Commentary: Iodine deficiency as a new challenge for industrialized countries: A UK perspective

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The World Health Organization (WHO) estimates that worldwide 2 billion people, including 285 million school-age children, still have iodine deficiency despite major national and international efforts to increase iodine intake, primarily through the voluntary or mandatory iodization of salt. Iodine deficiency has substantial effects on growth and development and is the most common cause of preventable mental impairment worldwide. Although endemic cretinism had been long recognized to be associated with iodine deficiency, the article from Pharoah, Buttfield and Hetzel in 1971 recognized the importance of severe iodine deficiency and its correction in early pregnancy in a classic interventional epidemiological study. The recent Copenhagen Consensus of 2008 (www.copenhagenconsensus.com) identified salt iodization as the third most important and cost-effective intervention for confronting ten great global challenges. Although the introduction of iodized salt has considerably improved the situation globally in the developing world, iodine deficiency remains an issue in continental Europe where it is estimated that up to 50% of the children live in iodine-deficient communities. Mild iodine deficiency impairs cognition in children, and moderate to severe iodine deficiency in a population reduces the intelligence quotient by 10–15 points. Iodine supplementation pre-pregnancy may prevent this adverse effect on the intellectual development of infants and children. Mild to moderate iodine deficiency occurs in areas that are not immediately recognized as iodine deficient.

Iodine deficiency has historically been considered an issue for developing countries rather than industrialized countries such as the UK. Endemic goitre associated with iodine deficiency was at one time widespread in the UK and Medical Research Council surveys in 1924 and 1944 reported visible goitre in up to 50% of the adult women and schoolgirls. No salt iodization programme was adopted in the UK unlike in other European countries. Since the 1940s, significant changes in farming practice in the UK were associated with a rise in the iodine content of milk, particularly during winter months when cattle are dependent on iodine-rich artificial feed. In addition, successive UK governments from the 1940s encouraged increased milk consumption in schoolchildren. By the 1980s, this resulted in the iodine content of milk alone being almost sufficient to meet the recommended daily requirement of 150 μg/day and has been described as an ‘accidental public health triumph’. Although national monitoring of milk iodine content continued, the major concern was to avoid the harmful effects of iodine toxicity rather than deficiency.

My interest in thyroid epidemiology was stimulated where as a research fellow in Newcastle-upon-Tyne working with Mike Tunbridge who had led the original Whickham survey documenting the prevalence of thyroid disorders in a representative sample of the UK in the early 1970s. Sixteen percent of the cohort had small but easily palpable diffuse or multinodular goitres. In men, the prevalence of goitre declined with age from 7% in those aged <25 years to 4% in those aged 65–74 years. Among the women, 26% had a goitre; the frequency ranged from 31% in those aged <45 years (mostly diffuse) to 12% in those aged over 75 years (who had a higher proportion of multinodular goitre). In the 20-year follow-up of the Whickham cohort, 10% of the women and 2% of the men had a goitre, as compared with 23 and 5% respectively, in the same subjects at the first survey. The presence of a diffuse goitre was not predictive of any clinical or biochemical evidence of thyroid dysfunction. In women, there was no association between goitre and thyroid antibody status in the initial survey but at the 20-year follow-up, there was a weak association. Although the order in which these
Recent epidemiological data from the US and The Netherlands suggest that the children of women with hypothyroxinaemia rather than high serum thyrotrophin (TSH) may have psycho-neurological deficits and delayed mental and motor function when compared with controls.\textsuperscript{10,11} A similar range of deficits had been observed in children in classic areas of iodine deficiency such as Papua New Guinea.\textsuperscript{3} I attended the Iodine Symposium at the American Thyroid Association meeting in 2009 where Professor Eastman described the findings of the Australian National Iodine Nutrition Study.\textsuperscript{12} Even in areas previously thought to be iodine sufficient, such as Australia and New Zealand, there was evidence of substantial gestational iodine deficiency, which may lead to low maternal circulating thyroxine concentrations. There were few data of the consequences of mild to moderate iodine deficiency in older children. A recent randomized, placebo-controlled, double-blind trial in 184 children aged 10–13 years in New Zealand (median UI 63 μg/l) had demonstrated that iodine supplementation (150 μg/l daily) for 28 weeks improved perceptual reasoning suggesting that mild iodine deficiency may prevent children attaining their full intellectual potential.\textsuperscript{13} Similar positive findings had been observed in European children who were moderately iodine deficient.\textsuperscript{14}

Recently, concern had also been expressed about the UK iodine status as up to 50% of the UK women of child-bearing age screened in smaller studies at single centres were iodine deficient.\textsuperscript{15} Household iodized salt is rarely available for purchase in the UK. In addition to a decreasing consumption of iodized salt, few, if any, manufacturers in the UK use iodized salt in the preparation and manufacture of foods. A recent study measured the iodine content in 36 different salt preparations available from 9 major national supermarkets in Cardiff, Wales.\textsuperscript{15} Iodine concentrations varied from undetectable in 32 samples, to trace quantities in 2. Only two samples contained meaningful concentrations of iodine (20 mg/kg) related to the prevention of iodine deficiency. No data were available for the UK population according to the International Council for Control of Iodine Deficiency Disorders (ICCIDD).\textsuperscript{16} The British Thyroid Association, thus, undertook to perform a systematic survey of the UK iodine status in 2009 and found that the median UI excretion in a sample of 737 girls was 80 μg/l and that more than two-thirds had a UI <100 μg/l.\textsuperscript{17} The study focused on young female subjects aged 14–15 years who are pre-pregnant as in the short- to medium term and it is their children who are most susceptible to the adverse effects of iodine deficiency. Milk intake was positively associated with UI and as milk iodine concentrations were unchanged, it was likely to be the reduced amount of milk now drunk by the population, which is responsible for the decline in iodine status.

The findings of the UK survey have major public health importance as the UK is now number eight on the list of the top 10 iodine-deficient countries (based on national median UI <100 μg/l in children) with the greatest numbers of school-age children with insufficient iodine intake in 2011.\textsuperscript{18} Iodine deficiency in an industrialized country presents a significant challenge as recently addressed in Australia.\textsuperscript{19} Despite the clear benefits in correcting iodine deficiency, a fear of iodine-induced thyroid dysfunction has at times delayed or limited the implementation of iodine supplementation in regions with iodine deficiency. In adults, mild iodine deficiency is associated with a decreased risk of overt and subclinical hypothyroidism, as well as autoimmune thyroiditis and an increased risk of non-toxic nodular goitre.\textsuperscript{20} A sudden increase in iodine supply to those in an iodine-deficient region may enhance thyroid autoimmunity through both a cellular and a humoral immune response and may result in hypothyroidism in those with damaged thyroid glands and hyperthyroidism in those with an underlying multinodular goitre or Graves’ disease, although it is unlikely to do so if the deficiency is not severe and if the increase is relatively small.\textsuperscript{21} Large epidemiological studies from Denmark have now carefully documented the pattern of thyroid disease after introduction of iodized salt in a mildly deficient population.\textsuperscript{22,23} An initial voluntary iodine fortification programme proved ineffective so a mandatory iodine fortification programme of bread salt and household salt was introduced in 2000 aiming to increase the iodine intake in adults by an average of 50 μg/day. This resulted in an increase in the population median UI concentrations from 53 to 68 μg/l in the original cohort to 93–108 μg/l when the cohort was reassessed 5 years later. Positive benefits both in terms of goitre prevalence\textsuperscript{24} and hyperthyroidism\textsuperscript{25} have been observed with a small increase in both thyroid peroxidase antibodies and thyroglobulin antibody titres in all age groups but was most pronounced in young women.\textsuperscript{26} Other smaller cohorts studied suggest that this enhanced thyroid autoimmunity might be reversible and reduce over time.\textsuperscript{27} It was too early in the natural history of autoimmune thyroiditis to detect an impact in terms of clinically relevant hypothyroidism but at 5 years a slightly higher serum TSH was seen in those subjects with positive anti-thyroid antibodies.

In developed countries, such as the UK, there is a strong public health objective to lower salt intake to reduce the risk of hypertension. It is estimated that only 10% of the UK salt intake is added to food at the

\[ \text{Australian National Iodine Nutrition Study.} \textsuperscript{12} \]
table so dialogue with the food and salt industries to establish the feasibility of adding iodized salt to processed food is essential. Although, accepting the available evidence-base for salt iodization to correct iodine deficiency, the UK thyroid community has still to convince others that there is a clinical phenotype associated with the levels of iodine deficiency documented in this UK sample. If we wish government to consider iodine prophylaxis to offset the adverse effects of iodine deficiency, data are required to provide reassurance that at the population level, the benefits far outweigh any disadvantages. Salt iodization is safe, equitable, largely self-financing and extremely cost-effective in an industrialized country. The alternative strategy is daily oral potassium iodide supplements for the most susceptible groups, such as women pre-pregnancy. However, it is accepted in the UK that only 50% of the pregnancies are planned and that iodine supplementation should ideally be at least 3 months prior to a pregnancy. Careful discussion is required with government departments and public health experts and it is hoped that these new data will be the catalyst to stimulate interest and awareness of iodine deficiency and its correction as an issue that remains of major public health importance in the UK.

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**References**


Commentary: A new dimension—Studies in schoolchildren

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The paper of Vanderpump indicates the new frontier in the cause of the elimination of iodine deficiency. It is the challenge of children pointed out by Labouisse of UNICEF in 1978 when he stated at a goitre meeting in South America, ‘Iodine deficiency is so easy to prevent that it is a crime to let a single child be born mentally handicapped for that reason’.

In children the problem is now being defined by the results of psychological assessment in conjunction with measurement of urine iodine excretion.

Vanderpump refers to WHO estimates that worldwide 2 billion people including 285 million school-age children still have iodine deficiency despite major national and international efforts to increase iodine intake primarily through the voluntary or mandatory iodization of salt.1,2

Recent papers indicate the psychological benefits of salt iodization or iodine supplements in children. Extensive studies have been carried out following the widespread use of iodized salt in China.3 Comparison of IQ in 8- to 14-year-old students by a modified Raven Test in IDD endemics from the same population before and after iodization revealed significant improvement.

Vanderpump refers to two recent important double-blind controlled trials. In the first in rural Albania 10- to 12-year-old children (n = 310) were given oral iodized oil (400 mgI), which showed improvement in information processing, fine motor skills and visual problem solving.4 The median urine iodine (UI) was 43 μg/l before the trial. In a randomized controlled trial in New Zealand, iodine supplementation with iodide tablets (150 μg daily) for 6 months improved perceptual reasoning in a sample of 184 mildly iodine-deficient children (aged 10–13 years) suggesting that mild iodine deficiency could prevent children from attaining their full intellectual potential.5 The median UI before the trial was 63 μg/l.

In Australia, a median level of 104 μg/l of UI has been observed in a total sample of 1709 children with some variation between the states.6 A current randomized controlled trial in South Australian schoolchildren is assessing cognition in 150 schoolchildren (aged 10–13 years) with median UI of 87 μg/l following an iodine tablet 150 μg/day for 6 months.7

The study of Vanderpump et al.8 in 737 schoolgirls (aged 14–15 years) found a median UI of 80 μg/l indicating mild iodine deficiency. Vanderpump reports in