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THYROID CANCER AFTER CHERNOBYL: OBFUSCATED TRUTH

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Causes and mechanisms of the registered incidence increase of pediatric thyroid cancer (TC) after the Chernobyl accident, unrelated to the ionizing radiation, were recently reviewed among other topics by Prof. Z. Jaworowski (2010). The main body of evidence (Cardis *et al.* 2005; Tronko *et al.* 2006; Davis *et al.* 2004) in favor of the cause-effect relationship between ionizing radiation and TC among children and adolescents after the Chernobyl accident is based upon the epidemiologic studies (Ron 2009). In the case-control study (Cardis *et al.* 2005) a retrospective estimation of doses was performed by questioning. The study by Davis *et al.* (2004) was similar in design. The 'Chernobyl victim syndrome' (Bay and Oughton 2005) was a widespread phenomenon: many patients strived for higher dose estimations to support their status as Chernobyl victims, and provided biased information. Cancer patients could have remembered circumstances related to the exposure better than the controls. Iodine supplementation months after the exposure was reported to reduce the cancer risk threefold (Cardis *et al.* 2005), although radioiodine would have already been absorbed and there would be no blockage in uptake that could have reduced thyroid dose (Boice 2005). Some aspects of the study design by Cardis *et al.* (2005), favoring an LNT-type dose-response relationship, were criticized by Scott (2006). The dose-response relationship in the recent epidemiologic study by Zablotska *et al.* (2011) is even stronger at the low dose level: it can be seen in the graph 2 in this paper that the dose-effect curve ($P<0.001$) is most steep in the area of minimal doses, then at higher doses it becomes more gently sloping, and the relationship disappears completely at the individual dose level of approximately 3 Sv. A dose-effect relationship of a similar form was reported also previously; but decrease or leveling of TC risk was observed at higher doses, e.g. > 10 Gy of external radiation (Ron *et al.* 1995). The decrease of risk at higher doses is explained by the effect of cell killing (UNSCEAR 2006; Boice 2005). However, no leveling of TC risk was found by Shore *et al.* (1985) at the doses of external radiation up to 10 Gy. In a case-control study following radiotherapy for childhood cancer, it was found that

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exposures around 60 Gy were associated with a high risk of TC (UNSCEAR 1994). For comparison, in a review of a series of studies in rats, a carcinogenic effect on the thyroid of 11 Gy from acute x-ray exposure was compatible to that from injection of 1.1 MBq of ^{131}I, which would give a dose of about 100 Gy, when significant cell killing might be expected (UNSCEAR 1993). The cell killing concept appears to be inapplicable for the doses around 3 Gy from radioiodine, when thyroid remains gross unchanged, the bulk of follicular epithelium remains viable, preserving capability of mitosis. In other words, the cancer field, i.e. exposed follicular cells as a field for potential carcinogenesis, remains in place. Therefore, it appears probable that both the dose-effect relationship at minimal doses and its disappearance at higher doses in (Zablotska *et al.* 2011) are caused by biases and other factors rather than by radiation, which would be in agreement with evidence in favor of low (if any) carcinogenicity of ^{131}I, used for diagnostic and therapeutic purposes (Hahn *et al.* 2001; Dickman *et al.* 2003; Boice 2005; Holm *et al.* 1991; Wartofsky 2010; DeGroot 1993). Interestingly, Zablotska *et al.* (2008) found in individuals, exposed as children or adolescents to ionizing radiation, a significant LNT-type dose-response relationship also for follicular thyroid adenoma, a benign condition, which is different in pathogenesis from papillary carcinoma prevailing among post-Chernobyl pediatric TC. It is worth mentioning here that a cause of the unusually high percentage of papillary carcinoma among TC cases in the screened Chernobyl populations is clear for a pathologist, acquainted with the diagnostic practice of that time: reliable diagnostics of a follicular TC often requires a great number of high-quality histological slides from the capsular area of a nodule, which was usually not done because of technical reasons and insufficient awareness of the minimally invasive follicular TC, absent in Russian-language literature. Paradoxically, if papillary TC was overdiagnosed after the Chernobyl accident (Jargin 2009a), follicular TC probably was underdiagnosed.

Tronko *et al.* (2006) in their cohort study used interviews as well as thyroid dosimetry data to estimate individual doses. The dosimetry measurements were performed within 2 months after the accident ($t_{1/2}$ of ^{131}I is about 8 days).The study design included, if indicated, repetitive examinations in the central clinics in Kiev (Tronko *et al.* 2006). Persons with higher dose estimates might have been, on average, more interested in further examinations. In the health care system of the former Soviet Union, an extent of a medical checkup has sometimes depended on a patient's initiative. The study by Zablotska *et al.* (2011) is analogous in design to that by Tronko *et al.* (2006). Other epidemiologic studies were probably loaded by the same and other biases (Jaworowski 2010), that can be found in studies on stochastic effects of low level radiation (Watanabe *et al.* 2008). Furthermore, detection of thyroid cancer is heavily depend-

ent on the degree of screening, which can increase the incidence 10-fold (UNSCEAR 1994). The screening effect, improved registration, reporting and other non-radiation-related factors have played their role in the post-Chernobyl incidence increase of TC (UNSCEAR 2000; Boice 2005), while proportion of radiogenic and nonradiogenic tumors among the post-Chernobyl TC cases remains unknown. Nonetheless, calculations in epidemiological studies are often based on a premise that all TC in the exposed population are radiogenic; and even latency periods were calculated for cancers without any proof that they had been caused by radiation (Jargin 2009b).

After the accident, numerous poorly substantiated publications appeared, where spontaneous diseases in Chernobyl clean-up workers or inhabitants of radiocontaminated areas, sometimes quite distant from Chernobyl, were a priori considered to be radiogenic (e.g. Grobova and Chernikov 1996; Chuchalin *et al.* 1997; Kogan *et al.* 1999; Derizhanova 2000; Degtiarova 2000; Lysenko *et al.* 2000). Previously we discussed several publications overestimating medical consequences of Chernobyl accident (Jargin 2007; 2009b-d; 2010b). Unreliability of others can be inferred by analogy: if earlier papers on the same topic were unreliable, later ones might be unreliable as well, because motivations and the attitude remained unchanged. For an inside observer it is evident that behind the avalanche of predominantly Russian-language papers, overestimating Chernobyl consequences, some of them referenced in Yablokov (2010), was a directive, which had been not unusual for the Soviet science. Research themes were often assigned to the scientists, while "expected results" were discussed at Scientific Councils (uchenyi soviet) sometimes being, in fact, prescribed in advance. Desired research results could be "recommended" by a superior, which was favored by the authoritative management style, ingrained also in science and medicine. Motives for overestimation of Chernobyl consequences have been obvious: exaggeration of this theme facilitated writing of dissertations, financing, international help, etc. The Chernobyl accident has been exploited to strangle worldwide development of atomic energy (Jaworowski 2010).

Travelling to the areas, formerly contaminated due to the Chernobyl accident, the author of this letter interviewed pathologists, cytologists and other specialists, who participated in diagnostics of the post-Chernobyl tumors. Most of them agreed that Chernobyl consequences had been overestimated; and the role of vested interests was pointed out. It was also stated that sets of histological specimens from a single patient were sometimes subdivided into several ones, creating "dead souls", which influenced statistics. It remains to be verified by the DNA examination of the specimens accumulated in tissue banks. Radio- and cancerophobia, sometimes amounting to panic, contributed to the overdiagnosis of cancer, which can be illustrated by the following citations from a Russian-lan-

guage professional publication (verbatim translation): "Practically all nodular thyroid lesions, independently of their size, were regarded at that time in children as potentially malignant tumors, requiring an urgent surgical operation" or "Aggressiveness of surgeons contributed to the shortening of the minimal latency period." (Parshkov 2006). Mechanisms of overdiagnosis were discussed previously (Jargin 2009a,c; 2010a). Obviously, mass screening in the areas, where pediatric TC had been rarely diagnosed before, on the background of poor equipment and shortage of modern literature, in the atmosphere of radio- and cancerophobia, of vested interests both in decision-making spheres and among researchers, must have inevitably resulted in overestimation. The principal causes of the overestimation of Chernobyl consequences likely include unreliability of Chernobyl-related (and some other) research, originating from the former Soviet Union, a nonchalant attitude towards scientific misconduct in general and manipulations with statistics in particular (Jargin 2009e,f; 2010b,c). Hopefully, the true state of affairs will be cleared sooner or later: Chernobyl cancer specimens are preserved in tissue banks, and evaluation of time-related markers of tumor progression should allow one day an estimate of the true "age" of these tumors, which would demonstrate, how many of them were misclassified as radiogenic cancer, having developed before the accident. Future dynamics of TC incidence in persons exposed during childhood due to the Chernobyl accident will also contribute to clarification: a tendency of incidence decrease was already noticed (UNSCEAR 2000; Reiners 2009), although maximum risk of radiation-induced thyroid cancers had been, according to previous knowledge, assumed to be approximately 15-30 years after the exposure (UNSCEAR 2000; Sarne and Schneider 1996; Mehta *et al.* 1989). Identifying cases from non-contaminated areas, falsely registered as Chernobyl victims, is technically possible as well, although it can be difficult as it would require cooperation of the authorities. A concluding point is that overestimation of Chernobyl consequences can create a wrong concept about carcinogenic action of radioactive iodine, which would be harmful for research and practice.

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