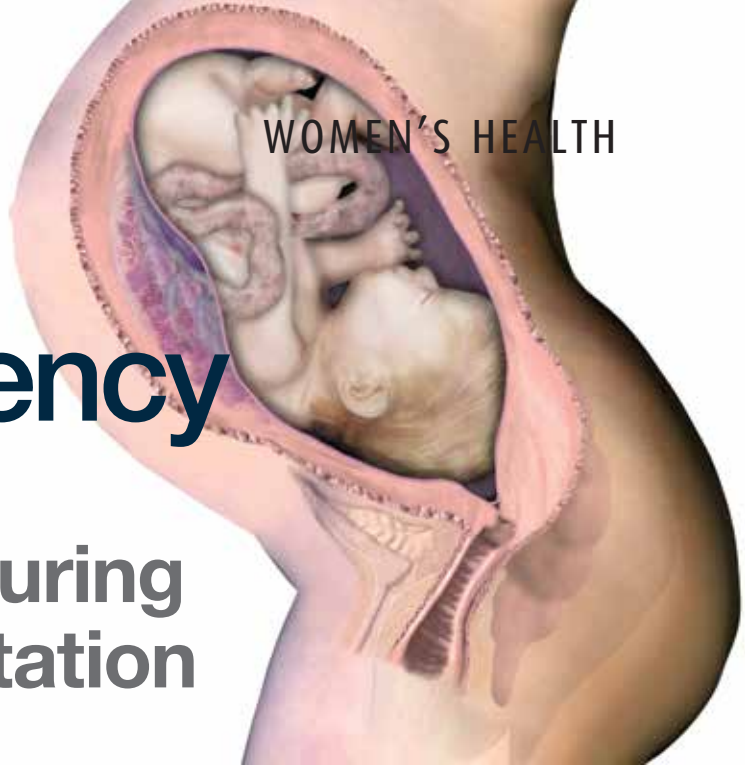

Iodine deficiency

The importance of supplementation during pregnancy and lactation

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Surveys have shown that most pregnant Australian women are iodine deficient, ingesting about half the daily requirement. Women need to be made aware of the increased need for iodine during pregnancy and lactation and the importance of iodine supplementation at this time.

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According to the World Health Organization (WHO), 'iodine deficiency is the world's most prevalent, yet most easily preventable cause of brain damage and more than two billion people worldwide are at risk of developing one or more of the effects of IDD [iodine deficiency disorders]'.[1] Dietary iodine deficiency results in a broad spectrum of disorders, collectively known as iodine deficiency disorders (IDD), comprising endemic goitre, hypothyroidism, obstetric complications, increased neonatal morbidity and mortality, and mild-to-severe brain damage that may vary from small loss of IQ to frank cretinism.[1]

The key points from this article are summarised in the box.

WHERE DOES IODINE COME FROM?

Iodine is a simple chemical element that is widely distributed in nature, and is found abundantly in marine creatures and seaweed. In the conventional Australian diet, iodine comes mainly from milk and dairy products and to a lesser extent from seafood and processed foods with added iodised salt such as bread. Vegetables, fruits and cereals are generally poor sources of iodine.

The disappearance of iodine deficiency in Australia in the 1950s could best be described as 'an accidental public health triumph' due to the widespread use of iodophors introduced over half a century ago as sanitising agents in the dairy industry.[2] These chemicals are a combination of iodine and a solubilising agent or carrier, such that the resulting complex provides a sustained-release reservoir of iodine and releases small amounts of free iodine in aqueous solution. Although milk is the best natural source of iodine, the amount of iodine in cow's milk is augmented by iodine leakage from the iodophore, more than doubling the natural concentration of iodine in the milk.

WHY DO WE NEED IODINE?

Iodine is an integral component of the thyroid hormone molecule, making up about two-thirds of the mass of tri-iodothyronine

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KEY POINTS

- Iodine deficiency during pregnancy is the most common global cause of neurodevelopment disorders in newborns and infants.
- Iodine requirements increase during pregnancy from 150 to 250 µg/day to meet the needs for increased thyroid hormone production.
- Failure of pregnant women to meet their iodine requirements may result in obstetric and fetal complications.
- Surveys have shown that most pregnant Australian women are iodine deficient, ingesting about half the daily requirement.
- An Australian study has shown a strong relation between mild-to-moderate iodine deficiency in pregnant women and subsequent loss of IQ in their offspring as demonstrated by poorer performance in NAPLAN testing compared with the offspring of iodine-sufficient mothers.[7] Similar data have recently emerged from the UK.[6]
- Mandatory iodisation of all salt used in bread-baking since 2009 has not corrected iodine deficiency in Australian women of reproductive age.
- The NHMRC recommends that all pregnant women and those planning a pregnancy (except those with known thyroid disease) take an iodine supplement of 150 µg/day.
- Iodine supplementation should be continued while breastfeeding to ensure adequate intake in the neonate.
- Surveys of pregnant women in Australia indicate that about 50% have not heard of the recommendation to take iodine supplements.
- Increasing iodine intake above 500 µg/day during pregnancy is excessive and of no benefit and should be avoided as it may cause harm.

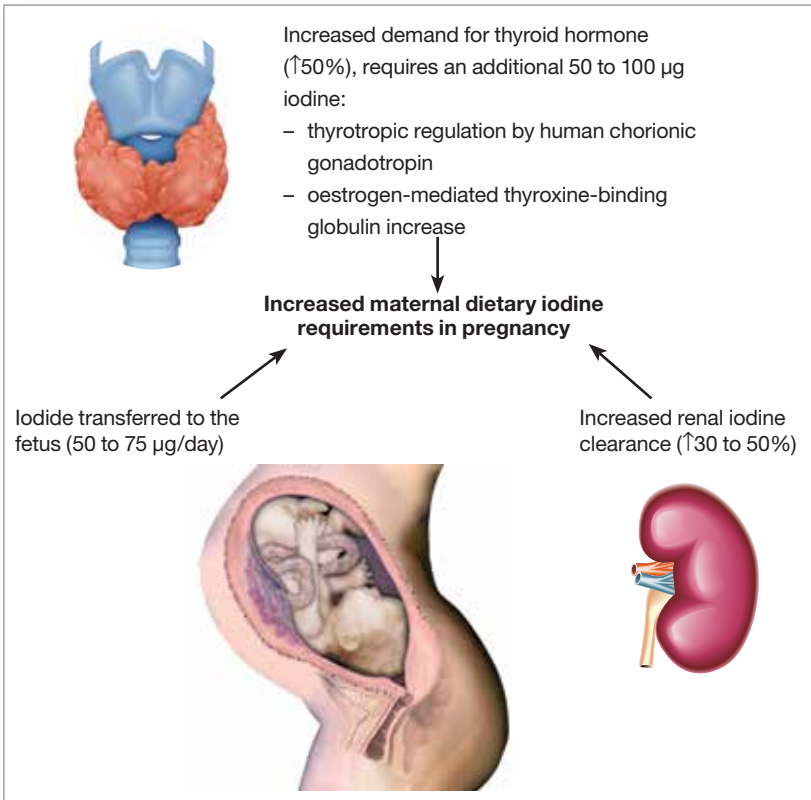

Figure. Reasons for increased iodine requirements during pregnancy.
Adapted from a diagram developed by Dr E.N. Pearce, Boston, USA.

(T3) and thyroxine (T4). Thyroid hormones regulate growth and metabolic rate in humans and are essential for optimal brain and physical development of the fetus and infant. The fetus is totally dependent on maternal T4 until late in gestation when the developing fetal thyroid gland becomes functional before birth. The breastfed infant is entirely dependent on iodine in the mother's milk to ensure normal thyroid function.

RE-EMERGENCE OF IODINE DEFICIENCY

The Australian National Iodine Nutrition Study (NINS) in school children, conducted a decade ago, confirmed that mild iodine deficiency had re-emerged in Australia.[3] This was due largely to changes in work practices in the dairy industry where iodophors were quietly replaced with other forms of sanitisers.[2] Contributing factors were thought to be consumer and food manufacturer preferences for noniodised salt over iodised salt.

In 2009, a good public health outcome was generated from the NINS with an agreement between State health ministers, the Federal Government and the New Zealand Government to implement mandatory iodine fortification of all salt used in the manufacture of bread and baked products. The aim was to restore adequate iodine intake to most of the population, although it was acknowledged that this would not correct iodine deficiency in pregnant women.

IODINE REQUIREMENTS DURING PREGNANCY

The National Health and Medical Research Council (NHMRC) recommended daily intake (RDI) of iodine for adults is 150 µg/day.[4] During pregnancy

there is a dramatic increase in iodine requirements. The maternal thyroid gland must increase thyroid hormone production by about 50% early in gestation to meet the demands of the mother, to ensure transplacental passage of T4 and iodine to the fetus, and to compensate for increased clearance of iodine by the kidney during pregnancy (Figure). Recently, the WHO, UNICEF and International Council for the Control of Iodine Deficiency Disorders (ICCIDD) recommended the RDI of iodine during pregnancy should be increased to 250 µg/day to maintain normal thyroidal iodine stores of 15 to 20 mg.[5] If the maternal thyroid gland cannot meet the demands of pregnancy, serious obstetric and fetal consequences ensue.

TABLE 1. MEDIAN URINARY IODINE EXCRETION (UIE) LEVELS FOR CLASSIFICATION OF IODINE STATUS[1,5]

Population group	Median UIE (µg/L)	Category of iodine intake
Pregnant women	<150	Insufficient
	150 to 249	Adequate
	250 to 499	More than adequate
	>500	Excessive
Breastfeeding women	<100	Insufficient
	>100	Adequate
Non-pregnant women	<100	Insufficient
	>100	Adequate

IODINE DEFICIENCY DURING PREGNANCY

As an adequate supply of T4 is essential for normal fetal and neonatal brain development, any deficiency in iodine will result in irreversible damage to the central nervous system. This can cause a spectrum of disorders from neurological cretinism to mild degrees of neurodevelopmental delay depending on the severity and timing of the deficiency.[1]

The negative impact of moderate-to-severe maternal iodine deficiency on fetal wellbeing is indisputable. However, the adverse effect on neurocognitive development of the offspring of women experiencing mild-to-moderate iodine deficiency has been difficult to quantify. Two recent observational studies, one in the UK[6] and the other in Tasmania,[7] have measured IQ or school performance of children between the ages of 8 and 10 years born to mothers whose urinary iodine excretion (UIE) during pregnancy was less than 150 µg/L. Results showed significant decreases in IQ and school performance in spelling, grammar and literacy. These studies add considerable weight to the argument that even mild maternal iodine deficiency can result in neurocognitive impairment in the offspring of those mothers.[8]

INDICATORS FOR ASSESSING IODINE DEFICIENCY

The severity of iodine deficiency in a population is classified according to UIE levels. Iodine intake can be derived from the UIE assuming an estimate of 24-hour urine volume and an approximate iodine bioavailability of 90% in the urine.[1] The median UIE of an iodine-sufficient population is 100 µg/L, corresponding to a daily iodine intake of 150 µg. In pregnancy, the median UIE should be 150 µg/L or more, corresponding to a daily iodine intake of 250 µg. The WHO criterion for optimal iodine intake in a population of pregnant women is a UIE of 150 to 249 µg/L (Table 1).[1,5]

Although measurement of UIE levels on a spot sample of urine is a simple test for assessing population iodine status for large groups of people, it is less precise for assessing iodine deficiency in an individual.[9] At any one time UIE in an individual reflects recent iodine intake only and not thyroidal iodine stores, so individual urine results must be interpreted in the context of the dietary history.[9] A decrease in serum thyroid hormone levels and a rise in thyroid-stimulating hormone (TSH) levels in response to mild-to-moderate iodine deficiency are often minor and again difficult to interpret in an individual. Recent studies point to a rise in serum thyroglobulin as being the most sensitive marker for iodine deficiency in an individual.[9] Finally, there is great diagnostic value in taking a dietary history because it is one of the most powerful tools in assessing iodine intake in an individual. As already emphasised, the major sources of iodine in the Australian diet are milk and dairy products, bread, iodised salt use in the home and seafood.

URINARY IODINE EXCRETION IN PREGNANT WOMEN

Unfortunately, a national survey of pregnant women was not undertaken at the time of the NINS. However, there have now been multiple, small studies of UIE levels in pregnant women, with results reported from New South Wales, Victoria, Tasmania, the ACT, South Australia and the Northern Territory. Every study showed median UIE levels of less than 150 µg/L, consistent with widespread inadequate iodine intake in pregnant women throughout most states (Table 2).[10-18] Extrapolating from these published data, daily iodine intake in pregnant women in Australia is about half the RDI for pregnancy.[19] A 2013 Australian national survey of UIE levels in women of childbearing age, conducted after the

TABLE 2. DATA FROM STUDIES OF URINARY IODINE EXCRETION (UIE) IN PREGNANT WOMEN IN AUSTRALIA BEFORE THE FORTIFICATION OF BREAD WITH IODISED SALT

Authors	Subjects	Location	Sample size	Median UIE (µg/L)
Gunton et al. 1999[10]	Pregnant Postpartum	Northern Sydney, NSW	81 28	104 79
Li et al. 2001[11]	Pregnant	Western Sydney, NSW	101	88
Hamrosi et al. 2005[12]	Caucasian Vietnamese Indian/Sri Lankan	Victoria	227 263 262	52 58 61
Travers et al. 2006[13]	Pregnant >28 weeks	Central Coast, NSW	815	85
Burgess et al. 2007[14]	Antenatal clinic	Hobart, Tasmania	285	76
Mackerras et al. 2011[15]	Indigenous teenagers	NT	24	49
Nguyen et al. 2010[16]	Antenatal clinic	Canberra, ACT	100	62
Blumenthal et al. 2012[17]	Antenatal clinic	Northwestern Sydney, NSW	367	81
Clifton et al. 2013[18]	Antenatal clinic	Adelaide, SA	196	84

mandatory use of iodised salt in bread commenced in 2009, has shown median UIE levels of less than 150 µg/L, indicating mild iodine deficiency persists in pregnant Australian women.[20]

STUDIES ON IODINE SUPPLEMENTATION DURING PREGNANCY

Evidence for a beneficial effect of maternal iodine supplementation on brain development in children born to women who were experiencing moderate-to-severe iodine deficiency during pregnancy is well accepted.[8,21] In addition, several studies of iodine supplementation in iodine-deficient pregnant women have demonstrated that correction of iodine deficiency can prevent enlargement of the maternal thyroid gland and normalise their serum thyroglobulin and thyroid function. However, with respect to mild-to-moderate iodine deficiency, the lack of well-designed, randomised controlled trials of iodine supplementation in women during pregnancy and lactation with measurement of beneficial effects on neurodevelopmental outcome of the offspring leaves many questions unanswered in terms of optimising brain development in the fetus and infant.[22]

IODINE SUPPLEMENTS

The agreed primary strategy for the prevention of iodine deficiency during pregnancy is universal salt iodisation. In countries where iodine deficiency is prevalent and universal salt iodisation has not been implemented, iodine supplementation has been recommended by the WHO and its collaborative partners.[5] It would be best if an adequate iodine intake during pregnancy could be achieved by a diverse healthy diet but I am not aware of any studies in Australia that have demonstrated iodine sufficiency in pregnant women without supplementation (Table 2). Ideally iodine supplementation should commence three to six months before conception and continue until the infant is weaned.

To establish an appropriate iodine supplement for pregnant and breastfeeding women in Australia, using both dietary information and back-calculation from published UIE levels, it was estimated that a supplement of 100 to 150 µg/day would ensure an adequate intake for more than 95% of the population.[19] The NHMRC has now recommended that all women who are pregnant, breastfeeding or considering pregnancy should take an iodine supplement of 150 µg/day, with the caveat that women with pre-existing thyroid disorders should seek advice from their medical practitioners before taking a supplement.[23] Similar recommendations have now been published by the American Thyroid Association and the American Endocrine Society.

Despite the fact that iodine nutrition has improved considerably in Australia and New Zealand since the fortification of bread with iodised salt in 2009, iodine intake in women of reproductive age – and presumably pregnant and breastfeeding women – remains suboptimal, reinforcing the need for supplementation.[20] Unfortunately, these messages are not reaching

pregnant women as almost 50% of pregnant women have not been educated about the need for iodine supplementation during pregnancy or seem to ignore the advice if it has been given.[24]

WHAT IS EXCESSIVE IODINE INTAKE AND CAN IT CAUSE HARM?

The philosophy of 'more is better' with respect to iodine intake is mistakenly becoming commonplace and should be discouraged as there is no scientific evidence for benefit above recommended intakes and this practice may cause harm (Table 1).[9] A proportion of women with a past or current history of autoimmune thyroiditis, especially those with Graves' disease, are at risk of developing either hypothyroidism or hyperthyroidism if their intake of iodine is excessive. There is general agreement among most authorities that an iodine intake of more than 1100 µg/day is excessive and potentially toxic[4] and it is prudent to advise women not to take more than 500 µg/day to ensure a wide safety margin.

CONCLUSION

During pregnancy there is a dramatic increase in iodine requirement from a recommended daily intake of 150 to 250 µg, with the maternal thyroid gland having to increase thyroid hormone production by about 50% early in gestation to meet the demands of the mother and fetus. Despite the fact that iodine nutrition has improved considerably in Australia and New Zealand since the fortification of bread with iodised salt in 2009, iodine intake in women of reproductive age remains suboptimal, reinforcing the need for supplementation. The NHMRC has now recommended that all women who are pregnant, breastfeeding or considering pregnancy should take an iodine supplement of 150 µg/day to ensure iodine levels are at an optimal level. Unfortunately, these messages are not reaching pregnant women as almost 50% of pregnant women have not been educated about the need for iodine supplementation during pregnancy. MT

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