

# Radiation exposure and cytotoxic endocrinopathy: It is time for action

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Unfortunate accidents such as the ones experienced in Chernobyl, Ukraine, in April 1986, and in Japan, in March 2011, remind us of the frailty of human life.

As doctors, however, our work is not to just grieve for the victims of these mishaps, but rather to help them manage and overcome the medical consequences of such disasters.

Terms like disaster management and disaster medicine relate to various health and medical aspects of caring for victims. Most of this work, however, is related to acute or subacute medical care, and tends to overlook the chronic sequelae that victims have to grapple with. Apart from acknowledging the more than 6000 cases of thyroid cancer in affected areas of Belarus, Ukraine and Russia, the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) does not elaborate on the possible endocrinopathies linked with nuclear radiation exposure, an important group of illnesses which impair the quality of life of victims.

One of the important medical conditions that may occur after exposure to nuclear irradiation is termed cytotoxic endocrinopathy.<sup>[1]</sup> Radiation has extensive, but differential, effects upon the endocrine system.

The anterior pituitary is highly sensitive to radiation, with growth hormone secretion being the most vulnerable.<sup>[2]</sup> Irrespective of whether the damage is in pituitary or

hypothalamic, growth hormone deficiency is universal (100%) in patients exposed to external radiotherapy (3750–4250 rads given in 15–16 fractions over 22 days). Deficiency of luteinizing hormone (LH), follicle stimulating hormone (FSH) (96%), adrenocorticotropic hormone (ACTH; 84%) and thyroid stimulating hormone (TSH; 49%), with hyperprolactinemia, can also occur.<sup>[3]</sup>

In sharp contrast, the posterior pituitary exhibits extraordinary resilience to radiation exposure.<sup>[2]</sup>

The hypothalamus is more prone to damage after radiation, as compared to the anterior pituitary. This may be due to hypothalamic neuronal damage, rather than reduced cerebral blood flow.<sup>[4]</sup>

A paradoxical situation of precocious puberty, rather than gonadotropin deficiency, has been reported in girls with exposure to low doses of radiation (2500–4750 rads) for management of brain tumors.<sup>[5]</sup> It is thought that low-dose radiation disrupts the normal restraint of the central nervous system on the hypothalamus and accelerates pubertal growth.

The thyroid gland is exquisitely sensitive to environmental thyroid disruptors, including irradiation. Thyroid cancers, especially papillary carcinoma and follicular tumors, which are more often >1.5 cm in diameter, multicentric, with local invasion and distant metastases, are common in patients with exposure to irradiation. Children are at higher risk, as reported from Belarus after the Chernobyl accident.<sup>[6]</sup>

Benign abnormalities, such as focal hyperplasia, single or multiple adenomas, chronic lymphocytic thyroiditis, colloid nodules and fibrosis, may occur is up to 20–30% of an irradiated population.<sup>[7]</sup> Maximum work related to endocrinology seems to have been carried out in thyroidology after the Chernobyl incident. The Chernobyl

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Tumor Bank, set up in 1988, has identified over 95% of thyroid tumors as being of the papillary carcinoma variety.<sup>[8]</sup>

A considerable rise in the incidence of thyroid cancer has also been reported from the Polish province of Opole, which suffered high levels of radiation exposure after the Chernobyl accident.<sup>[9]</sup> Similar findings have been noted in adult survivors of the atomic bombings of Hiroshima and Nagasaki.<sup>[10]</sup>

The parathyroid seems to be more resistant to radiation-induced cytotoxicity than its larger neighbor, the thyroid. However, individuals who have received neck irradiation should have their calcium level monitored, even though the latency period for development of hyperparathyroidism is very long (25–47 years).<sup>[11]</sup>

The testes are very radiosensitive organs, and the damage may be irreversible or reversible. The degree of damage and the effect on Sertoli and Leydig cell function depends on the radiation dose, and the age and pubertal status of the boy.<sup>[12]</sup> The ovaries, in contrast to the testes, have a fixed population of oocytes which cannot be replaced. Hence, radiation-induced ovarian damage is usually permanent.<sup>[13]</sup>

The adrenal gland seems relatively immune to radiation toxicity though its endocrine function involves steroidogenesis similar to that of the gonads. The reason for this is unclear.<sup>[2]</sup>

With the recent incident in Fukushima, Japan, there has been a focused global attention on earthquakes, disaster preparedness, disaster management, nuclear energy and nuclear safety. Along with these issues, sufficient importance should also be devoted to the assessment and study of radiation-induced endocrinopathy or cytotoxic endocrinopathy.

An article by Wiwanitkit in the current issue focuses on the important and timely topic of prophylaxis for radiation-induced thyroid dysfunction.<sup>[14]</sup> Another contribution by Niazi and Niazi highlights the importance of this topic as well.<sup>[15]</sup>

The mechanism behind this group of diseases should be unraveled and appropriate management strategies designed to achieve optimal endocrine function for the

people accidentally exposed to nuclear irradiation. The *IJEM* welcomes contributors and comments on this aspect of endocrinology and metabolism. As we remember the tragedy of Chernobyl, whose 25<sup>th</sup> anniversary falls on 26 April this year, let us contribute to improving the health of those affected by it and by similar such incidents. Let us sensitize our colleagues, and the world, to the importance of radiation-related endocrinopathy or cytotoxic endocrinopathy.

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