

### Thyroid Disease 60 Years After Hiroshima and 20 Years After Chernobyl

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**Thyroid cancer was the first solid tumor reported to be increased in frequency among atomic bomb survivors.** Subsequent surveys found a significant excess of papillary thyroid cancer but not of follicular, medullary, or anaplastic cancer. A straight line adequately describes the relationship between radiation dose and thyroid cancer incidence, relative risks are similar in males and females, and age at exposure substantively influences risk. Risk is highest for children exposed when younger than 10 years, and there is no significant increase in risk of thyroid cancer for those exposed after age 20 years. Radiation-induced thyroid cancers are rarely fatal, but the risk per unit dose following exposure in childhood is higher than for any other radiation-induced malignancy.

Radiation-induced thyroid cancer has been extensively studied in human populations other than atomic bomb survivors. These populations include patients treated with radiation for malignant and nonmalignant conditions, populations exposed to radioactive fallout from nuclear weapons tests, and populations living in the vicinity of nuclear installations such as Chernobyl in the former Soviet Union and Hanford in Washington State.

The latest research from the Adult Health Survey (AHS) in Japan reported in this issue of *JAMA* by Imaizumi and colleagues derives from a cross-sectional study of 4091 survivors of the Hiroshima and Nagasaki atomic bombings in 1945 who were invited to a special thyroid examination more than 50 years later. The prevalences of thyroid cancer (n=87), benign nodules (n=207), and cysts (n=324) were significantly increased and directly related to radiation dose, and the risk decreased with increasing age at exposure; however, autoimmune thyroid diseases (positive antithyroid antibodies, antithyroid antibody–positive hypothyroidism, or Graves disease) were not linked to radiation exposure.

There are several new findings of note. First, it is remarkable that a biological effect from a single brief environmental exposure nearly 60 years in the past is still present and can be detected. The radiation doses (mean, 45 cGy) were related to the distance from the hypocenters, and enormous effort was required to accurately estimate exposures for individuals. The existence of dose-response relationships strongly supports the authors’ assertion of a radiation-related excess of thyroid neoplasms nearly 60 years after exposure. Second, using highly sensitive assays to detect serum levels of antithyroid antibodies and thyroid-stimulating hormone, this study was not able to confirm the findings of a smaller but similar investigation of Nagasaki atomic bomb survivors that purported to show an association between radiation and autoimmune thyroid disease. The absence of a dose-response relationship for any measure of autoimmune disease in the study by Imaizumi et al is consistent with earlier studies of atomic bomb survivors and a recent study of persons exposed as children to iodine 131 releases from the Hanford nuclear site.

The study of atomic bomb survivors remains the single most important study of radiation effects in humans, but the exposure was brief, lasting less than a second, and thus provides no information on the effects from the prolonged

**See also p 1011.**
or protracted exposures most individuals experience throughout life. Experimental evidence suggests that the risk posed by ionizing radiation decreases when the dose is spread over time, in part because the body has more time to repair any radiation-induced damage. Studies of patient populations suggest a slight ameliorating effect of fractionated and prolonged radiation exposure and a downturn in risk at the highest therapeutic exposures. The studies of atomic bomb survivors also do not provide information on internal intake of radionuclides, such as radioactive isotopes of iodine that are administered to patients and also are components of fallout from nuclear weapons tests or releases from nuclear facilities. However, studies of persons exposed to radioiodines from Chernobyl in 1986 are now beginning to provide information on the effects of chronic exposures from internally ingested radioiodine on risk of thyroid cancer.

To date, thyroid cancer among children living near Chernobyl in 1986 is the only convincing late effect from the nuclear accident. Thousands of thyroid cancers have been detected, but, fortunately, fewer than 10 deaths have been reported. The first analytical study, published in 1998, suggested an association between radioactive iodine exposure and thyroid cancer prevalence, and subsequent studies have borne this out. However, the interpretation of data are not straightforward. Estimated radiation dose to the thyroid is mainly from iodine 131, which has an 8-day half-life. Other shorter-lived radioactive iodine isotopes, in particular iodine 133, could have contributed to the excess risk because of a higher exposure rate and more uniform exposure of the thyroid gland. The influence of intense screening of the exposed populations after the Chernobyl accident has yet to be defined.

Perhaps most intriguing is the likelihood of an important interaction between radioactive iodine exposure and dietary iodine deficiency. The populations living near Chernobyl had diets deficient in iodine and also were in areas of highest fallout of radioactive iodines. The continued administration of potassium iodine to block uptake of radioiodine reduced risk of thyroid cancer even when given months after the accident, when blockage of iodine 131 uptake was no longer possible. An explanation for this reduction in risk is not entirely clear. Restoring normal levels of stable iodine to the diet in areas of endemic goiter might reduce thyroid stimulation by endogenous thyroid-stimulating hormone in such a way that any underlying damage from prior radioiodine exposure would not emerge. Evidence from animal studies indicates that decreasing thyroid stimulation after administration of radioactive iodine reduces the frequency of thyroid tumors.

Comprehensive epidemiologic evaluation of 3440 persons residing near the Hanford nuclear site as children at the time of iodine 131 releases has not identified a significantly increased risk of thyroid cancer or autoimmune thyroid disease. The estimated radiation risk coefficient for thyroid cancer in the Hanford study was 11-fold lower (excess relative risk, 0.7 per Gy) than that in pooled analyses of atomic bomb survivor and patients exposed to therapeutic x-rays as children (excess relative risk, 7.7 per Gy). This finding suggests that protraction of exposure, distribution of dose within the thyroid gland, or both, might be important factors in reducing subsequent risk. In contrast to the studies of children living near Chernobyl, the Hanford population was exposed only to iodine 131 and not to other shorter-lived, more energetic isotopes of radioiodine, and their diets were not known to be iodine deficient.

Although comparisons with the current investigation by Imaizumi et al are problematic in that the Adult Health Survey investigation is of prevalent thyroid neoplasms among survivors who were all screened, the estimated excess prevalence odds ratio for thyroid cancer was about 1.0 per Gy for those aged 10 years at exposure and lower than that reported in the atomic bomb and radiotherapy patient incidence series. This finding suggests a decline in risk with time since exposure.

There is inconclusive evidence linking low-dose exposures to environmental radiation and the risk of autoimmune thyroid disease. Data from ecologic studies around Chernobyl have been inconsistent, and clinical thyroid disease related to the presence of antithyroid antibody levels has not been observed. Further, the moderate or severe iodine deficiency around Chernobyl may have moderated the effect of any thyroid disease process. Dose-response analyses also have been conducted between iodine 131 thyroid doses and autoimmune disease following releases from the Hanford nuclear site, but the risks for hypothyroidism and autoimmune thyroiditis were unrelated to dose, consistent with the current investigation by Imaizumi et al.

In summary, the association between radiation and risk of thyroid disease has been studied for more than 60 years, and new findings continue to be reported. The risk following exposures in childhood apparently lasts for life, although it appears that the risk declines many years after exposure. The radiosensitivity of the young thyroid gland is high and most likely relates to subsequent proliferative activity of the gland during puberty and growth, but the reasons for the absence of risk following adult exposures are not entirely clear. The risk of thyroid cancer seems to be enhanced if diets deficient in stable iodine result in chronic thyroid stimulation. Exposure to iodine 131 alone appears to be associated with a lower risk compared with acute exposures to the atomic bomb or medical radiotherapy, perhaps due to the associated low dose rate and nonuniform distribution of dose in the gland. It remains to be confirmed whether potassium iodine supplements administered weeks after exposure can reduce the risk of radiation-related thyroid neoplasms and nodules in humans or whether this only occurs in areas of endemic goiter. While relatively low-dose radiation exposure can cause a wide range of adverse thyroid effects, autoimmune thyroid disease is apparently not one of them.
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Strengthening Primary Care to Bolster the Health Care Safety Net

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The future of primary care is in jeopardy, and nowhere is this more evident than in the current debate on physician workforce. Reversing its projections that the United States would be faced with a physician surplus by 2000,1,2 the Council on Graduate Medical Education in early 2005 projected a physician shortage by 2020.3 This conclusion was reached despite the council’s estimate that the number of physicians per 100 000 population would actually increase 5% between 2000 and 2020. The projected shortage is supported by forecasts that the US population’s demand for specialized services will increase more rapidly than the growth in physician supply.4

Just as the national consensus in the early 1990s of a specialty physician surplus was associated with a subsequent increase in the number of medical graduates choosing a primary care specialty (family medicine, internal medicine, or pediatrics), it appears that recent claims of a specialist shortage are having the opposite effects. In at least 1 state, residents completing specialist training receive more job offers than those trained as generalists,5 and medical graduates’ interest in family medicine is on the decline.6

The proclamations of a looming specialist shortage are made even though there is no evidence that more specialty care improves population health. Nations with a strong primary care infrastructure have better health outcomes than those such as the United States that emphasize specialty medicine.7 One reason for this phenomenon may be that primary care is much more important than specialty care in providing services to those most in need (ie, vulnerable populations), which serves to narrow health disparities associated with ethnic group, socioeconomic, and geographic residence status.

Amid the physician workforce banner on whether there are too many or too few physicians,8 consensus can be found regarding one claim: physicians in the United States are not equitably distributed.9 Geographic maldistribution of physicians creates pockets of medically underserved communities while others have excess supply. Market forces in the US health sector have failed to supply physicians where they are needed equitably.10

See also p 1042.
to clear minefields that were originally laid to protect military encampments, checkpoints, and other military objects.

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CORRECTION

Omission of Financial Disclosure Information: In the Editorial entitled “Thyroid Disease 60 Years After Hiroshima and 20 Years After Chernobyl” published in the March 1, 2006, issue of JAMA (2006;295:1060-1062), the financial disclosure information provided by the author at the time the Editorial was accepted was inadvertently omitted. Dr Boice had reported that he has provided expert testimony concerning thyroid cancer among persons living near the Hanford nuclear site, an involvement that has ended.