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Conference on 'Over- and undernutrition: challenges and approaches'

Symposium on 'Geographical and geological influences on nutrition' Iodine deficiency in industrialised countries

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Iodine deficiency is not only a problem in developing regions; it also affects many industrialised countries. Globally, two billion individuals have an insufficient iodine intake, and approximately 50% of continental Europe remains mildly iodine deficient. Iodine intakes in other industrialised countries, including the USA and Australia, have fallen in recent years. Iodine deficiency has reappeared in Australia, as a result of declining iodine residues in milk products because of decreased iodophor use by the dairy industry. In the USA, although the general population is iodine sufficient, it is uncertain whether iodine intakes are adequate in pregnancy, which has led to calls for iodine supplementation. The few available data suggest that pregnant women in the Republic of Ireland and the UK are now mildly iodine deficient, possibly as a result of reduced use of iodophors by the dairy industry, as observed in Australia. Representative data on iodine status in children and pregnant women in the UK are urgently needed to inform health policy. In most industrialised countries the best strategy to control iodine deficiency is carefully-monitored salt iodisation. However, because approximately 90% of salt consumption in industrialised countries is from purchased processed foods, the iodisation of household salt only will not supply adequate iodine. Thus, in order to successfully control iodine deficiency in industrialised countries it is critical that the food industry use iodised salt. The current push to reduce salt consumption to prevent chronic diseases and the policy of salt iodisation to eliminate iodine deficiency do not conflict; iodisation methods can fortify salt to provide recommended iodine intakes even if *per capita* salt intakes are reduced to <5 g/d.

Iodine deficiency: Goitre: Industrialised countries: Thyroid disorders

Many industrialised countries are areas of historical iodine deficiency and goitre

Iodine (as iodide) is widely but unevenly distributed in the earth's environment. In many regions leaching from glaciation, flooding and erosion have depleted surface soils of iodide and most iodide is found in the oceans. Iodide ions in seawater are oxidised to elemental iodine, which volatilises into the atmosphere and is returned to the soil by rain, completing the cycle[(1)]. However, iodine cycling in many regions is slow and incomplete, leaving soils and drinking water depleted of iodine. Crops grown in these soils will be low in iodine and human populations and animals consuming food grown in these soils become iodine deficient. Iodine-deficient soils are common in industrialised countries; well-known examples are the Alpine region of Europe, the Midwest in North America, southern Australia and inland areas of western England and Wales. Iodine deficiency and goitre in these areas persists until iodine enters the food chain through the addition of iodine to foods (e.g. iodisation of salt) or dietary diversification introduces foods produced outside the iodine-deficient area.

Iodine is an essential component of the hormones thyroxine and triiodothyronine produced by the thyroid gland[(2)]. Thyroid hormones, and therefore iodine, are

Abbreviations: NHANES, National Health and Nutrition Examination Survey; TSH, thyroid-stimulating hormone; UI, urinary iodine concentration.
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essential for mammalian life. In 1917 it was shown that thyroid enlargement (goitre) is caused by iodine deficiency and can be prevented by iodine supplementation[3]. Goitre prophylaxis through salt iodisation was first introduced in industrialised countries (Switzerland and the USA) in the early 1920s[4]. In 1980 the first global estimate from WHO on the prevalence of goitre was reported; it was estimated that 20–60% of the world's population were iodine deficient and/or goitrous, with most of the burden in developing countries. During the period of 1970–1990 it was shown in controlled studies in iodine-deficient regions that iodine supplementation not only eliminates new cases of cretinism but also reduces infant mortality and improves cognitive function in the rest of the population[5]. Programmes to correct iodine deficiency were considered to have clear political appeal because its human, economic and social consequences could be averted by a low-cost intervention, universal salt iodisation. Since 1990 elimination of iodine deficiency has been an integral part of national nutrition strategies in most developing countries. In contrast, it has received little attention from public health authorities in many industrialised countries.

Dietary sources, absorption and requirements

The native iodine content of most foods and beverages is low. In general, commonly-consumed foods provide 3–80 μg per serving[6,7]. Foods of marine origin have higher iodine contents because marine plants and animals concentrate iodine from seawater. In the USA the median intake of iodine from food in the mid-1990s was estimated to be 240–300 μg/d for men and 190–210 μg/d for women[8]. Major dietary sources of iodine in the USA are bread and milk[9]. In Switzerland, based on direct food analysis, mean intake of dietary iodine is approximately 140 μg/d, mainly from bread and dairy products[7]. In many countries the use of iodised salt in households for cooking and at the table provides additional iodine. The iodine content of foods is also influenced by iodine-containing compounds used in irrigation, fertilisers and livestock feed. Iodophors used for cleaning milk cans and teats can increase the native iodine content of dairy products. Traditionally, iodate was used in bread making as a dough conditioner, but it is being replaced by non-iodine-containing conditioners, such as bromate. Dietary supplements often contain iodine. Based on data from National Health and Nutrition Examination Survey (NHANES) III (1988–1994) it has been estimated that supplements containing iodine are taken by 12% of men and 15% of non-pregnant women, the median intake of iodine from supplements being approximately 140 μg/d for adults[8]. Other sources of iodine include water purification tablets, radiographic contrast media, medicines (e.g. amiodarone) and skin disinfectants (e.g. povidone-iodine contains approximately 10 mg/ml).

Iodine is ingested in several chemical forms. Iodide is rapidly and nearly completely absorbed in the stomach and duodenum. Iodate, widely used in salt iodisation, is reduced in the gut and absorbed as iodide. In healthy adults the absorption of iodide is >90%[10]. Organically-bound iodine is typically digested and the released iodide absorbed. The body of a healthy adult contains 15–20 mg iodine, of which 70–80% is in the thyroid. In chronic iodine deficiency the iodine content of the thyroid may fall to <20 μg[11]. In iodine-sufficient areas the adult thyroid traps approximately 60 μg iodine/d to balance losses and maintain thyroid hormone synthesis[11]. Iodine comprises 65 and 59% of thyroxine and triiodothyronine by weight respectively. Degradation of thyroxine and triiodothyronine in the periphery releases iodine that enters the plasma iodine pool and can be taken up by the thyroid or excreted by the kidney[11]. Of the ingested iodine >90% is ultimately excreted in the urine. WHO recommendations for iodine intake are shown in Table 1; the WHO recommended nutrient intake for iodine is the intake estimated to cover the needs of 'nearly all' healthy individuals at the specified life stage[12].

Table 1. WHO recommendations for iodine intake (μg/d)[12] by age or population group

Age or population group	RNI
Children 0–5 years	90
Children 6–12 years	120
Adults >12 years	150
Pregnancy	250
Lactation	250

RNI, recommended nutrient intake.

Methods to assess iodine status

Four methods are generally recommended for assessment of iodine nutrition in populations[12]: the goitre rate; urinary iodine concentration (UI); blood thyroid-stimulating hormone (TSH); blood thyroglobulin. These indicators are complementary, in that UI is a sensitive indicator of recent iodine intake (days) and thyroglobulin shows an intermediate response (weeks to months), whereas changes in the goitre rate reflect long-term iodine nutrition (months to years). These methods have recently been extensively reviewed[13]. WHO recommends the use of total goitre rate to define severity of iodine deficiency in populations (surveys are usually conducted in school-age children) with the following criteria: <5%, iodine sufficiency; 5·0–19·9%, mild deficiency; 20·0–29·9%, moderate deficiency; >30%, severe deficiency[12]. The median UI from a representative sample of spot urine collections from different population groups is the most common way to classify a population's iodine status (Table 2). The median UI is recommended for assessing iodine nutrition in pregnant women, and recently WHO have recommended 150–249 μg/l as the median UI that indicates adequate iodine intake during pregnancy[12] (Table 2). A collection method and a new reference range for UI in newborns in the first week after birth has recently become available[14]. Although UI does not provide direct information on thyroid function, a low value suggests that a population is at higher risk of developing thyroid disorders.

TSH is used in many industrialised countries for routine newborn screening to detect congenital hypothyroidism;

Table 2. WHO epidemiological criteria for the assessment of iodine nutrition in a population based on medians or ranges of urinary iodine concentrations (μg/l)[12]*

	Iodine intake	Iodine nutrition
School-aged children		
<20	Insufficient	Severe iodine deficiency
20–49	Insufficient	Moderate iodine deficiency
50–99	Insufficient	Mild iodine deficiency
100–199	Adequate	Optimum
200–299	More than adequate	Risk of iodine-induced hyperthyroidism in susceptible groups
>300	Excessive	Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid disease)
Pregnant women		
<150	Insufficient	
150–249	Adequate	
250–499	More than adequate	
≥500	Excessive‡	
Lactating women†		
<100	Insufficient	
≥100	Adequate	
Children <2 years of age		
<100	Insufficient	
≥100	Adequate	

*There is no information about iodine nutrition for pregnant and lactating women in the WHO assessment table, and the upper limits of the median urinary iodine for lactating women and children <2 years of age are not specified.
†The values for median urinary iodine are lower than the iodine requirements, because of the iodine excreted in breast milk.
‡In excess of the amount needed to prevent and control iodine deficiency.

such screening offers a sensitive indicator of iodine nutrition in the newborn period[12]. Newborn TSH is an important measure because it reflects iodine status during a period when the developing brain is particularly sensitive to iodine deficiency. Serum TSH concentrations are transiently increased in iodine-deficient infants for the first few weeks of life, a condition termed transient newborn hypothyroidism. In areas of iodine deficiency an increase in transient newborn hypothyroidism, indicated by >3% of newborn TSH values above the threshold of 5 mU/l whole blood collected 3–4 d after birth, suggests iodine deficiency in the population[12]. Recent data from a large representative Swiss study suggest that newborn TSH is a sensitive indicator of even marginal iodine nutrition in pregnancy[15]. A new assay for thyroglobulin has been developed for dried blood spots taken by a finger prick[16], simplifying collection and transport. Dried blood spot thyroglobulin has been shown to be a sensitive measure of iodine status[16,17] and recently a reference standard and an international reference range in iodine-sufficient schoolchildren (4–40 μg/l) has been made available[16]. In contrast, thyroid hormone concentrations are generally poor indicators of iodine status[12], unless iodine deficiency is severe.

Epidemiology of iodine deficiency in industrialised countries

Only a few countries (Switzerland, some of the Scandinavian countries, Australia, the USA and Canada) were recognised as being clearly iodine sufficient before 1990. Since then, globally, the number of households using iodised salt has risen from <20% to >70%, dramatically reducing iodine deficiency[18]. Currently, WHO estimates that approximately two billion individuals have an insufficient iodine intake, including one-third of all school-age children[19] (Table 3). The WHO prevalence data emphasise that iodine deficiency is not only a problem of developing countries; the highest prevalence of iodine deficiency is in Europe (52·0%), where the household coverage with iodised salt is the lowest (approximately 25%), and many of these countries have weak or non-existent control programmes for iodine-deficiency disorders[20]. There are several limitations to these WHO prevalence data. First, extrapolation from a population

Table 3. Prevalence of iodine deficiency (total number (millions) and percentage) in the general population (all age-groups) and in school-age children (6–12 years) in 2007[19]

	Population with urinary iodine <100 μg/l†			
	General population		School-age children	
WHO regions*	*n*	%	*n*	%
Africa	312·9	41·5	57·7	40·8
Americas	98·6	11·0	11·6	10·6
Eastern Mediterranean	259·3	47·2	43·3	48·8
Europe	459·7	52·0	38·7	52·4
Southeast Asia	503·6	30·0	73·1	30·3
Western Pacific	374·7	21·2	41·6	22·7
Total	2000·0	30·6	263·7	31·5

*193 WHO member states.
†Based on population estimates for 2006[83].

indicator (median UI) to define the number of individuals affected is problematic, e.g. a country in which children have a median UI of 100 µg/l would be classified as being iodine sufficient, yet at the same time 50 % of children would be classified as having inadequate iodine intakes. Second, nationally-representative surveys represent only 60 % of the global population included in the WHO data, and sub-national data may under- or overestimate the extent of iodine deficiency[19]. Finally, there are insufficient data from the majority of the countries to estimate the prevalence of iodine deficiency in pregnant women.

Effects of mild-to-moderate iodine deficiency

Pregnancy

Iodine deficiency, when severe, has multiple adverse effects on growth and development in animals and human subjects, collectively termed the iodine-deficiency disorders[3,4]. The adverse effects on pregnancy of mild iodine deficiency, typical of industrialised countries, remain unclear. Six controlled trials of iodine treatment in pregnant women with iodine deficiency have been conducted in Europe[21–26]. Overall, these studies suggest that in areas of mild-to-moderate iodine deficiency the maternal thyroid is able to adapt to meet the increased thyroid hormone requirements of pregnancy[27]. Although supplementation in these studies was generally found to be effective in minimising an increase in thyroid size during pregnancy, only two of the six studies report that maternal TSH is lower (within the normal reference range) with supplementation, and none of the studies show a marked impact of supplementation on maternal and newborn total or free thyroid hormone concentrations[27]. Thyroid hormone concentrations may be the best surrogate biochemical marker for healthy fetal development. Thus, the results of these trials are reassuring. However, because none of the trials measured long-term clinical outcomes such as maternal goitre or infant development, the potential adverse effects of mild-to-moderate iodine deficiency during pregnancy remain uncertain. In industrialised countries with iodine deficiency it has often been suggested that pregnancy is an environmental factor contributing to a higher prevalence of goitre and thyroid disorders in women, compared with men. However, the data to support this premise are scarce. In European studies data from an uncontrolled prospective study in ten women[28], a retrospective study[29] and a cross-sectional study in smoking women[30] suggest goitres formed during pregnancy may only partially regress after parturition.

Childhood

There have been many cross-sectional studies comparing cognition and/or motor function in children from chronically iodine-deficient and iodine-sufficient areas, including children from European backgrounds[31–35]. These cross-sectional studies generally report reduced intellectual function and motor skills in children from iodine-deficient areas. However, observational studies are often confounded by other factors that affect child development. Furthermore, these studies could not distinguish between the persistent effects of *in utero* iodine deficiency and the effects of current iodine status. Two meta-analyses have reported on this issue[36,37], but they have included mainly data from regions of chronic severe iodine deficiency; in such areas populations experience a mean reduction in intelligence quotient of 12–13·5 points.

In a recent placebo-controlled double-blind 6-month intervention trial 10–12-year-old children with moderate iodine deficiency (*n* 310) in Albania were randomised to receive either 400 mg iodine as oral iodised oil or placebo. It was found that compared with placebo iodine treatment improves performance on tests of information processing, fine motor skills and visual problem solving[38]. These findings have recently been confirmed in mildly-iodine-deficient New Zealand children[39]. Thus it appears that in children born and raised in areas of moderate iodine deficiency cognitive impairment is at least partially reversible by iodine repletion[38,39]. In addition, recent controlled studies clearly demonstrate that iodine repletion in school-age children with iodine deficiency increases insulin-like growth factor-1 and insulin-like growth factor-binding protein-3 concentrations; in children who have moderate-to-severe deficiency their somatic growth is improved[40]. Chronic iodine deficiency increases the TSH concentration and produces a thyroid hormone pattern consistent with subclinical hypothyroidism[11], and subclinical hypothyroidism may increase the risk of CVD. Iodised oil rapidly normalises the increased TSH concentrations found in individuals who are iodine-deficient[11] and thus corrects subclinical hypothyroidism. An uncontrolled study has reported that iodine treatment of German adolescents who are goitrous decreases plasma cholesterol concentrations[41]. A recent controlled study has reported that in children with moderate iodine deficiency and elevated TSH concentrations as a result of iodine deficiency iodine treatment of improves their lipid profile and reduces their insulin (C-peptide) levels compared with controls[42]. This previously unrecognised benefit of iodine prophylaxis may be important because iodine deficiency remains common in many industrialised countries with increasing rates of obesity and CVD.

Treatment and prevention

Salt fortification with iodine

In the majority of industrialised countries affected by iodine deficiency the most effective way to control iodine deficiency is through salt iodisation[12]. Salt iodisation is the recommended strategy for control of iodine deficiency because: (1) salt is one of few foodstuffs consumed by virtually every individual; (2) salt intake is fairly consistent through the year; in many countries salt production and importation is limited to a few sources; (3) iodisation technology is simple and relatively inexpensive to implement; (4) the addition of iodine to salt does not affect its colour or taste; (5) the quantity of iodine in salt can be simply monitored at the production, retail and household

levels. WHO/UNICEF/International Council for the Control of Iodine Deficiency Disorders recommends that iodine is added at a level of 20–40 mg iodine/kg salt, depending on local salt intake[12]. Salt iodisation remains the most cost-effective way of delivering iodine and of improving cognition in populations who are iodine deficient[43]. Worldwide, the annual costs of salt iodisation are estimated to be US$ 0·02–0·05 per child covered, and the costs per child death averted are US$ 1000 and per disability-adjusted life-year gained are US$ 34–36[44].

The importance of food industry use of iodised salt in industrialised countries

WHO recommends universal salt iodisation to control iodine deficiency[12]. Universal salt iodisation is a term used to describe the iodisation of all salt for human (food industry and household) and livestock consumption. Although the ideal, even in countries with successful salt iodisation programmes, universal salt iodisation is rarely achieved, as many countries do not iodise all salt for livestock and food industries are often reluctant to use iodised salt. The limited use of iodised salt by the food industry is one of the main reasons for iodine deficiency in many industrialised countries. In countries such as England and Denmark household salt, i.e. salt for cooking and table use, contributes only 8–15 % to total salt intakes; most of the remainder comes from purchased processed foods[45,46]. Thus, in industrialised countries, where on average total adult *per capita* salt consumption is approximately 10 g/d, only about 1 g household salt is consumed daily[46]. If the food industry uses non-iodised salt and only household salt is iodised (at WHO recommended levels of 20 mg iodine/kg salt), then total iodine intake from iodised salt will only be approximately 20 µg/d, far below the daily requirement for all age-groups. Thus, in order to successfully control iodine deficiency in industrialised countries it is critical to convince the food industry to begin to use iodised salt in their products. For example, in The Netherlands all salt used by the baking industry is iodised, and this source is the major contributor to iodine sufficiency in the country[20]. Switzerland's long-running iodised salt programme has been successful partly because approximately 60 % of salt used by the food industry is iodised on a voluntary basis. As iodine at µg/g levels in iodised salt does not cause colour or flavour changes in any foods and in most countries the price difference between iodised and non-iodised salt is negligible, there should be no major barriers to adoption of iodised salt by food manufacturers.

How to reconcile the policy of reducing salt consumption to prevent chronic diseases and the policy of universal salt iodisation to eliminate iodine deficiency

Current WHO recommendations to prevent chronic diseases state that the population average *per capita* consumption of salt should be <5 g/d (<2 g Na/d)[47]. However, the WHO recommendation that salt be fortified with iodine at a level of 20–40 µg/g is based on the assumption of an average salt intake of approximately 10 g/d at the population level[12]. Thus, the level of iodine fortification may need to be adjusted by national salt iodisation programmes if health authorities are successful in reducing salt consumption. Since iodisation methods can easily fortify salt with adequate concentrations of iodine to provide recommended iodine intakes even if *per capita* salt intake falls to <5 g/d, these two important health policies are not in conflict[47]. Interaction with food manufacturers in industrialised countries will be fundamental to the success of both salt-reduction strategies and to universal salt iodisation.

Other fortification vehicles

Bread can be an effective vehicle for iodine by including baker's salt enriched with iodine[48]. Although iodising drinking water or irrigation water can also be effective[49], the higher cost and the complexity of monitoring are disadvantages. In Finland iodine-fortified animal fodder has increased the iodine content of foods derived from animal sources. In countries with iodine deficiency iodine should be routinely added to complementary foods or add-on formulas for infants during weaning to provide approximately 90 µg iodine/d[50].

Iodine supplementation

In some regions iodisation of salt may not be practical for control of iodine deficiency, at least in the short term, and iodine supplements can be used (Table 4)[12]. Iodised oil supplements are prepared by esterification of the unsaturated fatty acids in seed or vegetable oils and addition of iodine to the double bonds. It can be given orally or by intramuscular injection[12]. The intramuscular route has a longer duration of action, but oral administration is more common because it is simpler. Usual doses are 200–400 mg iodine/year[12] and it is often targeted to women of child-bearing age, pregnant women and children. Its disadvantages are an uneven level of iodine in the body over time and the need for direct contact with individuals with the accompanying increased costs. Iodine can also be given as potassium iodide or potassium iodate as drops or tablets. Single oral doses of potassium iodide monthly (30 mg) or biweekly (8 mg) can provide adequate iodine for school-age children[51].

Strategies to prevent or correct deficiency during pregnancy and lactation

For nearly all industrialised countries the primary strategy for sustainable elimination of iodine deficiency in pregnancy remains salt iodisation[12]. In countries or regions in which a salt iodisation programme covers ≥90 % of households and has been sustained for ≥2 years, and the median UI indicates iodine sufficiency (Table 4), pregnant and lactating women do not need iodine supplementation[12]. Several countries with long-standing successful iodised salt programmes have reported an optimal median UI in pregnant women[27]. Moreover, in countries affected by mild or moderate iodine deficiency (Republic of Ireland, Germany, Belgium, Italy, Denmark) thyroid volume increases

Table 4. Recommendations for iodine supplementation in pregnancy and infancy in areas in which <90% of households are using iodised salt and the median urinary iodine is <100 μg/l in schoolchildren[12]

Women of child-bearing age	A single annual oral dose of 400 mg iodine as iodised oil Or A daily oral dose of iodine as potassium iodide should be given so that the total iodine intake meets the RNI of 150 μg iodine/d
Women who are pregnant or lactating	A single annual oral dose of 400 mg iodine as iodized oil Or A daily oral dose of iodine as potassium iodide should be given so that the total iodine intake meets the new RNI of 250 μg iodine/d Iodine supplements should not be given to a woman who has already been given iodised oil during her current pregnancy or up to 3 months before her current pregnancy started
Children aged 0–6 months	A single oral dose of 100 mg iodine as iodised oil Or A daily oral dose of iodine as potassium iodide should be given so that the total iodine intake meets the RNI of 90 μg iodine/d Should be given iodine supplements only if the mother was not supplemented during pregnancy or if the child is not being breast-fed
Children aged 7–24 months old	A single annual oral dose of 200 mg iodine as iodised oil as soon as possible after reaching 7 months of age Or A daily oral dose of iodine as potassium iodide should be given so that the total iodine intake meets the RNI of 90 μg iodine/d

RNI, reference nutrient intake.

15–31% during pregnancy, while in iodine-sufficient countries (Finland, The Netherlands) there is little or no increase in thyroid volume during pregnancy[52]. These data suggest that effective salt iodisation can provide adequate iodine intake during pregnancy, but iodine-containing supplements taken during the prenatal period may have contributed to iodine intakes in these studies.

Implementation of salt iodisation is not always feasible, and non-implementation may result in inadequate iodine supply for women of child-bearing age and pregnant women. In this situation supplementation of these groups should be considered. WHO recommends that countries assess their salt iodisation programmes and then decide whether supplementation is indicated[12]. In order to ensure adequate iodine supply during pregnancy women should ideally be provided with adequate iodine intake (≥150 μg/d) for a long period before conception to ensure plentiful intrathyroidal iodine stores[53]. In Italy thyroid function in pregnant women from a mildly-iodine-deficient area who had regularly used iodised salt for ≥2 year before becoming pregnant was compared with that in women who began using iodised salt on becoming pregnant[53]. The findings suggest that prolonged use of iodised salt is associated with better maternal thyroid function, possibly as a result of having greater intrathyroidal iodine stores to draw on during pregnancy. In iodine-deficient countries or regions that have weak iodised salt distribution, i.e. in countries or areas in which <90% of households are using iodised salt and the median UI is <100 μg/l in schoolchildren, supplements should be given to pregnant women, lactating women and infants, according to the strategy shown in Table 4[12].

Iodine nutrition in the industrialised countries: the examples of France, the USA, Australia and the UK and the Republic of Ireland

According to the WHO the highest prevalence of iodine deficiency is in Europe, where the household coverage with iodised salt is the lowest[19]. It is remarkable that Western Europe has donated substantial funds and effort towards controlling iodine deficiency in less-industrialised countries in Africa and Asia, but has not yet corrected its own problem. Currently, about half the population in Western and Central Europe is mildly iodine deficient[19,20], and it is likely that unrecognised pockets of more severe deficiency may exist in remote or disadvantaged populations. There are several reasons for this position. Most European nations have weak or non-existent governmental programmes to address iodine deficiency. Awareness of the importance of iodine deficiency is underestimated as many countries have not conducted systematic assessment or monitoring of their populations. Thus, iodine prophylaxis is weaker in most European countries than elsewhere in the world, and laws relating to iodised salt vary widely in Europe, as do the types and amounts of iodine compound used for fortification[20].

France

Iodised household salt was introduced in France on a voluntary basis in 1952 (at 10–15 mg sodium iodide/kg salt)[54]. In the mid-1990s iodine status was investigated in a nationally-representative sample of French adults (4860 men aged 45–60 years and 7154 women aged 35–60 years)[54]. The median UI in males and females was reported

to be 85 and 82 μg/l respectively, indicating mild iodine deficiency, with an overall goitre rate of 11 % for males and 14 % for females. The prevalence of individuals with an adequate UI was found to be lowest among 55–60 year olds, with the only 35 % of men and 34 % of women in this age-group having a UI ≥100 μg/l. The age-related decrease in iodine intake was thought to be a result of a reduction in energy intake with aging and/or increased awareness of the health benefits of reducing Na intake, which may have reduced iodine intake from salt. Median UI were found to display wide marked regional variations; median UI were higher among residents living in the north-west and west than among those living in the centre and east, independent of age and gender. The central region (Auvergne, Limousin) and the north-eastern areas (Alsace, Lorraine, Champagne-Ardennes, Franche-Comté) were found to have the highest percentages (33 and 24 for women and 22 and 23 for men respectively) with UI values <50 μg/l. It was suggested that these regional variations in median UI were a result of variations in the iodine contents of local foodstuffs, as they are dependent on native soil and water iodine content as well as incidental addition of iodine to foods by agricultural practices, including iodine-containing fertilisers, herbicides, disinfectants and/or iodine-supplemented livestock feed[54].

In contrast to the results in adults, a study of approximately 1500 French children aged 6–14 years conducted in the mid-1990s has reported iodine sufficiency in four areas of France: Lorraine; Rhône-Alpes; Languedoc-Roussillon; Midi-Pyrénées[55]. The mean UI was found to be 130 (SD 74) μg/l (only 10 % of UI values <50 μg/l), with the prevalence of goitre, determined by ultrasound, being 4·1 % in boys and 3·1 % in girls.

Two studies in pregnant women in southern France have confirmed iodine deficiency in this group. Mean UI in pregnant women in south-west France (*n* 347) was found to be 69 (SD 4) μg/l at initial presentation (before 12 weeks of gestation) and 86 (SD 6) μg/l during the ninth month of pregnancy[56]. During pregnancy a marked decrease was found in free thyroxine and triiodothyronine concentrations, with an increase in TSH and thyroglobulin concentrations. A thyroid ultrasound was performed 1–5 d after delivery in 246 mothers. Thyroid hypertrophy (defined as thyroid volume >18 ml) was found to affect 15·4 % of women whose first trimester UI was <50 μg/l, but was present in only 3·5 % of women whose first trimester UI was >100 μg/l; 11 % of women were found to be goitrous (thyroid volume >22 ml). Similar findings have recently been reported in pregnant women in the third trimester of pregnancy in the Nice area (*n* 330); median UI was found to be 64 μg/l, with 86 % of women having a UI <150 μg/l[57]. Median free thyroxine was found to be 12·3 pmol/l, with 41·2 % of values being <12 pmol/l. Median TSH was reported to be 1·93 mU/l, with 26·3 % having a TSH >2·5 mU/l. Thus, iodine deficiency is common in pregnant women in southern France and may be associated with hypothyroxinaemia and hyperthyrotopinaemia.

The USA

Recent data from the USA indicate the general population is iodine sufficient, and iodine nutrition has improved since the 1960s–1970s when much of the population was consuming excess dietary iodine. Based on the success of the classic iodine supplementation studies in Ohio, general prophylaxis with iodised salt was first introduced in the state of Michigan in 1924[4]. In 1948 the USA Endemic Goitre Committee tried to introduce iodised salt to all states by federal law, but the bill failed[4]. However, the voluntary use of iodised salt increased across the country and adventitious iodine entered processed foods as iodine-containing compounds were used as bread conditioners and in the dairy industry. These trends were associated with a decline in the prevalence of goitre[58].

By the 1970s iodine excess had become a greater concern than iodine deficiency, as iodine intakes were estimated to be 150–700 μg/d[59]. In a ten-state study of approximately 36 000 individuals in 1975 the median UI was found to be 250 μg creatinine/g, with the goitre prevalence in all age-groups at 3·1 %; a higher prevalence of goitre was found among individuals with high UI values than those with low values[60]. In a subsequent study in approximately 7800 USA children aged 9–16 years the prevalence of goitre was reported to be 6·8 %; again with goitre being associated with higher, not lower, UI[61]. However, the higher iodine intakes were not found to be associated with discernable thyroid dysfunction.

In the early 1970s the NHANES began to track iodine nutrition in the USA population. NHANES I (1971–1974) reported a median UI of 320 μg/l[58]. Subsequently, results from the USA Total Diet Study suggested a decreased total iodine content of the food supply between 1984 and 1991[62], at least partially because of a reduction in the amount of iodine in milk and the replacement of iodine compounds with bromine salts by the baking industry. Although there are no national data on iodised salt use, it is estimated that only about 60 % of salt consumed in the USA is iodised (added as potassium iodide at a concentration of 77 mg iodine/kg salt)[58].

NHANES III (1988–1994) reported a median UI of 145 μg/l, less than half the median in NHANES I[58]. An increase in individuals with UI concentrations <50 μg/l was found (11·6 % in 1988–94 *v.* 2·4 % in 1971–4). However, the frequency of UI concentrations >500 μg/l was reported to be reduced from 27·8 % to 5·3 %, with the frequency of UI >1000 μg/l falling from 5·3 % to 1·3 %. Thus, using WHO criteria[12], the data from NHANES III suggested an improvement in iodine status in the USA population, indicated by a sharp decrease in the prevalence of iodine excess, with the median UI in the middle of the range (100–200 μg/l) signifying adequate iodine status. However, concern was expressed that iodine intakes would continue to fall, putting the population at risk of deficiency. This situation has not arisen; in NHANES III the median UI was shown to be stable over the 6 years of sampling and NHANES 2000 and 2001–2002 have reported median UI of 161 μg/l and 168 μg/l respectively[58]. Thus, it appears the iodine intakes in the USA have stabilised. However, in the 2001–2002 NHANES the UI of pregnant women was reported to be 173 (95 % CI 75, 229) μg/l, within the range recommended by WHO (150–249 μg/l), but the lower 95 % CI was <150 μg/l, partly because of small sample size[63]. Thus, until additional data

become available, in order to ensure adequate iodine intake to maintain euthyroidism for the mother and fetus during pregnancy, the American Thyroid Association has recommended that women receive 150 μg iodine supplements daily during pregnancy and lactation and that all prenatal vitamin–mineral preparations contain 150 μg iodine[63].

Australia

Australia is an industrialised country in which mild iodine deficiency has reappeared, after having been controlled for decades mainly by adventitious iodine in milk and milk products. In 1992 the median UI in the Australian population was reported to be >200 μg/l, indicating iodine sufficiency[64]. A national survey in 2003–4 of schoolchildren in mainland Australia aged 8–10 years (*n* 1709) has reported a median UI of 104 μg/l[64]. In New South Wales and Victoria children were found to be mildly iodine deficient, with median UI of 89 μg/l and 73·5 μg/l respectively. Based on WHO reference values by age, 5·6 and 9·3 % of boys and girls respectively were found to have increased thyroid volume, but no significant association was demonstrated between UI and thyroid volume. These results indicate marginal iodine intake in the Australian population at the national level, with several of the states being mildly iodine deficient. Tasmania was not included in this survey, but in a study in 2001, before bread fortification with iodine began, the median UI in Tasmanian schoolchildren was reported to be 84 μg/l, with 20 % of values <50 μg/l[65].

These data are supported by a recent cross-sectional study of 815 pregnant women (≥28 weeks of gestation) and 824 newborns in New South Wales[66]. Spot urine samples were measured for iodine concentration in the women and TSH was measured in newborns at 48–72 h after birth using a sensitive fluoroimmunoassay. The median UI in pregnant women was reported to be 85 μg/l, indicating mild iodine deficiency, with eighteen newborns (2·2 %) having TSH values >5 mIU/l. No correlation was found between neonatal TSH and maternal UI, but mothers with a UI <50 μg/l were shown to be 2·6 times (relative risk 2·65 (95 % CI 1·49, 4·73)) more likely to have a baby with a TSH level >5 mIU/l.

The major sources of dietary iodine in the Australian diet are thought to be milk and milk products, seafood and iodised salt[67]. However, few individuals purchase iodised salt and, except in Tasmania, few if any food manufacturers use iodised salt in the preparation and manufacture of foods. It has been suggested that for the last 40–50 years the largest source of iodine in the Australian diet has been milk containing iodine residues from sanitising iodophors used in dairying. In a 1975 survey mean iodine concentrations in cow's milk in southern Australia were reported to be 583–593 μg/l[67]. As a result of concerns that high iodine levels in milk could lead to iodine toxicity Food Standards Australia specified a milk iodine limit of 500 μg/l in the Food Standards Code of 1982[68], which led to the replacement of iodophors by chlorine-containing sanitisers. Iodine content of milk samples in Sydney from 2001 to 2004 (thirteen samples per year) were found to be highly variable but generally much lower than in the 1970s, with median concentrations of 140 (range 60–220) μg/l in 2001 and 195 (range 66–412) μg/l in 2004[67]. It was suggested that the reduced amount of iodine in milk is a major reason why iodine deficiency has reappeared in regions of Australia. In 2009 a decision was made by Food Standards Australia New Zealand to address iodine deficiency in the population by requiring the salt in bread to be replaced with iodised salt[69].

The UK and the Republic of Ireland

The re-emergence of iodine deficiency in Australia should raise concern in the UK, as the pattern of a rise and fall in iodine intakes as a result of changes in milk iodine levels may recur in Britain. Studies in the UK in the 1800s reported a high prevalence of goitre and occasional cretinism[70]. By 1900 the English goitre belt was well-defined; it extended from the West Country through Somerset and northwards into Derbyshire and the Peak District, with offshoots into North and South Wales. The high regional goitre rates in adults and children in the 1940s led to recommendations by the Medical Research Council in 1944 and 1948 for a programme of iodised salt throughout the UK, but no action was taken[71]. In Oxfordshire the goitre prevalence between 1948 and 1958 was found to be essentially unchanged in boys but increased in girls, from 27 % to 40 %[72]. Goitre remained a health problem into the early 1960s in Sheffield and Wales[73,74], as well as in Glasgow, where patients presenting with non-toxic goitre were reported to have low dietary iodine intake and low plasma inorganic iodine concentrations[70]. Although monitoring data are scarce, it appears that since the 1960s the prevalence of iodine deficiency and goitre has fallen in the UK. A 1990 survey has reported the absence of thyroid enlargement in children in a traditionally iodine-deficient area of South Wales[75].

The improvement in iodine intakes dating from the 1960s in the UK may have been a result, at least in part, of increasing iodine intake from milk and milk products. Iodine supplementation of livestock improves their reproductive performance and many UK dairy herds, beginning as early as the 1920s and 1930s, have been given iodine via iodised salt licks and/or iodine-enriched cattle feed[70]. This practice increases the iodine content of milk, particularly during the winter months, when cattle are more dependent on iodine-rich artificial feed. In addition, the use of iodophor disinfectants for cleaning teats and milk tankers and giving iodinated casein to cows to promote lactation have also contributed to higher iodine levels in milk[70]. The simultaneous increase in *per capita* milk consumption has resulted in the amount of iodine provided by milk in the UK sharply increasing; it was estimated that average daily iodine intake from milk increased between 1930 and 1980 from approximately 5 μg to 25 μg (in summer) and >100 μg (in winter)[70]. The increasing contribution of milk iodine is likely to be a major reason why estimated dietary iodine intakes in the UK increased between 1952 and 1982 from 80 μg to 255 μg/d[76].

However, several UK authors have suggested that the increasing trend to replace iodine compounds used in the dairy and baking industries with non-iodine alternatives

may be decreasing iodine intakes, similar to the situation that has occurred in Australia[77–82]. If adventitious dietary iodine falls, the population may be vulnerable to iodine deficiency because iodised salt makes up <5% of all salt consumed in the UK and the Republic of Ireland[77]. Recent measurement of the iodine content in retail salt (thirty-six samples) in Cardiff (Wales) has shown iodine concentrations to be undetectable in thirty-two samples, with two samples, labelled as iodised, containing approximately 20 mg iodine/kg[77].

Limited data from Scotland[78] and north-east England[79] suggest many pregnant women are iodine deficient. In a study in Middlesbrough (north-east England) in 2000–2001 pregnant women attending the antenatal clinic at 15 weeks of gestation (*n* 227) and non-pregnant age-matched controls (*n* 227) were enrolled[79]. Sixteen of the pregnant women (7%) and twenty of the non-pregnant controls (8·8%) were found to have UI <50 μg/l, with ninety (40%) of the pregnant women having UI between 50 μg/l and 100 μg/l. The 227 pregnancies resulted in 218 live births and no newborn was reported to have a clearly elevated blood TSH. Although it was suggested that the data indicate borderline iodine deficiency in pregnancy, using the current WHO cut-off value for inadequate iodine intake for this group (150 μg/l)[12] most of the women were clearly iodine deficient.

In the Republic of Ireland the distribution of newborn TSH as a measure of iodine nutrition has been examined in the population[80]. Samples drawn from the National Neonatal Screening Programme were assessed during the years 1995–2006. In 1995–6 the frequency of TSH values >5·0 mIU/l was found to be >3%, suggesting iodine deficiency in the population. However, a marked decline in the proportion of elevated values was observed in the subsequent years. At the same time, a small but significant increase ($P<0·001$) in mean blood TSH within the 0–5·0 mIU/l interval was observed between 1999 and 2006. It was suggested that the trend towards increasing TSH is of concern and should be monitored carefully. UI was measured in Irish women (*n* 54) during the first trimester of pregnancy (median 8 weeks of gestation) attending the National Maternity Hospital in Dublin[81]. The samples were taken at different times during the year with thirty-six samples taken in the summer months. The UI were found to show seasonal variation; the median UI in the women being 45 μg/l in summer and 68 μg/l in winter. These values are lower than those in a study of pregnant women in Dublin in the mid-1990s from the same research group[82], in which the median UI was reported to be 83 μg/l in summer and 135 μg/l in winter. Although these studies were small, they suggest dietary iodine intake in Irish pregnant women continues to fall well short of WHO recommendations. This outcome is not surprising, as only about 3–4% of total salt sales in Ireland are iodised[81]. Thus, dietary iodine intake in the Irish population depends on consumption of sea fish and marine products, which varies widely among regions and individuals, and milk and dairy products, the iodine content of which varies seasonally and may be decreasing as a result of reduced use of iodophor disinfectants by dairies. As in the UK, relying on unpredictable amounts of iodine in the food supply, driven mainly by commercial rather than health interests, is precarious. The few available data suggest that the Republic of Ireland and the UK are mildly iodine deficient. Representative data on current iodine status in children and pregnant women are urgently needed to inform health policy.

Conclusion

Mild iodine deficiency affects many industrialised countries, including Australia, New Zealand and approximately 50% of continental Europe. It is likely that pregnant women in the Republic of Ireland and the UK are also mildly iodine deficient, but there are few representative data. In most industrialised countries the best strategy to control iodine deficiency is carefully-monitored salt iodisation. However, because approximately 90% of the salt consumption in industrialised countries is from purchased processed foods, it is critical that the food industry use iodised salt. The current push to reduce salt consumption to prevent chronic diseases is not at odds with salt iodisation to eliminate iodine deficiency; as salt intakes fall, the iodine content of salt can be increased to deliver adequate iodine, even if *per capita* salt intakes are reduced to <5 g/d.

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