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Letter to the Editor

Overtreatment of Supposedly Radiogenic Cancer and Precancerous Lesions

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It is known that the incidence of thyroid carcinoma (TC) among people exposed to ionizing radiation at a young age from the Chernobyl accident (hereafter accident) increased significantly. The precipitous elevation of TC detection rate that began ~4 years after the accident could not be predicted either from studies of A-bomb survivors in Japan or from experience with radiotherapy. As discussed previously,[1] some dose-effect relationships have been caused or influenced by bias and confounding factors, especially by dose-dependent selection. Individuals informed about higher doses or residing in more contaminated territories would be on average more motivated to undergo medical examinations and be given more attention by medics. TC was rarely detected in young people in the USSR prior to the accident. In Belarus (1981–1985) the incidence rate was ~0.3 in people younger than 15 years and was 0.5 cases per million per year in the Ukraine. In the northern provinces of Ukraine, the incidence rate of TC was as low as 0.1 per million per year.[2] According to another source, the incidence of TC in patients younger than 14 years of age increased from 0.3 (1981–1985) to 30.6 (1991–1994) cases in Belarus, and from 0.4 to 4 per million per year in all of Ukraine.[3]

The above-cited pre-accident figures are very low compared with other industrialized countries. A table with the incidence rates of various countries is presented in the article.[4] In a later publication, an overview of worldwide statistics states that "The incidence of TC in children below 14 years of age is 0.5–1.2/million and 4.4–11/million for adolescents between 15 and 19 years of age, with a constantly growing number of cases in both Europe and America."[5] A comparison of these figures with those quoted above indicates that there were neglected TCs in the population prior to the accident. The fact that screening can elevate the TC detection rate considerably has long been known. Moreover, some people strived for recognition as victims of the accident to get better therapy for their diseases. TC cases from non-contaminated territories wrongly registered as Chernobyl victims must have been on average more advanced as there had been no mass screening outside the Chernobyl area. Accordingly, TCs found during the first decade after the accident were on average more advanced than those detected later. More details and references are in the book.[1]

Apparently, the considerations delineated above have been camouflaged. The time span of 1986 to 1990, when screening began and the TC frequency started to increase was chosen by the United Nations Scientific Committee on the Effects of Atomic Radiation for comparison with post-accident figures[6] because" 1986 and not earlier, data on TC incidence have been specifically collected by local oncologists" (UNSCEAR Secretary, e-mail message of October 22, 2013). Dr. Fridman claimed that the TC incidence in Belarus in the period from 1971 to 1985 did not significantly differ from that in other countries[7] with reference to the paper,[8] where no such information was found. Dr. Balonov stated without references that the pre-accident TC incidence in children younger than 10 years of age in Belarus and Ukraine was 2–4 cases/million/year,[9] i.e. much higher than the statistics quoted above.[2,3] Apparently, the mass screening after the Chernobyl disaster found advanced neglected malignancies that were misinterpreted as aggressive cancers developing because of radiation exposure after a short latency. This gave rise to the doctrine that radiogenic TCs tend to be rapidly growing and early metastasizing,[10,11] which has contributed to the excessive radicalism of treatment.

Here are several quotes concerning Chernobyl-related TC. "Practically all thyroid nodules in children, independent of their size, were regarded at that time as potentially malignant tumors, requiring urgent surgery."[12] The recommended treatment was "radical thyroid surgery including total thyroidectomy (TT) combined with neck dissection followed by radioiodine ablation"[4] and irradiation with 40 Gy.[13] Certain experts generally advised TT with neck dissection for thyroid cancer.[14] Less radical surgery was deemed "only acceptable in exceptional cases of very small solitary intra-thyroidal carcinomas without evidence of neck lymph node involvement on surgical revision."[15]

In a later study, 69% of post-Chernobyl pediatric TC patients underwent TT; among them, radioiodine was administered to 69% of the cases.[5] As per the same article, in patients diagnosed with TC after the Fukushima Daiichi accident, hemithyroidectomy was performed in 92% and TT in 8% of cases.[5] In another study, "given the presence of radiation exposure in the patients' histories", TT was performed in 405 of 465 papillary thyroid microcarcinomas (87.1%) with postoperative radioiodine therapy in 76.1%. Neck dissection was performed in ~50% of the cases.[16] Of note, recurrences were recorded only in 1.3% of the cases after a median follow-up of 5.2 years. The authors noted that microcarcinomas in their series were "rather indolent" and advised "more frequent

Abbreviations: TC, thyroid carcinoma; TT, total thyroidectomy.

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organ-preserving surgeries vs. TT even for potentially radiogenic papillary thyroid microcarcinomas."[16] The long-term overall survival of post-Chernobyl TC patients was deemed excellent between 1990 and 2014, with 21 deaths (1.9%) among pediatric TC patients, only two from progressive carcinoma, three from other tumors, three from non-oncologic diseases and six from trauma. Seven TC patients committed suicide.[5] These figures are indicative of the overdiagnosis of TC and overuse of TT.

Epidemiologists have warned against false-positive diagnoses of malignancy in thyroid nodules. Many experts argued that the worldwide increase in the TC incidence (not only in children) has been caused by screening, improvement of medical surveillance, and technological advances in diagnostics.[5,17] The author agrees with the statement that "The extent to which opportunistic thyroid cancer screening is converting thousands of asymptomatic persons to cancer patients without any known benefit to them needs to be examined carefully."[17] Health-related, cosmetic and social (stigmatization as a cancer patient) adverse effects of surgical hyperradicalism are known. The risk of complications associated with thyroid surgery (nerve injuries, hypoparathyroidism and others) is believed by some experts to be proportional to the extent of thyroidectomies,[18] although it is an area of controversy. The rate of adverse effects was additionally elevated because of the insufficient qualification of some surgeons engaged after the Chernobyl accident under conditions of a high workload.[3] The extent of surgery for well-differentiated papillary TC is a matter of debate, which is beyond the scope of this letter. In particular, performing a subtotal thyroidectomy instead of TT may be a better choice to preserve parathyroid function.[19] Elective neck dissection is usually performed in patients with clinically evident nodal disease even though there is no general agreement on this matter.[18,19] *Ceteris paribus*, TT should be avoided if thyroxine supplies are unreliable,[20] which might be of importance in view of international conflicts.

Analogous tendencies to overestimate aggressiveness were noticed regarding post-Chernobyl renal and bladder lesions, as discussed elsewhere with illustrations and references.[1,21] Surgeons might overuse nephrectomy instead of less radical procedures if they read that renal-cell carcinoma in patients exposed to low-dose ionizing radiation is on average more aggressive, while the surrounding parenchyma contains "proliferative atypical nephropathy with tubular epithelial nuclear atypia and carcinoma *in situ*."[22] The same experts found severe urothelial dysplasia and/or intraepithelial cancer in 56–73% (in different papers and cohorts) of routine biopsies from bladder mucosa of consecutive patients with benign prostatic hyperplasia, coming from contaminated territories or the city of Kyiv, which is not officially recognized as contaminated.[23,24] More details, references, and histological images are in the preceding publications.[1,21] These percentages seem to be unrealistic. The clinical and morphological findings designated as "Chernobyl cystitis" or "irradiation cystitis" with epithelial proliferation, hemorrhage, fibrin deposits, and increased angiogenesis[23,24] were increased by repeated cystoscopy with "mapping" biopsies, and electrocoagulation of vesical mucosa.

Radiation dose reconstructions in human populations are often imprecise. Screening effect, selection, and other biases in the epidemiological research might contribute to appearance in the future of new reports on enhanced cancer risks associated with a moderate increase in the radiation background. This would not prove causality. It is essential for radiation protection to determine the threshold dose for the carcinogenic effect. Large-scale animal experiments involving different species are a reliable tool to determine thresholds. Admittedly, large-scale studies with primates, which might be similar enough to humans to extrapolate the results directly, are expensive, and extrapolation from laboratory animals is associated with uncertainties.[25] Experiments with low radiation doses seem to be feasible in animal breeding facilities. The use of various species must enable more precise extrapolations to humans. The monitoring of exposed populations and epidemiological studies are important, but potential biases and confounding factors should be taken into account. In conclusion, claims of extraordinary aggressiveness of supposedly radiogenic cancers arising after exposure to low radiation doses, should not lead to overtreatment.

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Conflict of interest

The author has no conflicts of interest related to this publication.

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