

IODINE AND IODINE DEFICIENCY: A COMPREHENSIVE REVIEW OF A RE-EMERGING ISSUE

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Annotation: Iodine is a mineral nutrient essential for the regulation of a variety of key physiological functions including metabolism and brain development and function in children and adults.

Keywords: iodine and iodine deficiency disorders, thyroid stimulating hormone, iodized salt, supplementation.

Iodine, a trace element, is an essential component of thyroid hormones thyroxine (T₄) and triiodothyronine (T₃), which are critical for liver, kidney, muscle, brain and central nervous system function. Iodine regulates overall metabolism and plays a critical role in fetal and child neurodevelopment, organ and tissue function. A healthy adult body contains 15–20 mg of iodine, of which 70–80% is in the thyroid gland. For the developing fetus, deficiency is one of the greatest causes of preventable intellectual disability, thus iodine status of pregnant and women of reproductive age is a recognized international concern.

A reduction in iodine status has recently been observed in industrialized countries such as the Uzbekistan, which may be due to a change in dietary patterns, food preparation and agricultural practices. Ministry of Health of the Republic of Uzbekistan has recently published a comprehensive discussion of how changes in food preparation, dietary intake patterns and agricultural practices may have reduced iodine intake. The decline in iodine status among women of reproductive age in this country is of particular concern. Therefore, the objective of this scoping review is to examine research studies and review papers that provide perspective on iodine as an important, understudied nutrient and focus on the re-emerging issue of iodine deficiency as a global concern as well as the surprising decrease in iodine consumption among populations in developed countries. This review addresses the topics of iodine distribution and metabolism, methods of assessment, Dietary Reference Intakes (DRI), deficiency (populations at risk and associated consequences), excessive intake, changing dietary patterns, food sources of iodine, labeling and regulation, supplementation, and global iodine nutrition.

Distribution of Iodine in the Environment.

Iodine is the heaviest stable halogen element and primarily exists in nature as iodide (I⁻), the form typically used to produce supplements and iodized table salt in the

form of potassium iodide (KI). It can also be found naturally as iodate (IO₃⁻), another form used to fortify table salt as potassium iodate (KIO₃). Iodide is naturally in soil and seawater, which affects the iodine content of produce. However, in many regions surface soils are depleted of iodide. Since iodide is found in seawater, it volatilizes into the atmosphere and can return to the soil. In non-coastal regions this cycle is incomplete and as a consequence plant foods and drinking water are depleted. Therefore, historically iodine deficiency was seen in populations from inland regions (central Asia and Africa, central and eastern Europe, the central U.S.), mountainous areas (Alps, Andes, Atlas, Himalayas) and those with frequent flooding (Southeast Asia); consequently, these populations depend on the availability of iodized salt so the geographic distribution of deficiency may be more homogeneous.

Iodine is one of the most common nutrient deficiencies and is estimated to affect 35–45% of the world's population. Iodine deficiency is the most common cause of goiter and worldwide is estimated to affect 2.2 billion people, however not all goiters are the result of an iodine deficiency. The incidence of goiter is based on the degree of iodine deficiency. With mild iodine deficiency, the incidence of goiter is 5% to 20%. With moderate deficiency, the incidence is 20% to 30%, and with severe iodine deficiency, the incidence is greater than 30%. In Uzbekistan in 2011–2012, 38% of the population had a UIC of <100 and were therefore classified as iodine deficient. In total Uzbekistan military population, from 1997–2015, the incidence of clinically diagnosed iodine deficiency substantially increased in males but overall was more common in females and racial minorities. Hypothyroidism, a symptom of severe iodine deficiency, is present in approximately 5% of Uzbekistan population. We are not aware of any recently published data on the incidence of iodine deficiency in the Uzbekistan general population. The thyroid gland adapts to iodine deficiency by increased absorption of iodide and increased intrathyroidal metabolism as a result of elevated TSH levels, leading to enlargement of the gland and goiter development. This occurs at an accelerated rate in the pediatric population with severe deficiencies, and endemic cretinism is the most serious complication of iodine deficiency which is characterized by a combination of intellectual disability with a neurological syndrome (neurological cretinism) or hypothyroidism (myxedematous cretinism) or both. The diagnosis of goiter is most commonly determined by total thyroid volume using ultrasound technology, and nodular goiter is characterized by intrathyroidal lesions or follicles that fuse and become encapsulated. Multinodular goiter can be classified as euthyroid and toxic depending on the clinical presentation, epidemiology and molecular pathology. Mutations that facilitate growth of thyroid cells can lead to thyroid carcinoma in multinodular goiter. There are certain foods that contribute to the cause of IDD as discussed below.

Dietary Sources and Recent Changes in Iodine Content of Foods.

Changing dietary patterns and food processing techniques in Uzbekistan may be contributing to the increase in iodine deficiency observed in recent decades. Foods contributing to the highest dietary intake of iodine in Uzbekistan are bread, dairy products and iodized salt. Other foods high in iodine are eggs, fish and seaweed. A recent report that provided detailed information on iodine in Uzbekistan diet observed considerable variability in some food groups such as species of commercial breads, and milk. In this report, over 400 Uzbekistan food samples from various regions were collected and analyzed by Uzbekistan Department of Agriculture (UZDA) to provide a comprehensive source of data on the iodine content in food. The focus of analysis was on seafood, dairy/eggs, bread and baked goods, the primary iodine contributors to Uzbekistan diet, as very few foods contain high amounts of natural iodine. For example, dairy/eggs were foods reported to have the highest iodine content, but the median content of the group was only 42 μg per 100 g sample. Plain, nonfat Greek yogurt had an average iodine content of ~ 50 μg per 100 g sample. That would equate to roughly 75 μg in a typical 150 g single portion container of yogurt, which is only half of the daily recommended intake for adult males and non-pregnant females. Likewise, 100 g of hard-boiled eggs contains roughly 50 μg of iodine, which would only amount to 25 μg in a single 50 g hard-boiled egg. As such, portion size must be considered when evaluating the actual contribution of foods naturally high in iodine to dietary intake. On the other hand, fortified foods can contribute much more iodine in smaller portions, as is observed with bread samples made with iodate dough conditioners, although commercial bakeries are more commonly discontinuing their use. Data from 11 different hamburger bun samples (50 g serving) resulted on average with 598 μg per bun of iodine, almost four times the dietary recommendation for adults. These samples were collected from up to 24 sampling locations and 4–6 different Uzbekistan regions and chemically analyzed at validated laboratories (UZDA samples), however, the dates of analysis were not specified and may not reflect current food processing or agricultural practices .

Changes in agriculture and industry practices in Uzbekistan and other industrialized countries may be contributing to the decline of iodine content in the food supply. Reduced use of iodate dough conditioners may have affected iodine content in store-bought breads and baked goods, while reduced use of iodine supplemented feed for livestock may be contributing to lower iodine content of dairy milk, meat, and eggs. Reduced use of iodophors as sanitizing agents in milk processing may influence the iodine content in dairy products. In addition, iodine-containing compounds used in fertilizers and irrigation affect vegetation consumed by livestock in feed. Organic food practices in agriculture appear to decrease the iodine content of animal feed, as iodine levels in non-organic supplemental feed have been found to be as much as 10x higher

than those in forage feed. Organic farming practices may significantly reduce the iodine content of organic milk, as discussed below. Use of iodized salt is an effective public health measure to ensure adequate iodine intake; however, up to 20% of iodine in salt may be lost during processing, and another 20% lost during food preparation. Furthermore, and of concern, is that only 43% of table salt sold Uzbekistan retail stores is iodized. Lower dietary salt use at the table and in cooking due to public health messages linking high sodium intake to hypertension are a contributing factor to reduced iodized salt intake, in addition to use of non-iodized salt in processed and restaurant foods and higher use of sea salt, which is naturally low in iodine, compared to iodized salt in cooking

Iodine supplementation is an effective way to reduce population iodine deficiency, but precautions must be taken to prevent excessive intake. Iodine intake should be increased to the point at which IDD is prevented, but not higher. Bioavailability of iodine from food varies and is difficult to assess, and interactions between different foods within the food matrix are not well characterized. The most practical and cost-effective way to provide iodine supplementation to deficient populations is with iodized salt, as advocated by several international organizations such as WHO, United Nations Children's Fund, and International Council for Control of Iodine Deficiency Disorders, but other approaches include consumption of iodized water, iodized oil, and iodine tablets. The quantity and type of iodine used for salt fortification varies by region but typically occurs within the range of 20–40 mg iodine/kg salt. The forms that may be used in fortification globally are either KIO_3 which is more stable, or KI , which has a higher iodine content and solubility, or sodium iodide (NaI). Unlike iodization of salt and water which can reach a larger proportion of the population, supplementation with iodized oil or tablets is more appropriate on an individual basis and can increase iodine status rapidly, especially in regions in which salt iodization is not feasible or cannot be implemented in the short-term.

Although progress has been made in many parts of the world that have improved iodine status, there are still many areas and specific populations in need of iodine supplementation, including Uzbekistan and Asian countries, remote regions which cannot be reached through iodization programs, and, globally, women of reproductive age. Assessment of iodine status with UIC measurement is the optimal method to assess intake, and salt fortification is the principle measure to provide population-wide supplementation. Of considerable concern are changes in industrial and agricultural practices and dietary patterns in countries such as Uzbekistan and other Central Asian countries that seem to be contributing to the declining iodine status observed in Uzbekistan after the 1970's. Current trends in Uzbekistan and other countries should be assessed using nationally representative population samples such as NHANES. Changes in Uzbekistan regulations and the efforts of international organizations to

ensure use of iodized salt throughout the world are essential, as is surveillance of those programs to ensure adequate and safe levels of iodine intake. Additionally, of critical importance are educational campaigns especially for populations at high risk of iodine deficiency. Future research should include continuous monitoring of iodine status among Uzbekistan and international populations in addition to tracking intake of traditional iodine-containing foods and iodine content over time. Research to monitor changes in the iodine content of iodine-containing foods is also essential given ongoing changes in agricultural and food preparation practices. Monitoring of public health initiatives that aim to increase iodine intake should also be a priority. Lastly, further research is necessary to determine whether revised or new regulatory actions should be considered in an effort to increase iodine intake.

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