Scientific Advisory Committee on Nutrition

Paper for discussion: Iodine and Health

Agenda item: 3

Please see attached paper for discussion.

Iodine

1. Following the publication of a paper in the Lancet in June 2011 by Vanderpump *et al.*[1], which suggested teenage girls in the UK were mildly iodine deficient, the Scientific Advisory Committee on Nutrition asked for an overview of the current evidence base on iodine and health. Members are asked for their views on monitoring iodine status in all or selected population sub-groups in the National Diet and Nutrition Survey (NDNS) in the future.

Background

2. Iodine is an essential nutrient required for the thyroid hormones which are required for regulation of the body's metabolism and for skeletal and central nervous system development in the fetus and infant. Iodine deficiency is associated with impaired production of thyroid hormone.

3. 'Iodine deficiency disorders' (IDD) describes the wide range of serious adverse effects of iodine deficiency, ranging from enlargement of the thyroid gland (goitre) as it tries to increase production of thyroid hormones, to cretinism[2]. Goitre is generally not considered to be a matter of public health concern in the UK[3]. The consequences of persisting iodine deficiency are set out in Table 1.

Measuring iodine status in a population

4. Urinary iodine (UI) is the most reliable indicator to assess, monitor and evaluate iodine status in a population[4]. The World Health Organization (WHO) recommends that the excretion of UI be expressed as µg of iodine per volume of urine. In the past, results of UI have been expressed normalised to urine creatinine as µg of iodine excreted/ g of creatinine, but relating urinary iodine to creatinine is now considered unnecessary, expensive and unreliable[5,6,7].

5. In individuals, UI excretion varies from day to day and sometimes within a particular day. A casual 'spot' urine sample does not accurately estimate the status of individuals, due to large variations in UI excretion at different times of the day. However, UI excretion in a spot urine sample is a valuable index for evaluating the iodine status of a population[8]. The WHO states that approximately thirty spot urine samples from a defined sampling group are sufficient to assess that group's iodine status[9].

6. Most studies investigating IDD have been conducted in populations with severe or moderate iodine deficiency. Mild iodine deficiency is not associated with any adverse effects[10,11]. A UI excretion of less than 50 µg/g creatinine is usually associated with a high incidence of goitre in a

population[12,13]. According to the thresholds outlined in Table 2 (Als *et al.*, 2003[14]), 50 µg/g creatinine corresponds to 0.045 µmol I/mmol creatinine; levels below which are indicative of moderate iodine deficiency.

World Health Organization (WHO) cut-offs

7. WHO, the United Nations Children's Fund (UNICEF) and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) recommend an iodine intake of 150 µg/day for adults and adolescents above 12 years[9]. This level was justified as it corresponds to the daily urinary excretion of iodine (1.18 µmol/day) and to the iodine content of food in areas where iodine intake was adequate[7,9,15]. It also provides the iodine intake necessary to maintain the plasma iodide level above the critical limit of 1.0 µg/L, which is the average level likely to be associated with the onset of goitre[16]. The suggested norms used by the WHO to define iodine deficiency or sufficiency (Table 3) were not established on data resulting from metabolic studies, but were decided on an arbitrary basis[7,9].

UK Dietary Reference Values

8. The UK Reference Nutrient Intake (RNI[i]) was set by COMA[17] at 140 µg/day for adults and between 40 µg/day and 140 µg/day for children as a reference point for assessing the sufficiency of iodine intakes[18]. The Lower Reference Nutrient Intake (LRNI[ii]) for iodine was set by COMA at 70 µg/day for adults (Table 4).

9. Urinary levels of more than 300 µg/L are excessive and risk adverse health consequences[19,20]. COMA advises that the safe upper limit on iodine intakes is 17 µg/kg or not more than 1,000 µg/day[18]. This is consistent with guidance from the Expert Group on Vitamins and Minerals, which states that iodine intakes of 940 µg/day would not be expected to have any significant adverse effects in adults[21].

Iodine requirements in pregnancy

10. Dietary iodine requirements are higher in pregnant and lactating women than in non-pregnant women due fetal iodine requirements and increased renal iodine losses[22]. Population iodine sufficiency during pregnancy is defined by median UI concentrations of 150 µg/L- 249 µg/L[4]. A review by Zimmermann and Delange (2004) which looked at UI concentration and excretion data between 1990 and 2002,

i The RNI is the amount of a nutrient that is sufficient to meet the needs of most (97.5%) of the population

ii The LRNI is the amount of a nutrient that is sufficient to meet the needs of only 2.5% of the population suggested pregnant women from nine out of ten European countries[iii] were not iodine sufficient[23]. Iodine deficiency in pregnant women can lead to an inadequate supply of thyroid hormones to the fetus resulting in impaired fetal brain development, reduced intelligence scores and impaired motor skills in the offspring of deficient women[24,25]. WHO recommends a higher iodine intake for pregnant women of 250 µg/day[26]. UK dietary reference values do not include incremental additional iodine for pregnant women.

Sources of iodine in the diet

11. High levels of iodine are present in marine fish (up to 2.5 mg/kg), shellfish (up to 1.6 mg/kg) and sea salt (up to 1.4 mg/kg)[21]. Levels in cereals and grains vary depending on the iodine content of the soil, whilst levels in meat, chicken, eggs and dairy products reflect the iodine content of the animal feed used. The food colour erythrosine is also rich in iodine, but has low bioavailability[27].

12. In the UK, iodine is naturally present in cow's milk, but concentrations can fluctuate according to the level of supplementation in animal feed and/or from hygiene products used in the dairy industry[28]. Milk and dairy foods are the major contributors of iodine to the diets of the UK population, providing 33% of an adult's daily intake (and more than this for children)[29]. Fish is also a rich source, but as consumption is low in the UK, it only provides 11% of iodine intakes. Beer and lager also provide 11% of daily iodine intake for adults. Tables 5 and 6 set out the iodine content of selected foods and their percentage contribution to mean daily iodine intakes.

13. Iodine, as iodide, is present in multivitamin and mineral supplements and is a component of kelp products. It is also present in licensed medicines, topical antiseptics and radiographic contrast agents.

14. The level of iodine in milk and dairy produce was last analysed by the Food Standards Agency in 2008 to estimate the dietary exposure to iodine from key food groups. The average iodine content of 145 samples of cow's milk was 30 µg/100g (range 7–100 µg/100g)[30] and confirmed that the levels of iodine in cow's milk have not changed much since previous analyses in the late nineties[31,32] (Table 7). These results are, however, higher than the average iodine concentrations found in earlier studies (15-17 µg/100g)[33,34,35]. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) were unclear about the reasons for the increase, although possible sources included iodine in animal feed and iodine containing compounds used as sterilants of cows' teats and milking vessels[36]. Organic milk in the UK is 42% lower in iodine content than

iii Belgium, Denmark, France, Germany, Hungary, Ireland, Italy, Turkey, Switzerland conventional milk[37], which is mainly explained by variation in feeding practices.

15. The iodine content of animal feedstuff is controlled by legislation in the UK. Maximum permitted levels for iodine (mg/kg) complete feed with a moisture content of 12% (typical for most dry feeds) are 4 mg for equines, 5 mg for dairy cows and laying hens, 20 mg for fish and 10 mg for other species or categories[38]. These are total levels of iodine and include both added and naturally occurring amounts. In 2005, the amount permitted for cows was reduced from 10 mg, as there was a risk that the Tolerable Upper Limit[iv] (UL) could be exceeded. This decision was based on worst case scenario model calculations with milk and eggs, which showed that the UL for adults and adolescents could be exceeded if the previously authorised maximum iodine level in feed continued.

Iodine intake of the UK population

16. Data from the most recent NDNS (2008/10)[39] indicates mean daily iodine intakes from food sources only are above the RNI for adults aged 19 years and older (Table 8). The mean iodine intake for girls aged 11-18 years from food sources only (110 µg/day) is below the RNI (82%), although boys of the same age are meeting the RNI. Mean intake for children aged 4-10 years also exceeds the RNI. Mean intake for young children aged 1½-3 years is more than double the RNI.

17. Iodine intakes for 11-18 year olds and 19-64 year olds have reduced slightly since previous surveys in the NDNS series (Table 8), which is probably due to reduced milk consumption.

18. The proportion of girls aged 11-18 years with average daily intakes of iodine below the LRNI from food sources only was 18% compared to 7% of boys of the same age, 8% of women and 5% of men aged 19-64 years (Table 9). The proportion of girls aged 11-18 years below the LRNI, had increased from 14% since the previous survey in 1997. When intake from dietary supplements was included, the proportion of girls with low intakes did not reduce. There is no UK data on UI as this analysis is not currently performed in the NDNS.

19. UI concentrations of UK schoolgirls aged 14-15 years were investigated by Vanderpump *et al.*[1] in 2009. 737 girls attending schools across nine UK cities were invited to participate. The median UI

iv The UL of 600 µg/day for adults and pregnant and lactating women, was established on the basis of noted biochemical changes in thyroid stimulating hormone (TSH) levels and the TSH response to thyrotropin-releasing hormone (TRH) administration in dose-response studies. Changes were marginal and unassociated with any clinical adverse effects at estimated intakes of 1700 and 1800 µg/day. An uncertainty factor of 3 was considered adequate. The UL is not a threshold of toxicity but may be exceeded for short periods without an appreciable risk to the health of the individuals concerned.

excretion in the sample was 80.1 µg/L (interquartile range 56.9-109.0 µg/L). The researchers used the findings, which indicated this group had mild iodine deficiency, to suggest that the UK population as a whole was now iodine deficient. The results were based on a single spot urine sample from each participant. A food frequency questionnaire was used to assess sources of iodine and iodine concentrations were measured in tap water. There was no positive association between iodine content of tap water by geographical area and UI concentration.

20. Kibirige *et al.*, studied 227 women at 15 weeks gestation and 227 non-pregnant age-matched controls between 2000 and 2001 in North-East England. The authors concluded that up to 40% of pregnant women were mildly iodine deficient, based on UI excretion rates of 50-100 µg/L from spot urine samples[40]. A separate study by Bath *et al.*, carried out on women of child-bearing age at the University of Surrey suggested 30% of this group were mild-moderately iodine deficient based on a median UI concentration of 66 µg/L. 24-hour urines were obtained from 26 women selected from the student and staff population at the university in 2008[41]. The three UK studies are summarised in Annex 2.

21. There are no concerns about excessive iodine intakes in the UK. The UK COT considered that the intake of iodine at the concentrations that have been found in cow's milk are unlikely to pose a risk to health even in those children who are high level consumers[36]. Data from the most recent NDNS shows that levels of iodine from food sources only at the upper 2.5 percentile were 440 µg for men and 290 µg for women[39].

Iodine status worldwide

22. It is claimed that much of Europe is iodine deficient[42]. Following the analysis of UI data, the WHO suggested that 14 European countries have optimal iodine status, 15 have mild iodine deficiency and one (Turkey) has moderate iodine deficiency[20]. No data is available for 11 countries, including the UK. The WHO report suggests that iodine deficiency may be re-emerging in countries that were previously thought to be iodine sufficient, such as Australia and New Zealand.

23. The risk of iodine deficiency is increased in some regions of the world among people who consume foods primarily from iodine-deficient soils. The countries that have adopted salt iodisation programs (the addition of iodine to salt intended for human or animal consumption) have significantly reduced the prevalence of iodine deficiency worldwide[4]. The decreased use of iodised salts in industrially produced foods is thought to contribute to lower iodine statuses[43].

24. There is an inverse correlation between household access to iodised salt and prevalence of low iodine intake[44,45,46]. Globally, the proportion of people consuming iodised salt increased from less than 20% in the

1990s to about 70% in 2000[47]. The Americas has the highest number of households consuming iodised salt and the lowest proportion of its population with an insufficient iodine intake. In contrast, the European Region which has the lowest household consumption of iodised salt (27%), has the highest proportion of its population with an insufficient iodine intake[48].

25. In the US, iodised salt and seafood are the major dietary sources of iodine. At 164 µg/L, median UI concentrations measured in the National Health and Nutrition Examination Survey (NHANES) indicates the US population has adequate iodine nutriton[49]. Iodised salt for use at home is rarely available to buy in the UK and few manufacturers use it in the preparation and manufacture of foods[50,51].

Groups that may be at risk of low iodine status in the UK

26. Teenage girls aged 11-18 years in the UK generally have poor diets. For example, NDNS data indicates that this group on average have low consumption of fruit and vegetables (7% achieved '5-a-day' compared with 30% of adults aged 19-64 years) and oily fish (consumed by 10%; consumers had a mean daily intake of 31g) and have high mean intakes of non-milk extrinsic sugars (NMES;15.3% food energy).

27. Iodine is one of several micronutrients for which girls are not meeting the RNI. Compared with other groups, 11-18 year old girls have the lowest mean daily intake of minerals from food sources as a percentage of the RNI. For example, a high proportion of this age group have intakes below the LRNI[v] for iron (44%), calcium (15%), magnesium (50%) and potassium (31%), and is a consequence of a diet low in meat, dairy products and wholegrain cereals.

28. Individuals that have lower UI concentrations are also low dairy consumers[52]. NDNS data shows consumption of milk has fallen since previous surveys (Table 10). For example, mean daily consumption of liquid cow's milk fell from 136g in 1997 to 111g in 2008-10 for girls aged 11-18 years.

29. Low iodine intake is not unique to UK girls. Norwegian data shows that 13 year old girls have low intakes of iodine (90 µg/day) which was explained by their low milk intakes. Only a minor percentage of the adult population had a mean daily intake of iodine below the lowest recommended intake (70 µg) due to their high milk consumption, even though milk produced in Norway is half as rich in iodine (15 µg/100g) compared with UK milk[53].

30. Because they exclude dairy products and fish from their diets, vegans in Britain may be at risk of low iodine status[54]. The small number of

v Proportion with intakes from food sources (excluding dietary supplements) below the LRNI vegans sampled in the NDNS means the diets of this group cannot be specifically interrogated. Sufferers of milk allergy, lactose intolerance or fish allergy may also be at risk[55]. There is no evidence of other age/sex groups having low iodine intakes.

Conclusion

31. Reduced milk consumption appears to have contributed to the decrease in iodine intakes in the UK population. Recent NDNS data indicates that 18% of girls aged 11-18 years have intakes below the LRNI and so are at risk of low iodine status. Other studies have reported findings that suggest this age group is mild-moderately iodine deficient, although these results should be generalised with caution. The poor diets of this age group are well documented. Girls are more likely to avoid foods such as meat and dairy products and consume inadequate quantities of fruit and vegetables. As a consequence of their poor dietary habits, they are failing to achieve recommendations for total and saturated fat, NMES and a wide range of micronutrients, including iodine. The NDNS data do not suggest that any other population groups in the UK have low iodine intakes. Results from individual research projects support the findings of NDNS dietary data on the population group at risk of iodine deficiency. A decision on whether UI analysis should be carried out in the NDNS in the future should be balanced against other analytical priorities in the survey.

Annex 1 - Tables

Table 1: Iodine deficiency disorders according to physiological group (Hetzel, 1983[2])

Physiological group	Health consequences of iodine deficiency
All ages	Goitre Hypothyroidism
Fetus	Spontaneous abortion Stillbirth Congenital anomalies Perinatal mortality
Neonate	Endemic cretinism including mental deficiency with a mixture of mutism, spastic diplegia, squint, hypothyroidism and short stature Infant mortality
Child and adolescent	Impaired mental function Delayed physical development Iodine-induced hyperthyroidism
Adults	Impaired mental function Iodine-induced hyperthyroidism

Table 2: Arbitrary thresholds used to define iodine deficiency or sufficiency, presented as I/day, I/creatinine or I/L (Als *et al.*, 2003[14])

Units of UI concentration or excretion	No iodine deficiency	Mild iodine deficiency	Moderate iodine deficiency	Severe iodine deficiency
µmol I/day	1.18	0.79	0.39	0.20
µmol I/mmol creatinine	0.134	0.089	0.045	0.022
µmol I/L	1.18	0.79	0.39	0.20

To convert µmol I/day into µg I/day multiply by 127
To convert µmol I/mmol creatinine into µg I/g creatinine multiply by 1122.7
To convert µmol I/L into µg I/dL multiply by 12.7

Table 3: WHO suggested norms used to define iodine deficiency or sufficiency (WHO/UNICEF/ICCIDD, 2007[4])

	No iodine deficiency	**Mild iodine deficiency**	**Moderate iodine deficiency**	**Severe iodine deficiency**
UI µg/L	>100	50-99	20-49	<20
Goitre prevalence	<5%	5.0-19.9%	20.0-29.9%	>30%

100µg/L is equivalent to 0.79µmol/L

Table 4: Dietary reference values for iodine (Department of Health, 1991[18])

Age (years)	**Lower Reference Nutrient Intake (LRNI) (µg/day)**	**Reference Nutrient Intake (RNI) (µg/day)**
1-3	40	70
4-6	50	100
7-10	55	110
11-14	65	130
15-18	70	140
19-50	70	140
50+	70	140

Table 5: Iodine content of selected foods in the UK (Food Standards Agency, 2002[56])

Food	Description	Iodine content (µg/100g)
Cod, baked	Baked in the oven, flesh only	161[57]
Eggs, chicken, boiled		52[57]
Whole milk, pasteurised, average	Average of summer and winter milk	31
Semi-skimmed milk, pasteurised, average	Average of summer and winter milk	30
Skimmed milk, pasteurised, average	Average of summer and winter milk	30
Cheddar cheese	Mild and mature English cheddar	30
Whole milk yoghurt, fruit	Assorted flavours including bio varieties	27
King prawns, cooked	Purchased	12[57]
Beer, bitter, canned		8[58a]
Chicken breast	Grilled without skin, meat only	7
White bread, sliced		4

[a] Data presented as µg/100ml. The iodine content of beer and lager available in the UK has not been analysed as part of the Department of Health's rolling programme of nutrient analysis in over twenty years. As such, composition data may not be representative of the beverages currently on the market.

Table 6: Percent contribution of selected food groups to daily mean iodine intakes for adults aged 19-64 years in 2008/09 – 2009/10[29]

Food group	Percentage contribution
Milk and milk products total,	33%
of which cow's milk	23%
Fish and fish dishes	11%
Beer and lager	11%
Cereal and cereal products	10%
Egg and egg dishes	6%
Other	29%

Table 7: Iodine content of cow's milk from 1985 to 2007

Year	Iodine content of milk (µg/100g)
1985[33]	15
1990/91[35]	15
1991[34]	17
1995[31]	30
1998/99[32]	31
2007[30]	30

Table 8: Mean daily iodine intakes of the UK population, from food sources only

Population group (years)	Mean iodine intake (µg) (2008/09 - 2009/10 NDNS)[39]	Mean iodine intake (µg) (2000/01 NDNS)[59b]	Mean iodine intake (µg) (1997 NDNS)[60b]	Mean iodine intake (µg) (1994/95 NDNS)[c61]
Boys 4-10	153		154	
Girls 4-10	133		135	
Boys 11-18	138		171	
Girls 11-18	110		134	
Men 19-64	192	221		
Women 19-64	143	161		
Men 65+	216			187
Women 65+	169			149

[b] mean intake was recalculated for previous NDNS surveys of seven days duration to represent four days of assessment
[c] the apparent increase in iodine intakes for adults aged 65 years and older is due to the use of different milk composition data. For the 1994/95 NDNS, the analytical data available at that time indicated milk had on average 15-17µg iodine/100g; approximately half the iodine content of milk analysed during the late nineties onwards.

Table 9: Proportion of UK population groups with mean daily intake of iodine from food sources only below the LRNI

Population group (years)	%age below LRNI (2008/09 - 2009/10 NDNS)[39]	%age below LRNI (2000/01 NDNS)[d59]	%age below LRNI (1997 NDNS)[d60]	%age below LRNI (1994/95 NDNS)[61]
Boys 4-10	1		2	
Girls 4-10	3		4	
Boys 11-18	7		5	
Girls 11-18	18		14	
Men 19-64	5	2		
Women 19-64	8	6		
Men 65+	0			2
Women 65+	1			6

[d] the proportion below the LRNI was recalculated for previous NDNS surveys of seven days duration to represent four days of assessment

Table 10: Quantities of liquid cow's milk (whole, semi-skimmed, skimmed and '1% fat milk') consumed according to age group

Population group (years)	Milk consumption (g per day)[e]	
	Previous NDNS[f]	NDNS 2008/09 -2009/10[39]
All 1½-3	276[62]	279
Boys 4-10	220[63]	226
Girls 4-10	175[63]	180
Boys 11-18	208[63]	157
Girls 11-18	136[63]	111
Men 19-64	225[63]	156
Women 19-64	195[63]	126
Men 65+	236[63]	204
Women 65+	226[63]	191

[e] Excludes milk in recipe dishes. Excludes other milks and dairy products
[f] Milk consumption data for previous NDNS do not include '1% fat milk' as this product was not on the market at the time

Annex 2 – Summary of UK studies

Study reference	Study design	Sample	Study population	Exclusions	Urinary iodine (UI) status measure	Remarks
Vanderpump *et al.*, 2011 Carried out between June-July 2009 and November-December 2009	Cross-sectional study	20ml non-fasting sample of early morning urine (n=737) 5ml tap water samples (n=30) FFQ assessing sources of iodine (n=664)	Girls (14-15 yrs) attending secondary schools (n=810) from 9 UK centres (Aberdeen, Belfast, Birmingham, Cardiff, Dundee, Exeter, Glasgow, London, Newcastle/ Gateshead)	No information given	Median UI concentration 80.1 µg/L; 95% CI 76.7-83.6 µg/L Median UI was significantly different between centres: highest in Dundee (98.4 µg/L) & lowest in Belfast (64.7 µg/L)	Sampling during summer (p<0.0001), geographical location (p<0.0001), low milk intake (p=0.02), high intake of eggs (p=0.02) were associated with low UI Iodine concentrations of tap water were <3 µg/L, apart from London (5.2-18.2 µg/L) Dietary habits of the participants who did not provide a urine sample (n=73) were not significantly different from those who did
Kibirige *et al.*, 2004 Carried out between March 2000-March 2001	Case-control study	20ml non-fasting sample of early morning urine for pregnant (n=227) and non-pregnant women (n=227) Diet was not assessed	White or Asian pregnant women at 15 weeks gestation (n=227), mean age 28.3 years (range 15.9-39.2) attending an antenatal clinic at a Middlesbrough hospital Volunteer non-pregnant age-matched controls (n=227), mean age 28.5 years (range 15.3-39.9)	Women with known thyroid disease or other systemic illness	UI concentration <50 µg/L for 16 pregnant women (7%) and 20 non-pregnant controls (9%) 40% of pregnant women had UI of 50-100 µg/L	Asian women had a lower mean UI than white women (p<0.05)
Bath *et al.*, 2008 No information given on study period	Cross-sectional study	24-hour urine collections (n=26) Diet was not assessed	Women of childbearing age (n=26) from the staff and student population at the University of Surrey, Guildford, UK	Subjects on thyroxine; those who were or had been pregnant in the last 6 months	Median UI concentration 66 µg/L 5 subjects (19%) had UI of 50-100 µg/L	Abstract from the British Dietetic Association's 'New to Research Symposium'

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