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Iodine Nutrition — More Is Better

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In normal adults, the daily production rate of the two biologically active thyroid hormones, tetraiodothyronine (which is better known as thyroxine and has four iodine atoms) and triiodothyronine (which has three), is approximately 100 μg and 30 μg, respectively. All of the thyroxine, but only about 20 percent of the triiodothyronine, is produced by the thyroid gland; the remainder of the triiodothyronine is produced through the extrathyroidal deiodination of thyroxine. A minimum of approximately 70 μg of iodine is therefore needed to produce these two hormones in the thyroid gland each day. But more than that is required, because iodine — whether ingested, released from the thyroid when the iodotyrosine precursors of the hormones are deiodinated, or released when the hormones are deiodinated in extrathyroidal tissues — is rapidly excreted in the urine. Infants, children, and pregnant or lactating women need more iodine, because their thyroxine production rate is relatively high.

The World Health Organization (WHO) has recommended that children 5 years of age or younger ingest 90 μg of iodine daily; children 6 to 12 years of age, 120 μg daily; adults, 150 μg daily; and pregnant or lactating women, 200 μg daily.[1] The prediction of iodine intake is difficult, if not impossible, because the amount of iodine in individual foods and in water can vary by a factor of 100.[2,3] The standard measure of iodine nutrition in a community or country is the median urinary iodine excretion, expressed in micrograms per liter. The values correspond to 70 to 80 percent of the daily iodine intake, which often varies widely among people in the same community or country.

Iodine can come only from external sources — mostly food, but also water. It is not widely distributed in nature; in the past, iodine deficiency was common among people on every continent. Many people are still deficient in iodine, despite major national and international efforts to increase iodine intake, primarily through the voluntary or mandatory iodination of salt. Indeed, in some countries, even salt for animals is iodinated. These efforts have been successful in many countries. However, iodine deficiency persists in many other countries (e.g., Australia, Russia, and some countries in Africa and Europe) (Fig. 1). The WHO estimates that approximately 2 billion people, including 285 million school-age children, still have iodine deficiency, defined as a urinary iodine excretion of less than 100 μg per liter.

An increase in iodine intake is only the first

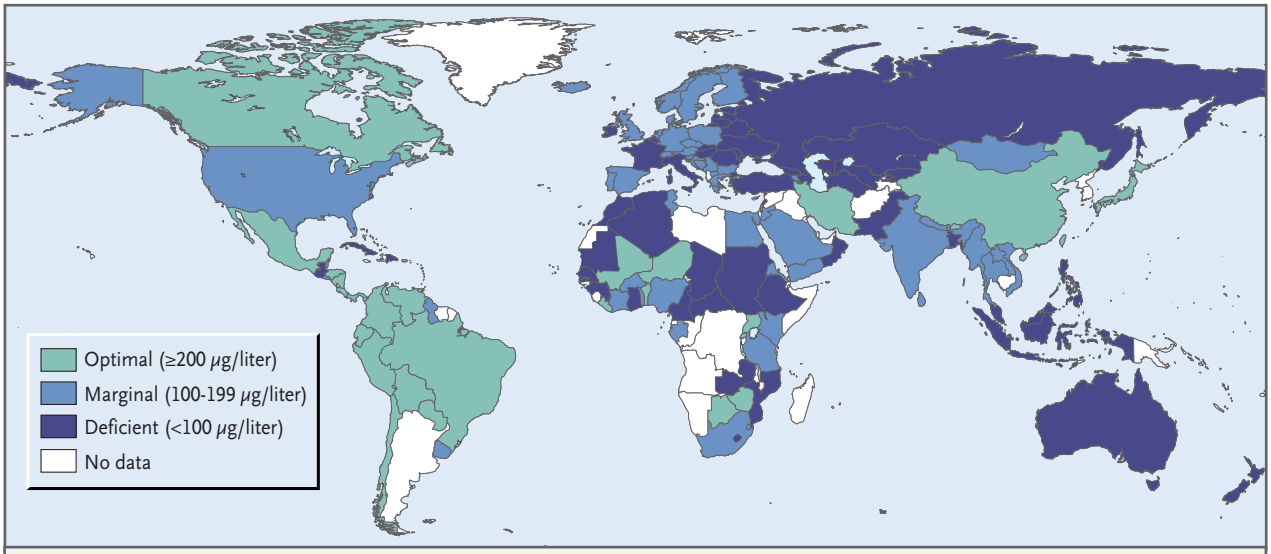

Figure 1. Worldwide Iodine Nutrition, Based on Measurements of Median Urinary Iodine Excretion.
Data are from the WHO[4] and the International Council for the Control of Iodine Deficiency Disorders (http://indorgs.virginia.edu/iccidd/mi/cidds.html).

step in the amelioration of iodine deficiency. The increase must be sustained, which has not always been the case. In the United States, where salt iodination is not mandatory but iodized salt (45 to 80 μg of iodine per gram of salt) is used in about 70 percent of households, the median urinary iodine excretion in adults declined from 320 μg per liter in 1971–1974 to 145 μg per liter in 1988–1994; and it was 168 μg per liter in 2001–2002.[5,6] Among pregnant women, the frequency of moderate iodine deficiency (urinary iodine excretion of less than 50 μg per liter) was 1 percent in 1971–1974 and 7 percent in both 1988–1994 and 2001–2002.[5,6] (According to the WHO, a median urinary iodine excretion of 100 to 199 μg per liter indicates that the iodine intake is adequate, but the U.S. data above suggest strongly that it should be considered marginal.) The causes of the decline include reduced salt intake and the reduced use of iodate in baking and iodine in animal husbandry, as well as the use of noniodized salt in processed foods. Iodine intake has also diminished in other countries — such as Australia, Guatemala, and Morocco — for similar reasons or because the iodination of salt was not monitored adequately or ceased.

What are the consequences of iodine deficiency and excess? The spectrum of chronic iodine-deficiency disorders is broad. Severe iodine deficiency in mothers and fetuses results in pregnancy loss and cretinism, with irreversible mental retardation, neurologic dysfunction, and growth retardation. Mild iodine deficiency results in learning disability, poor growth, and diffuse goiter in school-age children. These consequences of mild deficiency are easily understood — the production of thyroid hormones is reduced, and the thyroid gland enlarges to compensate for the reduction. In adults, mild iodine deficiency is also associated with nontoxic nodular goiter and, less often, with toxic nodular goiter, because the constitutive (thyrotropin-independent) growth and functional potential of some clones of thyroid cells increases.

The spectrum of disorders of iodine excess also includes hypothyroidism and hyperthyroidism. Milligram or higher doses of iodine may cause hypothyroidism in people with damaged thyroid glands and normalization of thyroid secretion in those with hyperthyroidism. This antithyroid action of iodine is often short-lived, owing to down-regulation of iodine transport into the thyroid gland, but such down-regulation does not occur in people with a damaged thyroid gland. Conversely, iodine in these quantities may induce hyperthyroidism in patients with a multinodular goiter or Graves' disease whose iodine intake is low, although it is unlikely to do so if the deficiency is not severe and if the increase in intake is relatively small.

A more important issue is whether some level of chronic iodine intake is harmful. Some classifications of iodine nutrition include categories of high or excessive iodine intake, because high levels of iodine intake have sometimes been associated with an increased risk of hyperthyroidism, hypothyroidism, or autoimmune thyroiditis. Indeed, fear of iodine-induced thyroid dysfunction has at times delayed or limited the implementation of iodine supplementation in regions with iodine deficiency. The divergent effects of such supplementation on thyroid disorders may be related to underlying thyroid autonomy or genetic susceptibility to the disorders. The evidence for these increased risks is based largely on the results of cross-sectional studies before and after iodine intake increased.

In this issue of the *Journal*, Teng et al.[7] provide new data on these risks. They studied people living in three regions of China in whom iodine intake was mildly deficient, more than adequate, or excessive (as defined by Teng et al.) and remained so for five years. The investigators found that more than adequate or excessive iodine intake was associated with a slightly increased cumulative five-year incidence of subclinical hypothyroidism and autoimmune thyroiditis, but not of overt hypothyroidism or hyperthyroidism. In many people, the first two disorders — both of uncertain clinical importance — were not sustained.

Overall, the small risks of chronic iodine excess are outweighed by the substantial hazards of iodine deficiency, which is still widespread. All these hazards — pregnancy loss, goiter, and mental retardation — are prevented by an adequate iodine intake. To achieve this, iodine intake should be increased in most countries, not only in those with iodine deficiency but also in those whose iodine intake is marginal, so the iodine intake is at least 300 to 400 μg daily. An increased intake is especially important for children and pregnant or lactating women. Given the highly variable iodine content of food and water, the best way to increase iodine intake is to increase the iodination of salt and to make salt iodination mandatory in most countries. Then, even mild iodine deficiency should be very rare.

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CLINICAL TRIAL REGISTRATION

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