koya PK, et al. Sex ratio at birth: Scenario from normal- and high-level natural radiation areas of Kerala coast in south-west India. Radiat Environ Biophys. 2015.

[12] Scherb H, et al. Letter to the Editor "Radiation and environmental biophysics". Radiation and Environmental Biophysics. 2016;55(1):3-4.

[13] Mudie NY, et al. Sex ratio in the offspring of parents with chronic radiation exposure from nuclear testing in Kazakhstan. Radiat Res. 2007;168(5):600-7.

[14] Bross ID. Why proof of safety is much more difficult than proof of hazard. Biometrics. 1985;41(3):785-93.

[15] Nakajima H, et al., Fukushima simulation experiment: Assessing the effects of chronic low-dose-rate internal 137Cs radiation exposure on litter size, sex ratio, and biokinetics in mice. J Radiat Res. 2015;56(Suppl 1):i29-35.

[16] Schull WJ, Neel JV, Hashizume A. Some further observations on the sex ratio among infants born to survivors of the atomic bombings of Hiroshima and Nagasaki. Am J Hum Genet. 1966;18(4):328-38.

[17] Scherb H, Voigt K, Kusmierz R. Ionizing radiation and the human gender proportion at birth-A concise review of the literature and complementary analyses of historical and recent data. Early Human Development. 2015;91(12):841-50.

[18] Spix C, et al. Case-control study on childhood cancer in the vicinity of nuclear power plants in Germany 1980-2003. Eur J Cancer. 2008;44(2):275-84.

[19] Sermage-Faure C, et al., Childhood leukemia around French nuclear power plants – the Geocap study, 2002–2007. Int J Cancer. 2012.

[20] Spycher BD, et al., Background ionizing radiation and the risk of childhood cancer: A census-based nationwide cohort study. Environ Health Perspect. 2015.

[21] Mathews JD, et al. Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: Data linkage study of 11 million Australians. BMJ. 2013;346:f2360.

[22] Pearce MS, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: A retrospective cohort study. Lancet. 2012;380(9840):499-505.

[23] Schull WJ, Neel JV. Radiation and the sex ratio in man. Science. 1958;128(3320):343-8.

[24] Scherb H, Kusmierz R, Voigt K. Human sex ratio at birth and residential proximity to nuclear facilities in France. Reprod Toxicol. 2016;60:104-11.