Iodine status in the UK population and implications for brain development

Dr Sarah Bath
MRC Research Fellow
Registered Dietitian

SENSE and NII meeting
London
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Overview

Iodine

Essential component of T4 and T3

Growth, development and metabolism

Brain and neurological development
Iodine Deficiency Disorders

Severe

- Severe impairment of cognitive function
- Deaf-mutism
- Spastic movements of arms and legs

Moderate

Impaired motor development at 24 months

Lower IQ at age 8

Poorer reading ability at age 9

Poorer spelling at age 9

Mild

Cretinism

Action of thyroid hormone on brain

Mother

\[ \text{T4} \]

\[ \text{T4} \rightarrow \text{Placenta} \]

\[ \text{T3} \]

Fetus

\[ \text{T4} \rightarrow \text{Placenta} \]

Deiodinase-2

Binds to TH receptors and regulates expression of T3-target genes

\[ \text{T3} \]
# Iodine intake recommendations

<table>
<thead>
<tr>
<th></th>
<th>UK: Reference Nutrient Intake (RNI)</th>
<th>EFSA: Adequate intake</th>
<th>US IOM: Recommended Dietary Allowance</th>
<th>Australia &amp; New Zealand: Recommended Dietary Intake</th>
<th>WHO: Recommended Nutrient Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children 7-10 years</strong></td>
<td>110</td>
<td>90</td>
<td>90 (7-8 yrs) 120 (9-10 yrs)</td>
<td>90 (7-8 yrs) 120 (9-10 yrs)</td>
<td>120</td>
</tr>
<tr>
<td><strong>Adulthood</strong></td>
<td>140</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>140</td>
<td>200</td>
<td>220</td>
<td>220</td>
<td>250</td>
</tr>
<tr>
<td><strong>Lactation</strong></td>
<td>140</td>
<td>200</td>
<td>290</td>
<td>270</td>
<td>250</td>
</tr>
</tbody>
</table>

Iodine during pregnancy and lactation

- Increased requirement during pregnancy to:
  - provide for increased T4 production
  - cover potential increased urinary loss
  - provide iodine for the fetus after the onset of fetal thyroid function

- Increased required during lactation:
  - Provide iodine for maternal thyroid function
  - Ensure adequate iodine in breast milk

Iodine excess

- Iodine excess can lead to hypothyroidism or hyperthyroidism
- Adults should not regularly consume more than **1000** mcg/day
- Some individuals may respond adversely to lower doses e.g. those with thyroid nodules
Assessment of iodine status

- Dietary assessment is not useful for estimating iodine intake
- Biomarker: Urinary iodine concentration (UIC)
  - High correlation between iodine intake (48-hr food diary) and 24-hr iodine excretion ($r=0.75$, $p<0.001$)
- Spot urine samples used for population studies

<p>| Median urinary iodide concentration (μg/L) |</p>
<table>
<thead>
<tr>
<th>Adulthood</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inadequate</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Adequate</td>
<td>100-199</td>
</tr>
<tr>
<td>More than adequate</td>
<td>200-299</td>
</tr>
</tbody>
</table>

- UIC should **NOT** be used to assess individuals
- Iodine-to-creatinine ratio adjusts for urine dilution

What is the iodine status of population groups in the UK?
Iodine Deficiency in the UK

- Iodine deficiency was widespread in Britain
- Cretinism reported in some areas
- Goitre was still present until the 1960s

Phillips D 1997

Areas of endemic goitre in the past

Derbyshire neck
How goitre was eradicated

Iodine concentration of milk increased

Milk consumption increased

Three-fold increase in iodine intake between 1950s and 1980s*

*Phillips D 1997;
UK was one of few countries with no data on iodine status of population (until 2011) *

*WHO 2007
Iodine status of UK schoolgirls*

- Urinary iodine concentration measured in 737 adolescent girls aged 14-15 years
- Nine centres across the UK
- Median urinary iodine concentration 80.1 µg/L
- Iodine excretion indicated mild deficiency in the cohort
- Concern that iodine deficiency may be widespread in the UK

*Vanderpump et al. Lancet 2011
UK now classified as mildly iodine deficient*

* Andersson et al J Nutr 2012
Iodine intake and status of UK women of childbearing age recruited at the University of Surrey in the winter

Sarah C. Bath, Michelle L. Sleeth, Marianne McKenna, Alan Walter, Andrew Taylor and Margaret P. Rayman*

Department of Nutritional Sciences, Faculty of Health and Medical Sciences, University of Surrey, Guildford, Surrey GU2 7XH, UK

- Median estimated iodine intake: 167 μg/day
- 14% had intake below estimated average requirement (EAR)
- 42% had intake below pregnancy EAR

Dark bars: Subjects took iodine-containing supplement
Importance of iodine pre-pregnancy

- Need to optimise thyroid stores of iodine prior to pregnancy\(^1\)

- Use of iodised salt for over 2 years reduced risk of maternal thyroid failure, compared with short term use of iodised salt\(^2\)

- Use of iodised salt prior to pregnancy resulted in improved thyroid profile than in women commencing iodine supplements during pregnancy\(^3\)

Median UIC (85.3 µg/L) classifies the group as mildly-to-moderately iodine deficient
Oxford pregnant women

- 230 primiparous UK women recruited at 12 weeks gestation in the ultrasound clinic for the Selenium in Pregnancy Intervention Trial (SPRINT)
- Only 2% of women took supplements containing iodine

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What are the implications of mild-to-moderate iodine deficiency during pregnancy on the developing brain?
Trials of iodine in pregnancy

No adequately powered randomised, placebo-controlled trials of iodine supplementation with child outcomes

Just three intervention studies in pregnancy:

- two suggest benefit of iodine supplements on child neurodevelopment up to 24 months\(^1,2\)
- One found no difference between iodised salt and two doses of iodine supplements (150 or 230 µg)\(^3\)

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Results from observational studies in regions of mild-to-moderate iodine deficiency
Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC)

Sarah C Bath, Colin D Steer, Jean Golding, Pauline Emmett, Margaret P Rayman

Collaborative study between University of Surrey and University of Bristol

Bath et al 2013 Lancet 382, 331-337
ALSPAC
(Avon Longitudinal Study of Parents & Children)

- Total of 14,541 pregnant women enrolled
- Biological samples (including urine) available
- Data have been collected on the health and development of the offspring over the last 20 years
Our current study investigated 1040 ALSPAC women. The women were selected on the basis of:

- availability of a urine sample in first trimester

and

- their children having a measure of intelligence quotient (IQ) at age eight years
Iodine status in ALSPAC

- Women’s iodine status grouped as:
  - < 150 µg/g or
  - ≥ 150 µg/g
  - i.e. deficient/sufficient*

- The group was classified as mildly-to-moderately deficient
  (median 91.1 µg/L)

- 67% of women had values < 150 µg/g

* WHO et al. 2007 Assessment of iodine deficiency disorders and monitoring their elimination. Geneva: WHO.
### Confounders

<table>
<thead>
<tr>
<th>Child</th>
<th>Maternal</th>
<th>Dietary</th>
<th>Socio-economic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Age</td>
<td>Iron intake</td>
<td>Maternal education</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Smoking</td>
<td>n-3 fatty acid intake</td>
<td>Paternal education</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>Alcohol</td>
<td>Fish oil supplements</td>
<td>Housing status</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>Parity</td>
<td></td>
<td>Crowding in the home</td>
</tr>
<tr>
<td>Birth weight</td>
<td>Stressful life-events</td>
<td></td>
<td>Family adversity</td>
</tr>
<tr>
<td></td>
<td>Parenting score</td>
<td></td>
<td>HOME score</td>
</tr>
<tr>
<td></td>
<td>Postnatal depression</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results

After adjustment for 21 confounders a significantly higher odds of suboptimum:

- Verbal IQ (OR 1.58 95% CI 1.09, 2.30)
- Reading Accuracy (OR 1.69 95% CI 1.15, 2.49)
- Reading Comprehension (OR 1.54 95% CI 1.06, 2.23)

Table source: Bath et al 2013 *Lancet* 382, 331-337
Degree of iodine deficiency

- Verbal IQ (p=0.002)
- Total IQ (p=0.04)
- Reading comprehension (p=0.04)

Figure: Means (95% CIs) for child cognitive outcomes according to maternal iodine status in the first trimester. Values are adjusted for the effect of confounders (model three). Child verbal and total IQ were assessed at age 8 years and reading accuracy and comprehension at age 9 years. IQ=intelligence quotient.

Figure source: Bath et al 2013 *Lancet* 382, 331-337
Iodine in pregnancy in UK

Avon (n=1023):
• UIC: 91 μg/L
• Iodine/creatinine: 110 μg/g

Cardiff (n=480):
• UIC: 117 μg/L

Tayside (n=433):
• UIC 137 μg/L
• 40% had intake < ½ recommended

Middlesborough (n=227):
• 40% had UIC below 100 μg/L

Oxford (n=229):
• UIC: 56 μg/L
• Iodine/creatinine: 116 μg/g

Surrey (n=229):
• UIC: 85 μg/L
• Iodine/creatinine: 123 μg/g

UK: mildly-to-moderately iodine deficient

- Median UIC 95μg/L
Knowledge and awareness of iodine

Study of 1026 UK pregnant women/new mothers

- 64% had not received information on iodine
- Only 16% aware of the role of iodine in pregnancy
- 56% unable to identify iodine-rich food sources
  - Only 9% correctly identified milk as a source

1. Combet et al. 2015 Br J Nutr doi:10.1017/S0007114515001464
Effect of iodine during childhood on cognition in regions of mild-to-moderate iodine deficiency
New Zealand – mild iodine deficiency\(^1\)
- Placebo or 150 µg iodine/day for 28 weeks
- In iodine group there was a significant improvement in scores on two of five subscales of cognitive testing

Albania – moderate iodine deficiency\(^2\)
- 400mg iodised oil or placebo
- In iodine group there was improvement in 4/7 subscales of cognitive test

A multi-centre pilot study of iodine status in UK schoolchildren, aged 8–10 years

Sarah C. Bath¹ · Emilie Combet² · Patrick Scully¹ · Michael B. Zimmermann³ · Katharine H. C. Hampshire-Jones¹ · Margaret P. Rayman¹

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surrey</td>
<td>Winter: 51</td>
</tr>
<tr>
<td></td>
<td>Summer:</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Scotland</td>
<td>Winter: 53</td>
</tr>
<tr>
<td></td>
<td>Summer:</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>N. Ireland</td>
<td>Winter: 30</td>
</tr>
<tr>
<td></td>
<td>Summer: 36</td>
</tr>
</tbody>
</table>

Would growing up in an iodine sufficient environment overcome the effects of deficiency during pregnancy?
Evidence from Australia\(^1\)

- Study of iodine deficiency during pregnancy, but not childhood
- Pregnant women recruited in 1999 - 2001 prior to a programme of iodine fortification in the area
- Women dichotomised on basis of WHO cut-off (\(<150 \text{ or } \geq 150 \mu g/L\))
- Children aged 9 born to mothers with low iodine status (\(<150 \mu g/L\)) had poorer spelling scores
- Marginal effect on grammar and English Literacy
- Children grew up under assumed iodine sufficiency
- Suggests irreversible damage can occur during pregnancy

Sources of iodine

- **Seafood**
  - 120g baked cod = 190 μg\(^1\)
  - 160g grilled mackerel = 56 μg\(^1\)

- **Milk and dairy products**
  - Seasonal variation\(^2\)
  - Glass milk (average) = 60 μg\(^1\)
  - Pot of yoghurt = 75 μg\(^1\)

- **Eggs**
  - Two eggs = 50 μg\(^1\)

- **Iodised salt**
  - Poor availability in the UK\(^3\)

- **Nutritional Supplements**
  - Kelp supplements should be avoided\(^4\)

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Food sources of iodine

Rose et al., 2001; Bates et al., 2014; Bath et al. 2012.
Iodine in fish

McCance and Widdowson 2014 Composition of foods integrated dataset
Food Fact Sheet

Iodine

This Food Fact Sheet will tell you more about iodine, its food sources and how much you need.

What is iodine?

Iodine is a mineral that is important for health. It is needed to make hormones in the thyroid. These hormones are needed for many body processes, including growth, regulating metabolism and for the development of a baby's brain during pregnancy and early life.

Do we get enough iodine in the UK?

For many years iodine intake in the UK was thought to be more than adequate but recent research has shown mild iodine deficiency in schoolgirls and pregnant women. There is now concern that many adult women may not be getting enough iodine, particularly in pregnancy.

How much iodine do I need?

<table>
<thead>
<tr>
<th>Life stage</th>
<th>Iodine required per day (mcg)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>150</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>250</td>
</tr>
<tr>
<td>Breastfeeding women</td>
<td>250</td>
</tr>
</tbody>
</table>

*World Health Organisation requirements

What happens if I do not have enough iodine?

A low intake of iodine over a long period of time may cause your thyroid to work harder to keep the right amount of thyroid hormones in your blood. This can mean that your thyroid increases in size in order to trap iodine; this swelling - or 'goitre' - may be visible in your neck. However, visible goitre due to low iodine intake is rare in the UK. It is more likely that having too little iodine in your diet will lead to low levels of thyroid hormones. If you have a deficiency of iodine when you are pregnant, your baby's brain may not develop as well as it could and this could affect your child's ability to learn in later years; for instance, your child could have a lower IQ or poorer reading ability.

Before and during pregnancy and breastfeeding

As iodine is required from the early stages of pregnancy, you should make sure you have been having enough iodine in your diet for several months before you get pregnant. This is because you can build up good stores of iodine in your thyroid before you become pregnant which helps it to function well during pregnancy. Therefore, if you are of childbearing age, and especially if you are planning a pregnancy, you should ensure that you meet the adult requirement for iodine.

During pregnancy, the amount of iodine you need increases. This is because you have to make sufficient thyroid hormones to transfer to your baby to help its brain develop correctly. You also supply all the iodine that the baby needs. Iodine deficiency in pregnancy may have serious consequences for your child so it is very important that you meet the higher iodine requirement if you are pregnant. Breastfeeding mums still need a higher amount of iodine, so their breast milk has enough iodine for their baby. This is because the brain is still developing at that early stage.

Where is iodine found in the diet?

Iodine is found in a range of foods, the richest sources being fish and dairy products. Seaweed is a concentrated source of iodine, but it can provide excessive amounts (particularly so in the case of brown seaweed such as kelp) and therefore eating seaweed more than once a week is not recommended, especially during pregnancy.

Milk and dairy products are the main sources of iodine for most people. Research has shown that organic milk has a 40% lower iodine content than conventional milk.

In many countries, iodine is added to table salt to give "iodised salt". Iodised salt is not widely available in the UK but can be found in some branches of several supermarket chains. As government recommendations are to reduce salt intake for health reasons, you should not rely on iodised table salt as a means of increasing your iodine intake.

The actual amount of iodine in food varies according to the iodine content of the soil, farming practice, fish species and season. This makes it difficult to estimate iodine per portion. The figures in the table are therefore for guidance only. Remember to follow Government advice on foods to avoid during pregnancy.

What about an iodine supplement?

Most adults following a healthy, balanced diet that contains milk, dairy products and fish, should be able to meet their iodine requirements. A supplement containing iodine can help meet your iodine needs if you do not consume sufficient iodine-rich foods. If you have thyroid disease, are taking other medication, or have experienced iodine deficiency over many years, you should speak to your GP before taking additional iodine. Iodine in supplements should be in the form of 'potassium iodide' and should not exceed the daily adult requirement of 150 mcg. Do not use seaweed or kelp supplements as an iodine source; this is because the amount of iodine in such supplements can vary considerably from the value claimed on the label and can provide excessive quantities of iodine.

It can be difficult to meet the higher recommendations for iodine during pregnancy and breastfeeding through diet alone, especially if you do not eat rich sources of iodine. Many, but not all, multivitamin and mineral pregnancy supplements contain iodine, so you need to check the label. The supplement should provide 140 or 150 mcg, so the remainder of the requirement for pregnancy can be met by your diet. If you consume high quantities of iodine-rich foods during pregnancy, you may not need an iodine supplement; talk to your doctor if you are uncertain.

Can I have too much iodine?

Yes - excessive iodine intake can cause thyroid problems and should be avoided. As a guide, adults should not exceed 600 mcg/day.

Who is at risk of iodine deficiency?

Anyone who avoids fish and/or dairy products (e.g. due to allergy or intolerance) could be at risk of iodine deficiency. Soy milk is often fortified with iodine (check the label) and therefore will not replace the iodine in cow's milk. Vegetarians and particularly vegans are at risk of iodine deficiency as they do not eat rich iodine sources (fish and/or dairy products).

Summary

Iodine is important for the production of thyroid hormones. It is dangerous to have too little or too much iodine. Good dietary sources include fish, shellfish and dairy products. During pregnancy, iodine is essential for the correct development of the baby's brain.
Recommendations for targeted supplementation of pregnant women

- **Australia and New Zealand:**
  - 150 µg/day supplement for pregnant and lactating women and those planning a pregnancy\(^1\)

- **United States and Canada recommend**
  - Pregnant and lactating women take 150 µg/day\(^2\)

- **No official recommendation in the UK**
  - Modelling suggests economic benefit of iodine supplementation during pregnancy in regions of mild/moderate deficiency\(^3\)

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Disadvantages of iodine supplements in pregnancy

- Transient stunning effect on the thyroid gland from an abrupt increase in daily iodine intake?\(^1\)
- Adverse effects on the psychomotor development index associated with supplements containing \(\geq 150 \, \mu g/d\) in pregnancy \(^2,3\)
- Compliance may be poor \(^4\)
- Iodine supplementation may be instituted too late in pregnancy \(^5\)

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Should an iodised salt policy be introduced in the UK?
Iodised salt and public-health campaigns

- Conflicting public-health messages
  - Salt reduction for CVD vs. iodised salt for iodine health
- Possible for both strategies to work in tandem\(^1\)
- Alternative vehicles to fortify iodine e.g. Australia and NZ
  - Legislation in October 2009 to iodise all salt used in bread making\(^2\)

Short Communication

Availability of iodised table salt in the UK – is it likely to influence population iodine intake?

Sarah C Bath, Suzanne Button and Margaret P Rayman*

Iodised salt only available to 21.5% of supermarket shoppers\(^1\)

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Conclusions

- Mild-to-moderate iodine deficiency appears sufficient to affect fetal brain development
- Women of childbearing age should ensure that they meet iodine requirements
- Iodine deficiency during pregnancy is an important area of public-health concern
- Further research is required, particularly an RCT of iodine in pregnancy with child cognitive outcomes
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https://www.surrey.ac.uk/nutrition/Research