

***CONSIDERATION OF MANDATORY FORTIFICATION WITH IODINE
FOR AUSTRALIA***

Nutrition Assessment Report

April 2008

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1. Assessment of Iodine Status

Assessing iodine intake using dietary assessment methods is recognised as difficult as these are potentially confounded by: 1) the potentially wide variation of iodine contents in similar foods from different regions, and 2) the potential presence of iodine uptake inhibitors often referred to as goitrogens (ICCIDD *et al.*, 2001; Gibson, 2005). Population iodine status is more accurately reflected by urinary iodine concentration (ICCIDD *et al.*, 2001). Thyroid volume, as assessed by neck palpation, or preferably ultrasonography, provides a measure of long-term iodine status (Gibson, 2005). Other less direct indicators of iodine status include blood concentrations of thyroid-stimulating hormone (TSH), thyroglobulin, and the thyroid hormones thyroxine and triiodothyronine (thyronine).

1.1 Enlarged Thyroids and Goitre

Chronically low iodine intakes lead to adaptive responses by the thyroid, including enlargement of the gland over time (ICCIDD *et al.*, 2001). Thyroid volume is therefore a long-term measure of iodine status. Increased thyroid volume is known as goitre once volume in children exceeds the 97th percentile of age or body surface area specific World Health Organization (WHO) reference values (Gibson, 2005). Raising iodine intake leads to a reduction of goitre size in children, and has historically been used to assess the success of interventions to address iodine deficiency (ICCIDD *et al.*, 2001). The goitres of adults are not similarly reduced by addressing iodine deficiency; therefore, iodine status in populations has historically been assessed by measuring goitre in children.

A number of systems exist to grade goitre assessed by palpitation. One developed by the WHO, International Council for the Control of Iodine Deficiency Disorders (ICCIDD) and UNICEF assigns a grade 0, 1 or 2 to indicate not visible or palpable, palpable but not visible, or visible enlargement respectively (Gibson, 2005).

1.2 Urinary Iodine Concentration

Urinary iodine concentration (UIC) is the preferred measure of iodine status of the ICCIDD and WHO (ICCIDD *et al.*, 2001). It closely reflects iodine intake at lower levels and is a sensitive indicator of recent changes in iodine intake (Gibson, 2005).

1.2.1 World Health Organization Classification of Population Iodine Status

The WHO and ICCIDD have developed a system of classifying populations into categories of iodine status based on their median UIC (MUIC) as shown in Table 1. The median is used instead of the mean because the distribution of UIC in a group is not normal; the tendency is for the mean to exceed the median (ICCIDD *et al.*, 2001). The WHO and the ICCIDD state that, in school-aged children, a MUIC of less than 100 µg/L, and more than 20% of the population having a UIC of less than 50 µg/L, together indicate *mild* iodine deficiency; a median concentration of less than 50 µg/L is indicative of *moderate* iodine deficiency (ICCIDD *et al.*, 2001). In children less than two years old and in lactating women a MUIC below 100 µg/L indicates an *insufficient* iodine intake, whereas in pregnant women, who have higher iodine

requirements than children or other adults, an MUIC below 150 µg/L indicates an *insufficient* iodine intake (ICCIDD, 2007). Table 1 provides further details on ICCIDD criteria for the assessment of population iodine status.

Table 1: ICCIDD Criteria for Assessing Iodine Status, Based on Median Urinary Iodine Concentrations in School-Aged Children

Median urinary iodine (µg/L)	Iodine intake	Iodine status
< 20	Insufficient	Severe iodine deficiency
20 – 49	Insufficient	Moderate iodine deficiency
50 – 99	Insufficient	Mild iodine deficiency
100 – 199	Adequate	Optimal
200 – 299	More than adequate	Risk of iodine-induced hyperthyroidism in susceptible groups
>300	Excessive	Risk of adverse health consequences

The latest guidelines from the ICCIDD state that in children less than two years old and in lactating women a MUIC below 100 µg/L indicates an *insufficient* iodine intake (ICCIDD, 2007). In pregnant women, who have higher iodine requirements than children or other adults, a MUIC below 150 µg/L indicates an *insufficient* iodine intake.

These categories of MUIC are not indicative of the iodine status of individuals and should only be used to assess populations. As an individual's UIC reflects recent iodine intake there can be considerable day-to-day variability. Therefore, spot samples cannot be used to diagnose the iodine status of an individual. Thomson *et al.* (1996) have shown that urine samples over a 24-hour period are necessary for diagnosis of iodine deficiency in an individual and for research purposes.

1.3 Neonatal Thyroid Stimulating Hormone

TSH in children and adults is relatively insensitive to mild and moderate iodine deficiency, but is appropriate for the diagnoses of congenital hypothyroidism in newborns (Gibson, 2005). The WHO recommends neonatal TSH be measured in heel-prick blood samples taken 72 hours after birth to avoid confounding by the initial surge of TSH (WHO, 1994).

1.4 Other Potential Markers of Iodine Status

Other indicators of iodine status include thyroglobulin and thyroid hormone i.e. thyroxine and triiodothyronine (thyronine) concentrations (ICCIDD *et al.*, 2001; Gibson, 2005). Of these blood markers, thyroglobulin appears to be the most specific indicator of recent iodine status; this new biomarker is still gaining acceptance amongst the research community (Gibson 2005). The blood concentrations of thyroxine and thyronine are also quite insensitive to milder forms of iodine deficiency.

1.5 Goitrogens

Inadequate intakes of iodine are not the only cause of thyroid dysfunction and goitre. Substances, collectively known as goitrogens, can inhibit the absorption and/or utilisation of iodine by the thyroid, or otherwise interfere with normal thyroid hormone synthesis (Sarne, 2007). These substances can occur as natural food components, in the form of pharmaceuticals, and as environmental contaminants.

In food they are found naturally in vegetables from the Brassicaceae family such as cabbage, in soybeans, cassava, and a range of plant foods specific to some geographic regions, most notably South America (Gibson, 2005, Sarne 2004). Drinking water has also been shown to contain goitrogenic substances in some instances; these have generally been bacterial by-products or inorganic material from sediment (Sarne 2004). High natural fluoride levels have been associated with impaired thyroid hormone production, and in the presence of iodine deficiency may exacerbate the impact of this deficiency (BEST, 2006).

A range of pharmaceutical agents also act as goitrogens (Sarne, 2007). However, goitrogenic substances have only been clearly identified as major contributors to underproduction of thyroid hormone in the absence of iodine deficiency in a small number of instances where consumption of these substances is unusually high (BEST, 2004; Delange and Hetzel, 2005; Sarne, 2007).

2. Evidence of Iodine Deficiency in Australia

Several studies have been conducted since 1999 in Tasmania, New South Wales and Victoria following identification of a probable re-emergence of iodine deficiency in those parts of the nation. Iodine deficiency was observed in all investigated groups including school children, pregnant women and adults generally. These studies have predominantly relied on spot urine samples to assess iodine status, consistent with standard practice.

The 2003-4 National Iodine Nutrition Study (NINS) measured the urinary iodine concentration of 1709 children aged 8-10 years from both rural and urban locations in New South Wales, Victoria, South Australia, Western Australia, and Queensland (Li *et al.*, 2006). Tasmania was excluded because of its recent efforts to address iodine deficiency locally. The Northern Territory was excluded for logistical reasons. Findings indicate mild deficiency in New South Wales and Victoria with South Australia being borderline; for further details see Table 2.

Table 2: Australian National Iodine Nutrition Study Median Urinary Iodine Concentration Data

State	Median Urinary Iodine Concentration ($\mu\text{g/L}$) ¹	Interquartile Ranges	Iodine Status
New South Wales	89	65.0-123.5	Mild deficiency
Victoria	73.5	53.0-104.3	Mild deficiency
South Australia	101	74.0-130.0	Borderline deficiency
Western Australia	142.5	103.5-214.0	Adequate
Queensland	136.5	104.0-183.8	Adequate
Weighted Total	98 ²		Mild Deficiency

The NINS finding was consistent with an earlier Melbourne study of 607 school children showing a MUIC of 70 $\mu\text{g/L}$, with 27% having a urinary iodine concentration less than 50 $\mu\text{g/L}$ (McDonnell *et al.*, 2003). A study in 301 5-13 year olds living in New South Wales in 2000 also had similar findings to the NINS with a MUIC of 84 $\mu\text{g/L}$, and 14% of children having an MUIC less than 50 $\mu\text{g/L}$ (Guttikonda *et al.* 2003). The only study in Australia to assess the change in iodine status in the same group over time was undertaken in Tasmania (Hynes *et al.*, 2004). The urinary iodine concentration of 170 children was assessed in 1998-99 and then again in 2000-01. Although the MUIC did not change markedly in 2 years (76 $\mu\text{g/L}$ to 75 $\mu\text{g/L}$), the study showed that the percentage of children with urinary iodine concentration below 50 $\mu\text{g/L}$ increased from 13.5% to 21.2% over the two year period; confirming a state of mild iodine deficiency in the area and suggesting a downward trend in iodine intake.

The iodine status of adult populations, especially pregnant women, has also been a topic of recent research, though only in New South Wales and Victoria. Two independent Sydney studies of pregnant women conducted in 1998-99 showed approximately 20% had urinary iodine levels less than 50 $\mu\text{g/L}$ with the MUIC of the groups being 100 $\mu\text{g/L}$ or less (Gunton *et al.*, 1999; Li *et al.*, 2001). A subsequent study involving 50 postpartum women attending a Sydney hospital reported a MUIC of 46 $\mu\text{g/L}$; 58% had a urinary iodine concentration of less than 50 $\mu\text{g/L}$ (Chan *et al.*, 2003). A MUIC of 85 $\mu\text{g/L}$ was reported in 796 pregnant women from the Central Coast area of New South Wales. Women that gave birth at private hospitals had a higher MUIC than those who did so in public hospitals, 101 $\mu\text{g/L}$ vs. 82 $\mu\text{g/L}$, however both groups had considerably lower MUIC than the 150 $\mu\text{g/L}$ recommend for

¹ According to the WHO and ICCIDD, an MUIC of 50-99 $\mu\text{g/L}$ indicates mild iodine deficiency in a population.

² As reported in: The prevalence and severity of iodine deficiency in Australia. Prepared for the Australian Population Health Development Principal Committee of the Australian Health Ministers Advisory Committee. December, 2007

pregnant women. A study of 802 pregnant women between 1998 and 2002 in Melbourne showed an increased percentage of pregnant women, 38-48% depending on ethnicity, had urinary iodine levels less than 50 µg/L, and MUIC levels of between 52 and 61 µg/L (Hamrosi *et al.*, 2005).

A study undertaken in over 2,500 Sydney neonates between 1998 and 2000 showed 5.4-8.1% of infants had whole blood thyroid-stimulating hormone concentrations greater than 5 mIU/L (McElduff *et al.*, 2002). Less than 3% of neonates would be expected to have a blood thyroid-stimulating hormone concentration greater than 5 mIU/L in an iodine replete population (WHO). A subsequent study involving of 50 Sydney neonates reported 6% as having TSH levels exceeding 5mIU/L (Chan *et al.*, 2003). The most recent published work reported that 2.2% of 816 neonates from the Central Coast of New South Wales had thyroid-stimulating hormone concentrations of > 5 mIU/L (Travers *et al.*, 2006). Part of the inconsistencies in these findings may have resulted from some samples being taken earlier than 72 hours after birth, a period when confounding by the initial surge of TSH following birth is most likely to occur (WHO, 1994).

Two of the above studies also investigated normal healthy adult populations and patients with diabetes (Li *et al.* 2001; Gunton *et al.*, 1999). In both studies, the healthy populations and people with diabetes had a MUIC <100 µg/L, with over 20% having levels less than 50 µg/L, indicative of mild iodine deficiency. A recent study conducted in 173 adults living in the Riverina region of Victoria reported a MUIC of 79 µg/L with 18.5% below 50 µg/L (Uren *et al.*, 2008). Although all age groups were mildly iodine deficient, 50-59 year olds had the lowest MUIC (67 µg/L). The sample was a convenience sample of people that responded to advertisements. Each category analysed had only a small sample of participants. Although this means the result may not accurately reflect the broader population's iodine status they are consistent with the other studies mentioned above. For further details of all the studies mentioned above see Table 3.

Table 3: Summary of Recent Australian Research Assessing Iodine Status

Reference:	Group	n	MUIC (µg/L)	% < 50 µg/L	Iodine Status
McDonnell <i>et al.</i> , 2003 (Melbourne)	Males 11-18 years	167	82	17	mild deficiency
	Females 11-18 years	410	64	31	mild deficiency
Guttikonda <i>et al.</i> , 2003 (NSW)	Males & females 5-13 years	301	82	14	mild deficiency
Chan <i>et al.</i> , 2003 (Sydney)	Postpartum women	50	47	58	insufficient
Travers <i>et al.</i> , 2006 (NSW)	Pregnant women	796	85	17	insufficient
	Children 6-13 years	94	84	14	mild deficiency
Li <i>et al.</i> , 2001 (Sydney)	Pregnant women	101	88	21	insufficient
	Adult volunteers	86	88	18	mild deficiency
	Patients with diabetes	85	69	24	mild deficiency

Reference:	Group	n	MUIC (µg/L)	%< 50 µg/L	Iodine Status
Gunton <i>et al.</i> , 1999 (Sydney)	Pregnant women	81	104	20	insufficient
	Postpartum women	28	79	19	mild deficiency
	Patients with diabetes	135	65	34	mild deficiency
	Adult volunteers	19	64	26	mild deficiency
Hamrosi <i>et al.</i> , 2005 (Melbourne)	Pregnant – Caucasian	227	52	48	insufficient
	Pregnant – Vietnamese	263	58	38	insufficient
	Pregnant – Indian/Sri Lankan	262	61	41	insufficient
	Adults 18-39 years	35	89	11	mild deficiency in all groups
Uren <i>et al.</i> , 2008 (Riverina Region Victoria)	Adults 40-49 years	38	80	21	
	Adults 50-59 years	34	67	32	
	Adults 60-69 years	41	79	22	
	Adults ≥ 70 years	25	77	0	

2.2 Tasmania

In 2001 the Tasmanian state Government encouraged the voluntary use of iodised salt by the local bread industry through a memorandum of understanding; as a result an estimated 80% of bread sold in Tasmania contains iodised salt (Seal *et al*, 2003). Monitoring of the initiative showed an increase in the MUIC of 8-11 year-old school children from 75 µg/L before fortification to 105 µg/L approximately four years post fortification (Hynes *et al*, 2004; Seal *et al*, 2007). A comparison of MUIC in pregnant women attending the antenatal clinic at the Royal Hobart Hospital indicated a more modest rise from 76 µg/L before fortification to 86 µg/L post fortification, this difference was not statistically significant ($P = 0.2$) (Burgess *et al*, 2007).

2.3 Conclusion

There is a substantial body of research clearly showing a re-emergence of mild iodine deficiency in South Eastern Australia. Iodine deficiency has been identified in children and adult populations as well as pregnant women, and somewhat less conclusively in neonates.

3. Health Risks of Iodine Deficiency

3.1 Adverse Effects of Iodine Deficiency

The spectrum of iodine deficiency disorders (IDD) is wide, varying according to the severity and duration of the deficiency and the life stage of the populations effected. The term IDD was first coined to provide a collective term to expand on goitre and cretinism; the latter being a form of severe mental retardation (Hetzl, 2000). It encompasses all presentations of the deficiency disease, including the effects of iodine deficiency on neuropsychological development. Table 5 provides WHO's

description of the spectrum of effects of IDD focusing on the more obvious and severe forms throughout the life cycle.

Table 5: Iodine Deficiency Disorders throughout the Life Cycle

Foetus	Abortions Still births Congenital abnormalities Increased perinatal mortality Increased infant mortality Neurological cretinism: mental deficiency, deaf mutism, spastic diplegia, squint Myoedematous cretinism: dwarfism, mental deficiency Psychomotor defects
Neonate	Neonatal goitre Neonatal hypothyroidism
Child and Adolescent	Goitre Juvenile hypothyroidism Impaired mental function Retarded physical development
Adult	Goitre with its complications Hypothyroidism Impaired mental function Iodine induced hyperthyroidism

Adapted from ICCIDD *et al.* (2001)

The signs of mild iodine deficiency are not easily discerned in any age group. However, moderate iodine deficiency in both children and adults is associated with a negative effect on motor performances, motor skill, perceptual and neuromotor abilities and reduced intellectual quotients (IQ). IQ is a tool commonly used to measure mental performance. The average IQ is, by definition, 100 with a standard deviation of 15 points (Megafoundation, 2005).

3.2 Importance of Iodine in Pregnancy and During Early Development

Iodine deficiency during pregnancy has often been described as the most common cause of intellectual impairment worldwide. While severe iodine deficiency during foetal development can lead to the extreme form of mental retardation known as Cretinism, mild and moderate deficiency may also lead to lesser impairments in mental development, hearing, motor control, and reaction time (Delange, 2001). Recent research also indicates mild and moderate deficiency in children can impair their physical growth (Zimmerman *et al.* 2007).

The ICCIDD suggest that the most critical period of iodine nutrition is from the second trimester of pregnancy to the third year after birth (ICCIDD, 2001). The adverse effects of iodine deficiency on the central nervous system can be irreversible, and are compounded by continuing deficiency during infancy (Zoeller and Rovet, 2004). Many of the effects of iodine deficiency shown in adults are usually the result of chronic iodine deficiency rather than of recent deficiency.

Iodine is required for the synthesis of thyroid hormones, which are in turn required for brain development. Major human brain development occurs during foetal growth and early years of life so that adequate iodine is important from conception until at least the third year of life (ICCIDD *et al.*, 2001).

The foetal thyroid does not begin functioning until about the 24th week of gestation and until that time is reliant purely on the transfer of the thyroid hormones thyronine and thyroxine across the placenta. Even at term, neonates still derive some thyroxine directly from the mother (Delange, 2000).

Brain development continues into early childhood, thus iodine nutrition remains a critical factor (Zoeller and Rovet, 2004). Before the introduction of weaning foods, the iodine intake of the infant depends on the iodine content of breast milk or formula. Levels of iodine in breast milk reflect the maternal diet (Dorea, 2002). Because of foetal reliance on maternal thyroid hormones, and the infant's reliance on breast milk, the dietary requirement for iodine intake are higher for pregnant and lactating women than for the rest of the population (Delange, 2004).

3.2.1 Neurological Consequences for Children of Mothers with Mild Iodine Deficiency during Pregnancy

The effect of mild iodine deficiency (MUIC 55-99 µg/L) on neurological development is a matter of current debate. A recent review concluded that there is evidence of delay in reaction time but no evidence of impaired mental development in infants of mothers that were mildly iodine deficient during pregnancy (Delange, 2001). However, a subsequently published study of Chinese children aged 7-13 months suggests that even mild prenatal iodine deficiency, as assessed by cord blood thyroid stimulating hormone concentrations, is associated with reduced performance in some tests of mental development (Choudhury and Gorman, 2003). This study suggested a dose-response relationship where small differences in the severity of iodine deficiency results in small changes in mental development in a linear fashion.

3.2.2 Neurological Consequences for Children of Mothers with Moderate Iodine Deficiency during Pregnancy

A number of publications have shown an association between moderate iodine deficiency (MUIC 25-49 µg /L) and impaired psychoneuromotor and intellectual development in children, including those born to moderately deficient women (Delange, 2001). The findings include low visual-motor performance, impaired motor skill and diminished IQ.

Haddow *et al.* (1999) reported an average IQ deficit of 7 points in children aged 7-9 years born to mothers with undetected thyroid deficiency, i.e. a thyroid-stimulating hormone concentration in the 96-99th centile of 25 000 women tested. Although the case-control study was not designed to investigate the effects of iodine deficiency the authors suggested that even mild asymptomatic hypothyroidism might have an effect on intelligence.

An Italian cross-sectional study reported that 11 of 16 children born to moderately iodine deficient mothers were diagnosed with attention deficit and hyperactivity disorder (ADHD), whereas none of the 11 children of mothers in an area of adequate iodine intake had ADHD (Vermiglio *et al.*, 2004). Further research in this area is required to draw any firm conclusion about this apparent association. However, an earlier study reporting a significantly increased risk of ADHD in those with generalised resistance to thyroid hormone³, and a subsequent work suggesting a link between TSH concentration and ADHD, add support to this possible relationship (Alvarez-Pedrerol *et al.*, 2007; Hauser *et al.*, 1993).

3.3 Neurological Consequences of Mild and Moderate Iodine Deficiency in Children

A cross-sectional study of 1,221 school children in southern Europe (Spain) with a MUIC of 90 µg/L showed that IQ was statistically significantly lower in children with urinary iodine concentrations below 100 µg/L than in those with excretions above 100 µg/L (IQ 96.4 ± 17.5 vs. 99.3 ± 15.8) (Santiago-Fernandez *et al.*, 2004). Further, children with urinary iodine concentrations below 100 µg/L were more likely to have an IQ below the 25th centile, i.e. IQ below 87.3.

Moderate iodine deficiency in both children and adults has been linked to a negative effect on motor performances, motor skill, perceptual and neuromotor abilities and diminished IQ (Delange, 2001). These effects were observed in studies of children who were not severely deficient and did not exhibit signs and symptoms of endemic cretinism. Zimmerman *et al.* (2006) randomised 310 moderately iodine deficient (MUIC 43 µg/L) 10-12 year olds in Albania to receive either iodine supplements or placebo. After 24 weeks the children receiving supplements showed statistically significant improvements in tests of information processing, fine motor skills and visual problem solving compared to those receiving placebo. An earlier study in 196 moderately to severely iodine deficient 7-11 year olds in Benin found that those children who had improved iodine status after 11 months also showed statistically significant improvements in tests of mental function (van den Briel *et al.*, 2000).

As well as having an impact on children, iodine deficiency has been shown to have an adverse effect on the IQ of older populations, potentially as a result of being born in iodine deficient areas (Delang and Hetzel, 2005). A meta-analysis of 18 studies undertaken by Bleichrodt and Born (1994) calculated that the mean IQ of individuals with moderate to severe iodine status was 13.5 IQ points lower than that of individuals with adequate iodine status.

³ Thyroid hormone resistance refers to a state in which normal concentrations of thyroid hormones are insufficient to generate the a standard response.

3.4 Mild and Moderate Iodine Deficiency and Growth

Despite the negative impact of severe iodine deficiency on growth being well established (Delang and Hetzel, 2005); the effect of mild or moderate iodine deficiency on growth has until very recently been unclear. Cross-sectional studies have shown either no correlation or a modest positive correlation between iodine intake and growth in children (Zimmerman, 2007). However, in a recent randomised controlled trial in 310 moderately iodine deficient, 10-12 year-olds those given adequate iodine had significantly improved height-for-age and weight-for-age z scores after six months compared to those not receiving additional iodine (Zimmerman *et al.*, 2007). Correcting mild iodine deficiency, in 100 5-14 year-olds did not result in a significant improvement in growth after six months compared to those not receiving additional iodine.

3.5 Iodine Deficiency, Goitre, and Thyroid Disease

The form and frequency of different types of thyroid disease as well as the average age of onset have been linked to population iodine status. Severe iodine deficiency leads to underproduction of thyroid hormones, i.e. hypothyroidism, as there is insufficient iodine available for the normal production of thyroid hormones (Delange and Hetzel, 2005). However, in mild and moderate iodine deficiency the overproduction of thyroid hormone i.e. hyperthyroidism, is the more common problem (Aghini-Lombardi *et al.*, 1999; Delange and Hetzel, 2005; Laurberg *et al.*, 2000).

Below is a summary of comparisons between populations with different iodine status and the associated distribution of thyroid diseases. The separate issue of the impact of fortification programs on thyroid health is covered in Supporting Document 4 (Safety Assessment) of the Assessment Report.

3.5.1 Mild and Moderate Iodine Deficiency and Hyperthyroidism

Comparisons of mild with moderately iodine deficient populations in Denmark with populations that have adequate or above adequate iodine intake in Iceland, indicate hyperthyroidism to be more common in iodine deficient populations (Laurberg *et al.*, 2000). Further, in Denmark it was found that hyperthyroidism was more common in the moderately deficient part of the country than in the mildly deficient part (Bülow Pedersen *et al.*, 2002).

The iodine status of a population also influences the distribution and age of onset of different forms of hyperthyroidism. In deficient areas the most common form of hyperthyroidism is multinodular toxic goitre (Aghini-Lombardi *et al.*, 1999; Laurberg *et al.*, 2000). In an area of above adequate iodine intake Graves' disease was the most common form of hyperthyroidism, developing earlier in life in an area of deficiency (Laurberg *et al.*, 2000). No such differences in the incidence of subacute thyroiditis have been reported (Laurberg *et al.*, 2000).

3.5.2 Mild and Moderate Iodine Deficiency and Hypothyroidism

Comparison of data from a moderately iodine deficient area of Denmark and an area of adequate/above adequate intake in England suggests that hypothyroidism is more common in areas of adequate or above adequate iodine intake (Laurberg *et al.*, 2000; Vanderpump, *et al.*, 1995). Other comparisons confirm that hypothyroidism is more common in areas of above adequate iodine intake, than those with mild or moderate deficiency; less clear is what can be expected in populations with adequate but not above adequate intakes (Laurberg *et al.*, 2000). In Denmark it has also been shown that hypothyroidism was more common in the area of mild iodine deficiency than in the area of moderate deficiency (Pedersen *et al.*, 2002).

Szabolcs *et al.* (1997) compared thyroid health in groups of nursing home residents over 60 years of age from the same geographic and ethnographic region, the Carpathian basin. Subjects from Northern Hungary, Slovakia, and Eastern Hungary showed deficient, adequate, and abundant iodine intake respectively. The study reports urinary iodine per gram creatinine as opposed to per litre urine, not allowing for direct application of the criteria for the description of iodine nutrition in Table 1. Eastern Hungary, where subjects' iodine intake was highest, had the highest prevalence of clinical hypothyroidism. Northern Hungary where iodine intake was lowest had the lowest prevalence of clinical hyperthyroidism.

3.6 Conclusion

Adequate iodine intake is essential for normal mental and physical growth and development. Iodine deficiency, even when categorised as mild, can lead to deficits in mental and nervous system function. The effect of iodine deficiency on growth and development is greatest when the deficiency occurs during foetal development and within the first two-to-three years of life when the nervous system is undergoing the greatest and most rapid development. In addition to the timing of the iodine deficiency its severity has a strong influence on the magnitude of any negative consequences. The developing foetus and the young child are therefore the most vulnerable with respect to iodine deficiency as the consequences for these two groups are the most serious, and because in these two groups they are irreversible.

As older children and adults are no longer undergoing major neural development the consequences of iodine deficiency are predominantly associated with thyroid health. Areas of moderate deficiency tend to have the greatest prevalence of hyperthyroidism, with this being slightly less prevalent in areas of mild deficiency or adequacy. Conversely it is areas of adequate or above adequate iodine supply that have a higher prevalence of hypothyroidism.

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