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# Mild iodine deficiency and thyroid disorders in Hong Kong

## 香港中輕微的碘缺乏症和甲狀腺疾病

**Objectives.** To review evidence of iodine deficiency and clinical thyroid disorders in Hong Kong.

**Data sources.** Publications on local dietary iodine intake, the iodine content of local food items, and clinical thyroid problems in the Hong Kong population.

**Data extraction.** Data was extracted and evaluated independently by the authors.

**Data synthesis.** Iodine is an essential nutrient. Iodine deficiency can lead to goitre, hypothyroidism, mental deficiency, and impaired growth. It is now appreciated that determination of goitre incidence in children alone may grossly underestimate the problem of iodine deficiency in a population. In total, the evidence indicates that iodine deficiency exists in Hong Kong, leading to clinical problems of transient neonatal hypothyroidism, goitrogenesis, and thyroid disorders in pregnant women and neonates, as well as thyroid dysfunction in the elderly.

**Conclusion.** A supplementation programme aimed at a relatively uniform iodine intake is recommended to avoid deficient or excessive iodine intake in subpopulations.

### Key words:

Goiter;  
 Hypothyroidism;  
 Iodine, deficiency;  
 Pregnancy;  
 Thyroid diseases

### 關鍵詞：

甲狀腺腫；  
 甲狀腺機能減退；  
 碘，缺乏；  
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**目的：**總覽香港中碘缺乏症和臨床甲狀腺疾病的證據。

**資料來源：**有關本地人從食物中攝取碘，本地食品碘含量及香港人口中臨床甲狀腺疾病的出版刊物。

**資料選取：**資料由筆者選取並獨立評價。

**資料綜合：**碘是基本的營養要素。缺乏碘可導致甲狀腺腫、甲狀腺機能減退、弱智和發育不良。人們已意識到僅考慮兒童中甲狀腺腫的病例可能會大大低估全部人口中缺乏碘的問題。總之，證據顯示香港人存在碘缺乏的問題，缺乏碘可導致新生兒短暫性的甲狀腺機能減退、甲狀腺腫、孕婦及新生兒的甲狀腺疾病、以及老年人的甲狀腺機能減退等臨床疾病。

**結論：**筆者推荐了一項旨在均衡攝取碘的計劃，以避免在不同人口中出現缺乏碘或過量攝取碘的情況發生。

## Introduction

Iodine is an important trace element and an essential substrate for the synthesis of thyroid hormones. The two major thyroid hormones, triiodothyronine ( $T_3$ ) and tetraiodothyronine ( $T_4$ ), are iodinated molecules which exert diverse effects on cellular metabolism, growth, and development.

Due to the importance of thyroid hormone-dependent processes, iodine deficiency has deleterious effects on individuals, especially pregnant women and growing children. The clinical and subclinical manifestations of iodine deficiency are collectively referred to as iodine deficiency

disorders (IDD). Iodine deficiency disorder is a serious global public health problem, estimated to affect one billion people worldwide.<sup>1</sup> Dietary iodine deficiency is the major cause of intellectual deficit worldwide.<sup>2-4</sup> In areas of endemic goitre and cretinism, the problem of iodine deficiency is not difficult to recognise. However, it has been realised only in recent years that milder forms of iodine insufficiency exist in non-goitrous areas, presenting in a more subtle manner—with increased pregnancy loss, increased perinatal and infant mortality, neonatal hyperthyrotropinaemia, neonatal hypothyroidism, growth retardation, and intellectual disability in children.<sup>5</sup>

Since the establishment of the International Council for Control of Iodine Deficiency Disorders in 1986, there has been greatly increased awareness of iodine deficiency as a major preventable cause of mental retardation. The World Health Organisation (WHO) aimed to eliminate IDD by the year 2000. Its recommended daily iodine intake levels are:

- at least 90 µg for children of 0-59 months;
- 120 µg for children aged 6-9 years;
- 150 µg for individuals older than 12 years, adolescents and adults; and
- 200 µg for pregnant and lactating women.<sup>6</sup>

Recent reports have shown that, with the exception of Japan, various degrees of dietary iodine deficiency exist in South-East Asia.<sup>7</sup> It has been estimated that 40% of individuals with IDD worldwide live in China, especially in the mountainous and inland regions.<sup>8</sup> To eliminate IDD, the most common and widely used intervention is iodine supplementation, using salt as the vehicle.<sup>9</sup> Salt iodisation involves the addition of a small amount of iodine (20-100 mg of iodine per kg of salt, or parts per million [ppm]). Added iodine is in the form of potassium iodate rather than potassium iodide, due to the greater stability of the former,<sup>10</sup> particularly in countries with warm, damp, or tropical climates. Research has shown that supplementation by salt iodisation in populations with IDD results in effective clinical improvement and considerable reduction in all manifestations of IDD, including cretinism and goitre.<sup>11,12</sup> Furthermore, salt iodisation has been proven to be extremely cost-effective, at approximately US\$0.5 per person per year. Currently, 75% of affected countries worldwide have legislation relating to iodisation of salt, and 68% of affected populations have access to iodised salt. In China, legislation allowing iodisation of salt was passed in 1996, and in southern China and Guangzhou, salt has since been iodised at 20-50 ppm, with the aim of retention of 20 ppm at the consumers' level.<sup>13</sup>

Hong Kong—a coastal city in southern China—is not an endemic goitrous area, and IDD is not known to be prevalent. Most of the salt supply in Hong Kong comes from the southern provinces of China. A recent survey conducted by the Hong Kong Consumer Council of local brands of salt sold in supermarkets and grocery stores, showed either no iodisation or low levels of iodisation, however.<sup>14</sup> It is generally believed that iodine deficiency as a cause of clinical thyroid problems does not exist in Hong Kong, an affluent city with a plentiful supply of seafood. There is circumstantial contradictory evidence refuting this belief, however. This paper reviews the current situation with respect to iodine intake and thyroid dysfunction in Hong Kong.

### **Iodine intake in Hong Kong**

To determine whether IDD exists in Hong Kong, it would be necessary to document the dietary iodine intake of the Hong Kong population. The lack of detailed information on iodine content for most Chinese food items, however, makes estimation of dietary intake difficult. Urinary iodine estimation is an accepted alternative to determine the iodine intake of a population.<sup>6</sup> Using a cut-off value for fasting urine iodine concentration of 0.79 µmol/L (100 µg/L), it was found that 45.3% of children, 51.7% of adults, and 55.3% of the elderly in Hong Kong had urine iodine concentrations below this criterion.<sup>15</sup> Fasting urine concentrations below 0.79 µmol/L are defined by the WHO as a state of iodine insufficiency.

Two surveys investigating the urine iodine excretion of children in Hong Kong have also been completed. One conducted in 1995 to 1996, showed a median value of 0.96 µmol/L (121 µg/L),<sup>15</sup> while the other, performed in 1996 to 1997, showed a median value of 190 µg/L.<sup>16</sup> These values are on the whole higher than those reported for adults in Hong Kong. This is probably due to the different eating habits of children, which lead to a comparative increase in iodine intake. For example, children's intake of iodine may be higher due to the fortification of iodine in milk (at the level of 40 to 50 ppm), the consumption of roasted seaweed as snacks, and the increase in the popularity of Japanese foods, such as sushi and seaweed rolls, in this age-group.

### **Transient neonatal hypothyroidism**

A pointer to possible dietary iodine insufficiency in Hong Kong is the high percentage of newborns with elevated cord blood thyroid stimulating hormone

(TSH) values, and the high incidence of transient neonatal hypothyroidism. One of the parameters for iodine deficiency is the incidence of elevated TSH in newborn babies.<sup>6</sup> The neonatal thyroid screening programme, determining cord blood TSH level, was launched in 1982 in Hong Kong. This programme was initiated at the Queen Mary Hospital<sup>17</sup> and subsequently extended by the Clinical Genetic Service of the Department of Health in 1984, to include all hospitals in Hong Kong. Data from this programme initially revealed that the mean cord blood TSH value was 7.0 mU/L. Fifty percent of neonates had a cord blood TSH level greater than 5.6 mU/L and approximately 22% of neonates had a cord blood TSH value greater than 10 mU/L (equivalent to a whole blood TSH value of 5 mU/L).<sup>17</sup> The high incidence of elevated cord blood TSH values in neonates in Hong Kong has not changed over the past two decades. In iodine-sufficient or iodine-replenished areas, the percentage of babies with elevated TSH values (>5 mU/L in whole blood samples) detected through neonatal screening programmes is less than 3%.<sup>6</sup>

It is now appreciated that both neonatal thyroid function and neonatal TSH level serve as very good indices of the iodine supply for the population as a whole, since newborns are more sensitive than adults to iodine deficiency.<sup>6,18</sup> In Europe, where mild-to-moderate iodine deficiency exists in some countries, the incidence of transient primary hypothyroidism is six times higher than that observed in the US where salt is iodised.<sup>19,20</sup> In Hong Kong, approximately 23% of the cases of congenital hypothyroidism detected by the Neonatal Thyroid Screening programme were transient in nature.<sup>17,21</sup> At Queen Mary Hospital, with a cord blood TSH level >25 mU/L used as the cut-off, retesting was indicated in approximately 1.5% of screened neonates. Infants with transient congenital hypothyroidism had a low serum T<sub>4</sub> level, and a TSH level >40 mU/L on the confirmatory blood sample or a TSH level between 20 and 40 mU/L on three occasions. These children were treated with thyroid-replacement therapy but were able to maintain normal thyroid function when thyroxine treatment was routinely withdrawn in order to reconfirm the diagnosis at the age of 3 years. The cause of this transient neonatal hypothyroidism was not attributed to transplacental transfer of inhibitory TSH-receptor antibodies.<sup>22</sup> In iodine-sufficient areas, the incidence of transient neonatal hypothyroidism is low. For example, in the US, only 2% of cases with congenital hypothyroidism are transient in nature, and the cause is mainly attributed to transplacental transfer of maternal TSH receptor-blocking antibodies.<sup>23</sup>

## Maternal goitrogenesis and foetal hypothyroidism

One of the subpopulations at risk for IDD is pregnant women. Pregnancy increases the maternal requirement for iodine intake. This is due to the increased renal clearance of iodine from the kidney, as well as to the transfer of iodine and iodothyronines to the foetus.<sup>24</sup> Monodeiodination of iodothyronines within the placenta also increases the demand for iodine as the placenta enlarges. Previous studies conducted in Europe revealed that a marginally low iodine intake of <50 µg per day was sufficient to pose a significant challenge to both the maternal and neonatal thyroid gland, resulting in goitre formation in the mother and hypothyroidism in the neonate.<sup>25</sup>

To evaluate the problem of dietary iodine insufficiency during pregnancy, a cross-sectional study of 253 healthy, southern Chinese pregnant women and their neonates was conducted in Hong Kong in 1996.<sup>26</sup> The results demonstrated the existence of borderline iodine supply for many, with 35.8% of pregnant women having a urinary iodine concentration below 0.79 µmol/L. This borderline iodine intake in pregnant women had a significant effect on both maternal and foetal thyroid function as evidenced by the following:

- (1) a negative correlation between maternal serum TSH concentration and urinary iodine concentration;
- (2) higher cord blood TSH levels in infants whose mothers had a low urinary iodine concentration compared with those whose mothers had normal urine iodine concentrations; and
- (3) women who had given birth to infants with a cord blood TSH level ≥16 mU/L had lower urinary iodine concentrations and serum free T<sub>4</sub> levels compared with those who had given birth to infants with normal cord TSH levels, and their infants also had higher cord blood thyroglobulin (Tg) levels.

To further evaluate the impact of iodine insufficiency in pregnant women and their neonates in Hong Kong, a prospective study was undertaken.<sup>27</sup> Two hundred and thirty healthy women were studied from the first trimester of pregnancy until 3 months after delivery. Increased urinary iodine excretion was seen from the first trimester onwards. There was a progressive reduction in circulating free T<sub>4</sub>, free T<sub>3</sub> concentration, and free thyroxine index (FTI) with increasing gestation, with subnormal levels at term of 53%, 61%, and 5%, respectively. Thyroid stimulating hormone was increased two-fold at term. Overall, thyroid volume (TV) as determined by ultrasonography

was increased by 30% between the first and the third trimester. Twenty-five percent of pregnant women at term demonstrated goitre enlargement according to the WHO definition of >18 mL. In contrast, studies conducted in areas with adequate iodine intake due to national dietary iodine supplementation programmes, such as in the US, have shown no enlargement of the thyroid gland or, at most, enlargement of <5% during pregnancy.<sup>28</sup> Furthermore, it has been noted that the change in TV in women during pregnancy in the Hong Kong study was correlated negatively with their urine iodine concentration ( $r = -0.15$ ,  $P < 0.02$ ) at term.<sup>28</sup> Six percent of these women showed excessive thyroïdal stimulation, as evidenced by a lower serum FTI and higher Tg levels when compared with subjects without evidence of thyroïdal stimulation. In addition, these subjects had lower urine iodine concentrations, a lower serum FTI but higher Tg and free T<sub>3</sub>/free T<sub>4</sub> ratios, as well as a larger TV throughout pregnancy. Their neonates also had higher cord blood TSH, Tg, and a slightly larger TV. Fifty percent of neonates had subnormal free T<sub>4</sub> at birth. Thus, pregnancy in a borderline iodine-sufficient environment results in maternal hypothyroxinaemia, maternal goitrogenesis, as well as neonatal hypothyroxinaemia, hyperthyrotropinaemia, and thyroid hyperplasia.

### Goitre incidence in children

Thyroid enlargement or goitre is the most prominent consequence of iodine deficiency. The prevalence of clinical goitre in school children has been widely adopted as a population screening measure for iodine deficiency,<sup>6</sup> with a total goitre rate (TGR) of 5% or more indicating that iodine deficiency is a public health problem in that area. A study of school children in a selected region of Hong Kong noted a TGR of 3.5%.<sup>16</sup> On the basis of this finding alone, it seems that there is no need for general iodine supplementation in Hong Kong. However, although goitre and borderline iodine deficiency do not appear to be prevalent in the school-aged child, iodine deficiency clearly is a clinical issue during later life, particularly during pregnancy and in old age.

### Hypothyroidism

Another circumstantial feature suggesting the possible existence of iodine deficiency in Hong Kong is the low prevalence of autoimmune thyroiditis and hypothyroidism seen. The prevalence of elevated TSH (>5 mU/L) in the elderly population has been reported at only 1.0%,<sup>29</sup> compared with 10% in Caucasians residing in iodine-sufficient areas.<sup>24</sup> Furthermore,

examination of thyroid function tests in the elderly female population in Hong Kong revealed an increased T<sub>3</sub>/T<sub>4</sub> ratio and a rising trend in Tg with ageing.<sup>29</sup> This pattern of thyroid function test results is commonly seen in situations where there is borderline thyroid reserve associated with iodine insufficiency.

Epidemiological data show that differences in iodine intake may affect the prevalence of autoimmune thyroid disease. It has been reported that the prevalence of autoimmune thyroid disease is low in regions with low dietary iodine. Robuschi et al<sup>30</sup> reported a low prevalence (0.6%) of subclinical hypothyroidism in Italy where there is low dietary iodine intake, compared with a prevalence of 14% in the US, where the dietary iodine intake is much higher. In Japan, where there is a very high iodine intake, hypothyroidism is very common and a positive correlation between the prevalence of excess iodine intake and high serum TSH has been found in various areas of Japan.<sup>31</sup>

### Hyperthyroidism

The incidence and causes of hyperthyroidism in a population can also reflect iodine intake. An epidemiological study conducted in Denmark, found that hyperthyroidism was significantly more common in an area of low iodine intake compared with another area with high iodine intake.<sup>32</sup> Although the incidence of Graves' disease (GD) was similar in both areas, the area with low iodine intake had significantly more cases of multinodular toxic goitre—especially in elderly women—resulting in significant morbidity, such as cardiac arrhythmias, osteoporosis, and muscle wasting. Unfortunately, data on the age-specific incidence of various forms of hyperthyroidism is not available in Hong Kong for comparison.

### Elimination of iodine deficiency disorders in Hong Kong

Overall, the collective evidence reviewed indicates that the dietary iodine intake of the Hong Kong population is borderline sufficient, but is inadequate to meet extra requirements at times of thyroïdal stress, such as during pregnancy, neonatal, and pubertal growth. In addition, this review makes clear that using goitre rates in children only as an indicator may result in a serious underestimation of the nature and magnitude of the problem of IDD in many regions, including Hong Kong.

It is important to recognise the existence of iodine deficiency, however mild, during pregnancy. It has

been shown that even a mild degree of maternal iodine deficiency and maternal hypothyroidism during pregnancy can result in poorer psychological and neurological performance in the child, as well as neonatal hypothyroidism.<sup>33-35</sup> Transient low levels of circulating thyroxine at the critical stage of brain development in the newborn has been shown to result in an intelligent quotient loss of 5 to 10 points.<sup>36</sup>

Iodine supplementation has to be early, as treatment initiated in the third trimester can improve brain growth and developmental achievement, but has no influence on the neurological status of the affected child.<sup>3</sup> Besides, early iodine supplementation can prevent goitre development in both the pregnant mother and the foetus.<sup>37</sup> According to the WHO recommendations, daily iodine intake for pregnant and lactating women should be 200 µg per day.<sup>6</sup>

Iodine supplementation during pregnancy is essential in Hong Kong because seafood is not commonly consumed.<sup>15</sup> According to a dietary survey, 50 to 80% of subjects never consumed high iodine-containing foods, such as seaweed, kelp, or laver, and seafood intake was low in those subjects with low iodine status. Infrequent consumption of iodine-rich foods may stem from public ignorance of the physiological functions of iodine and the devastating consequences of its deficiency.<sup>38</sup> There are only a few places in the world that could ensure adequate dietary iodine intake through natural food sources. The majority of the world's population achieve adequate iodine intake through national supplementation programmes, namely the iodisation of salt or other vehicles.

Currently there is no programme to eliminate iodine deficiency in Hong Kong due to the assumption that IDD is non-existent, and the misconception that a high incidence of thyrotoxicosis and thyroid cancer is related to excessive iodine intake. In Hong Kong, the majority of patients with thyrotoxicosis have GD. There is, in fact, no published evidence to demonstrate that increases in iodine intake cause GD. Current evidence indicates:

- (1) remission rates with antithyroid drug treatment of GD are lower in areas with higher iodine intake<sup>39</sup>;
- (2) the response to thionamide drugs is rapid in GD patients who reside in IDD areas and the dose required to control the disease is smaller<sup>40</sup>; and
- (3) excess iodide administered to hyperthyroid patients with GD increases TSH receptor-antibodies.<sup>41</sup>

It is possible that large quantities of iodides administered to patients with latent GD may result in frank

hyperthyroidism. However, there is to date no published evidence to support this speculation.

With respect to thyroid cancer, the overall incidence is not influenced by the iodine intake of the population. However, the distribution of differing types of thyroid carcinoma appears to be related to the intake of iodine, with fewer of the more aggressive follicular and anaplastic carcinomas, and more papillary carcinomas in iodine-rich areas. Populations commencing iodine prophylaxis exhibit an increase in the ratio of papillary to follicular carcinomas.<sup>42</sup>

There is also concern that an increase in iodine intake may result in an increased incidence of thyroid dysfunction—iodine-induced hyperthyroidism (IIH)<sup>43</sup> and iodine-induced hypothyroidism.<sup>44</sup> It has long been known that thyrotoxicosis may develop in people with normal thyroid glands when they are exposed to large amounts of iodine, such as post-radio-contrast media or with amiodarone treatment; and that thyroid function may return to normal when the iodine is withdrawn. Hyperthyroidism is seen in certain individuals residing in low iodine intake regions when they are exposed to an intake of iodine that is more than they are usually accustomed to, particularly in the presence of existing nodular changes in the thyroid gland.

An increased incidence of hyperthyroidism following the introduction of iodised salt has been reported in severely iodine-deficient countries.<sup>45</sup> However, populations in these areas were exposed to iodine excesses due largely to poor monitoring of the quality of the iodised salt and of the iodine intake of the population.<sup>43</sup> The incidence of IIH during national iodine prophylaxis programmes in many countries has been low, and usually disappears several years after the initiation of the programme.<sup>45</sup> Iodine-induced hyperthyroidism is most commonly encountered in older people with long-standing nodular goitre, and in regions of chronic iodine deficiency, but instances of IIH in the young have also been reported.<sup>46</sup> This customarily occurs after an incremental rise in mean iodine intake in the course of a national iodisation programme, and is transient. Hence it should not be regarded as a contraindication to an iodisation programme, given the enormous long-term benefits of the elimination of iodine deficiency on the whole population, especially in the improvement in children's mental and physical health, as well as in women's health. With a systematic programme involving small increments in the level of salt iodisation and close monitoring of the programme, the problem of IIH can be minimised.

Contrarily, iodine-induced hypothyroidism, through a habitual intake of large amounts of seaweed (1-43 mg/d of iodine, ie 10-4300 times the daily iodine requirement) was reported in Japan.<sup>44</sup> Most hypothyroidism is reversible, although severe cases may be irreversible.<sup>47</sup> Histologically, the thyroid gland develops focal lymphocytic thyroiditis with a more severe degree of destruction in these cases.

Overall, the iodine intake of the Hong Kong population should be brought up to a level at which IDD can be avoided but no higher. Health care policies are urgently needed to establish intervention programmes aimed at a relatively uniform iodine intake, avoiding deficient or excessive iodine intake in subpopulations. In the interim period, at-risk subpopulations including pregnant and lactating women, and young children of up to 3 years should receive physiological doses of potassium iodate supplementation.

## Conclusion

Iodine deficiency disorder is a major public health problem worldwide. Although Hong Kong is not a goitrous or an endemic iodine-deficient area, evidence suggests the existence of mild iodine deficiency, which can result in clinical IDD. A supplementation programme aimed at a relatively uniform iodine intake is recommended, to avoid deficient or excessive iodine intake in subpopulations.

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