



Iodine May 2012

Indications

Iodine is one of the halogen series of elements (along with fluorine, chlorine and bromine); it was formerly used as an antiseptic, but is now regarded as too toxic for that purpose. In spite of its toxicity, iodine is an essential micronutrient element in humans; its only known function is as a component of the secretions of the thyroid gland, principally tri-iodothyronine and thyroxine. The current WHO RDA for iodine is 150 micrograms per day (or 250 micrograms per day during pregnancy) [1].

80 – 90% of the iodine in the blood is in the form of thyroxine; most of the remainder (5 – 15%) makes up the plasma inorganic iodide, which is the fraction of the circulating iodine that is filtered at the glomerulus and passes into the formed urine. Regulation of body iodine does not occur via changes in the glomerular filtration rate (as is the case with other essential elements) and the kidney has no mechanism to conserve iodine. The urine is the major (92%) route for iodine excretion [2] and the urine iodine concentration correlates closely with both the plasma inorganic iodide and the dietary intake of iodine. The **daily iodine intake** can be calculated from the **urine iodine concentration (ppm) x 0.0235 x body weight (kg)** [3].

A common method for correction of iodine deficiency is salt iodization – the addition of potassium iodate to salt for human and livestock consumption to give a concentration of c. 15 ppm of iodine – with the urinary iodine concentration as the principal indicator of effect. There is no mandatory iodization of salt in the United Kingdom and, to date, no systematic monitoring of the population iodine status.

Interpretation

The urine iodine concentration is recommended by the WHO as the best single indicator of iodine nutrition, with the following stratification of reference values [1]:

Urine iodine $\mu\text{mol/L}$	Urine iodine $\mu\text{g/L}$	Iodine intake	Iodine nutritional status
0–0.15	< 20	Insufficient	Severe deficiency
0.16–0.38	20–49	Insufficient	Moderate deficiency
0.40–0.78	50–99	Insufficient	Mild deficiency
0.79–1.56	100–199	Adequate	Optimal
1.57–2.36	200–299	More than adequate	Risk of iodine-induced hyperthyroidism
$\geq 2.37 \mu\text{mol/L}$	≥ 300	Excessive	Risk of hyperthyroidism and autoimmune thyroid disease

The reference value for urine iodine corrected for creatinine is 0.16 – 0.42 mmol iodine / mol of creatinine [4].

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Iodine deficiency diseases continue to constitute a major health problem in many countries with some 656 million people suffering from goitre worldwide; iodine deficiency diseases remain a problem even in some developed countries [5].

Biolab's recent results for urine iodine (n = 1000) suggest that more than 50% of the UK population has some degree of iodine deficiency, This is in agreement with the current literature [6].

Iodine supplementation.

Normally there is a high tolerance to ingested iodine with a wide safety margin [7,8,9]. An upper dietary limit of 2 mg per day has been proposed, which is exceeded only exceptionally. On a high seaweed diet in Japan, intakes of 5 mg per day have been reported to cause no ill-effects and some individual may consume more than this amount.

It is, however, not correct to assume that the administration of iodine is entirely non-hazardous, as it can have profound and variable effects on thyroid gland function. Iodine is a known goitrogen at high intake levels, an action which is used in clinical medicine in a number of circumstances.

Substantial increases in the dietary intake of iodine can have paradoxical and counter-intuitive effects. Common causes of iodide toxicity include heavy applications of iodine (for example as povidone-iodine) to open wounds, large injections of iodine radio-contrast media and amiodarone treatment for cardiac arrhythmias (amiodarone contains 75 mg of iodide per 200mg tablet and both hypothyroidism and hyperthyroidism are listed as potential adverse effects of its use).

In such cases there is a definite progression of events:

- a rapid decrease in release of T3 and T4 from thyroglobulin;
- decreased I^- uptake by the thyroid gland;
- decreased organification of I^- and hence decreased T3 and T4 synthesis.

These changes will culminate in hypothyroidism, with low plasma T3 and T4 and a high TSH.

If the thyroid gland was normal before excess iodine administration, then, as the iodide level in the gland falls in response to decreased iodine uptake, normal thyroid function is restored. However, if there was previous thyrotoxicosis or Hashimoto's disease, permanent hypothyroidism with goitre may result.

Conversely, thyrotoxicosis may result from excess iodine administration if the gland was previously adenomatous. In adults with a goitre due to iodine deficiency, iodine supplementation may also precipitate thyrotoxicosis (the Jod Basedow phenomenon).

The thyroid-suppressive action of iodine is still used as an acute therapeutic intervention (iodine solution is given orally to control thyrotoxicosis pre-operatively), in thyrotoxic crisis ('thyroid storm') and for thyroxine cardiotoxicity. In the "pre-carbimazole" era, high dose iodine (1.0 to 6.0 mg per day) was used as a long term treatment for hyperthyroidism.

Though there is often tolerance to high doses of iodine (as is reported from Japan) adverse effects can occur as a result of either high supplemental doses or following modest increases in intake in populations after the introduction of iodised salt. In the UK, the Guidance Level for iodine supplements was set at 500 μ g per day (i.e. 0.5 mg) by the Food Standards Agency in 2003, which could result in a maximum Total Safe Intake of 940 μ g per day (0.94 mg). The equivalent US Tolerable Upper Intake Level from all sources is 1,100 μ g (1.1 mg). Both the UK Reference Nutrient Intake and the US RDA are 150 μ g (0.15 mg). However, the US Institute of Medicine advises that those with autoimmune thyroid disease or nodular goitre may respond adversely to doses of iodine within this range and considerable caution should be used. The mild iodine deficiency that is now seen in the UK can be easily corrected by emphasis on iodine-rich foods (cow's milk and goat's milk products, fish - especially mackerel - and the use of iodised salt), together with modest supplements of 150 to 300 μ g (0.15 – 0.30 mg) per day for several months.

The adverse effect of very high intakes of supplemental iodine on thyroid function was observed in Peace Corp workers in West Africa who demonstrated a high rate of thyroid dysfunction and goitre after using iodine-treated water [10]. Their estimated daily iodine intakes for a period of several months was reported to be in the region of 50 mg per day. Observed effects included goitre, raised TSH levels and raised levels of thyroid peroxidase antibodies. The prevalence of these abnormalities substantially reduced when high iodine intakes ceased.

To emphasise that significant changes in thyroid function can result from even modest increases in iodine intake, a recent Danish study [11] reported on the increased incidence of overt hypothyroidism in subjects in the age range of 20 – 59 years following on the iodine fortification of salt. This measure was introduced in Denmark in 1998 and resulted in an across-the-board increase in iodine intake in the Danish population. Possible causes of the observed increase in the incidence of hypothyroidism were suggested as:

- an increase in autoimmune thyroid disease, provoked by excess iodine,
- intra-thyroidal synthesis of iodinated arachidonic acid derivatives, which normally acts as a negative feedback protection against a sudden iodine load,
- an iodine-induced increase in the rate of apoptosis of thyroid follicular cells.

Conclusions on iodine supplementation

- a) The predominantly mild iodine deficiency now seen in the UK can be corrected with iodine-rich foods (cow's milk and goat's milk products, fish - especially mackerel - and the use of iodised salt), together with modest supplements of 150 to 300 µg (0.15 – 0.30 mg) per day of iodine from kelp for several months.
- b) High-dose iodine (greater than 2 mg per day) has a number of medical uses and practitioners should consider carefully before they recommend high dose nutritional supplementation with iodine.
- c) There are a number of potential effects on thyroid function that may derive from increasing the amount of iodine ingested; even marginal increases in intake over long periods of time have been shown to adversely affect thyroid function in some subjects.

Patient preparation for urine iodine testing

The patient should discontinue nutritional supplements and medication the day before the collection of a urine sample (iodine is a component of the material used in pharmaceutical capsules).

Specimen requirements

A random urine sample is the specimen of choice for the assessment of iodine intake. The WHO reference interval [1], quoted above, is based on random urine specimens.

Postal samples should reach Biolab within 48 hours of collection.

Methodology

Iodine is measured by inductively coupled plasma-mass spectrometry (ICPMS).

Turn around time

3-4 working days.

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