Paediatric Food Allergy Symposium
Monday 6th March

15.00 Iodine Deficiency in Cow’s Milk Allergy
Rachel Wood
Specialist Paediatric Dietitian in Allergy and Gastroenterology, Royal Manchester Children’s Hospital
Paediatric Food Allergy Symposium

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Iodine deficiency in cow’s milk allergy

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Specialist Paediatric Dietitian in allergy and gastroenterology
Royal Manchester Children’s hospital
6th March 2017
Overview

- Causes and consequences of iodine deficiency
- Identifying deficiency and potential risks of this
- Case studies
- Where’s the evidence
- Supplementation
  - Formulas
  - Vitamin and minerals
  - Shop bought milks
- How it affects our practice
Interactive voting question

Is there a risk of iodine deficiency in the UK?

- Yes
- No
- Don’t know
Interactive voting question

What are the richest sources of iodine in the diet?

1. Cows milk
2. Fish
3. Egg
4. Infant formula
5. All of the above
What is Iodine?

- Mineral that forms part of the thyroid hormones thyroxine (T₄) and T₃.
- These are necessary for regulating metabolism, thermoregulation, protein synthesis and growth.
- Iodine content of food variable
  - Level in cereals and grains dependent on soil they are grown
  - Levels in meat, chicken, eggs and dairy dependent on iodine content on animal feed
  - Inorganic iodine salts are water soluble and are leached out of the soil
  - Organic milk in the UK is 42% lower in iodine than conventional milk
### Percent contribution of selected food groups to daily mean iodine intakes for adults aged 19-64 years in 2008/09 – 2009/10c

<table>
<thead>
<tr>
<th>Food group</th>
<th>Percentage contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk and milk products total, of which cows’ milk</td>
<td>33%, 23%</td>
</tr>
<tr>
<td>Fish and fish dishes</td>
<td>11%</td>
</tr>
<tr>
<td>Beer and lager</td>
<td>11%</td>
</tr>
<tr>
<td>Cereal and cereal products</td>
<td>10%</td>
</tr>
<tr>
<td>Eggs and egg dishes</td>
<td>6%</td>
</tr>
<tr>
<td>Other</td>
<td>29%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Food group</th>
<th>Portion</th>
<th>Average iodine/portion (mcg) (actual iodine content will vary)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk and dairy products</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cow's milk</td>
<td>200ml</td>
<td>50-100**</td>
</tr>
<tr>
<td>Organic cow's milk</td>
<td>200ml</td>
<td>30-60**</td>
</tr>
<tr>
<td>Yoghurt</td>
<td>150g</td>
<td>50-100**</td>
</tr>
<tr>
<td>Cheese</td>
<td>40g</td>
<td>15</td>
</tr>
<tr>
<td>Fish</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haddock</td>
<td>120g</td>
<td>390</td>
</tr>
<tr>
<td>Cod</td>
<td>120g</td>
<td>230</td>
</tr>
<tr>
<td>Plaice</td>
<td>130g</td>
<td>30</td>
</tr>
<tr>
<td>Salmon fillet</td>
<td>100g</td>
<td>14</td>
</tr>
<tr>
<td>Canned tuna</td>
<td>100g</td>
<td>12</td>
</tr>
<tr>
<td>Shellfish</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prawns</td>
<td>60g</td>
<td>6</td>
</tr>
<tr>
<td>Scampi</td>
<td>170g</td>
<td>160</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td>1 egg (50g)</td>
<td>25</td>
</tr>
<tr>
<td>Meat/Poultry</td>
<td>100g</td>
<td>10</td>
</tr>
<tr>
<td>Nuts</td>
<td>25g</td>
<td>5</td>
</tr>
<tr>
<td>Bread</td>
<td>1 slice (36g)</td>
<td>5</td>
</tr>
<tr>
<td>Fruit and vegetables</td>
<td>1 portion (80g)</td>
<td>3</td>
</tr>
</tbody>
</table>

**Depending on the season, higher value in winter**
Iodine Requirements

UK Dietary Reference Values for iodine (DH, 1991)

<table>
<thead>
<tr>
<th>Age</th>
<th>Lower Reference Nutrient Intake (LRNI) (µg/day)</th>
<th>Reference Nutrient Intake (RNI) (µg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>4-6 months</td>
<td>50</td>
<td>60</td>
</tr>
<tr>
<td>7-9 months</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>10-12 months</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>1-3 years</td>
<td>40</td>
<td>70</td>
</tr>
<tr>
<td>4-6 years</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>7-10 years</td>
<td>55</td>
<td>110</td>
</tr>
<tr>
<td>11-14 years</td>
<td>65</td>
<td>130</td>
</tr>
<tr>
<td>15-18 years</td>
<td>70</td>
<td>140</td>
</tr>
<tr>
<td>19-50 years</td>
<td>70</td>
<td>140</td>
</tr>
<tr>
<td>50+ years</td>
<td>70</td>
<td>140</td>
</tr>
</tbody>
</table>

The World Health Organisation recommendations are in the table.

<table>
<thead>
<tr>
<th>Population group</th>
<th>World Health Organisation Recommended Nutrient Intake (RNI) (µg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 0-5 years</td>
<td>90</td>
</tr>
<tr>
<td>Children 6-12 years</td>
<td>120</td>
</tr>
<tr>
<td>Adults &gt;12 years</td>
<td>150</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>250</td>
</tr>
<tr>
<td>Lactation</td>
<td>250</td>
</tr>
</tbody>
</table>

*WHO, 2007

<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>200</td>
</tr>
<tr>
<td>Breastfeeding women</td>
<td>200</td>
</tr>
</tbody>
</table>

*European Food Safety Authority (EFSA) recommendations.
What about Iodised Salt?

- Not commonly available or used
- Government trying to reduce intake of salt
Iodine deficiency

- Body normally regulates thyroid hormone concentrations
  - If iodine levels fall below 100mcg, iodine uptake increases and the production of thyroid hormone increases
  - If levels fall below 10-20mcg/day hypothyroidism occurs
  - Goitre the earliest clinical sign of deficiency
- In the fetus and neonates protein synthesis in the brain and central nervous system is dependent on iodine or iodine containing compounds.
  - hence the effect it has on the baby’s brain development during pregnancy and early life
  - Can cause irreversible effects
  - Mild to moderate maternal deficiencies can be linked to Attention deficit hyperactivity disorder
Table 2: Iodine deficiency disorders according to physiological group (Hetzel, 1983)

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

![Diagram of Normal Thyroid and Goiter](image-url)
Measuring Iodine

- Urinary Iodine Excretion (UIE) – 24-hour collection is reference standard
- Impractical and poor compliance
- Single non-fasting casual urine sample most used
- UIE varies according to recent iodine intakes
- The quantitative relationship of UIE and iodine intake not fully evaluated.
- Due to homeostatic adaptation UIE may be expected to underestimate dietary intake of iodine at low exposures
What is the risk with the allergic child?

- Cows milk allergy
  - main source of iodine in infant and child's diet
  - Breast fed or reluctance to take Hypoallergenic formulas
  - Also at risk of vitamin D and calcium deficiency
- Fussy eating
- Further restrictions/allergies
  - Iron and iodine deficiency
- Shop bought alternative milks not routinely supplemented with Iodine
Case Study 1

- 8 ½ year old male
- Allergies to milk, egg, fish, wheat, peanuts
- Breast fed until nearly 3 years of age
  - Mum excluded cow’s milk from diet
- Dislikes soya, but tolerates it
- Fussy eater
  - difficult to establish on regular diet, reluctant to try new foods
  - “Fear” of reactions – avoids socialising
- Good growth
  - weight 75th centile height 91st centile
Case Study 1

- Failed milk challenge on ward last year – breathing difficulties
- Takes oat milk fortified with calcium
- Small amount of wheat being introduced at home
- Dislikes egg and fish but no recorded recent reactions - baked egg introduction at home
- Reluctance from family to reintroduce

<table>
<thead>
<tr>
<th>SPT’s</th>
<th>Histamine</th>
<th>Milk</th>
<th>Cod</th>
<th>Wheat</th>
<th>Egg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sept 2010</td>
<td>5mm</td>
<td>8mm</td>
<td>0mm</td>
<td>8mm</td>
<td>8mm</td>
</tr>
<tr>
<td>March 2015</td>
<td>4mm</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3mm</td>
</tr>
</tbody>
</table>
Case Study 1

- Presented with Goitre June 2013 with symptoms from September 2012 age 4 years
  - Normal antibodies
  - Under the Endocrine team
- Dietary analysis done but inaccurate measures due to variation of iodine in foods
- Thyroxine and Fruitivits (multivitamin and mineral supplement) started.
- Goitre resolving, urinary iodine only back to normal
- Investigations into developmental delay/ADHD
Case Study 2

- Now 18 year old male
- Growing well weight <25\textsuperscript{th} C Height <50\textsuperscript{th} C
- Initially avoiding milk and soya due to suspected allergy.
- Never had eggs, fish, wheat, nuts, peanuts, legumes and tomatoes because of brother’s allergies.
- Passed soya challenge 10/2011
- Passed egg in cake challenge 02/2012
- Milk allergy – on the final stages of desensitisation program
Case Study 2

- Review Jan 2014 diagnosed with Goitre
  - Iodine deficiency related hypothyroidism started on Thyroxine – antibody normal
- Mother suffers with overactive thyroid
- Maternal grandma and great grandma have underactive thyroid
- Maternal grandfather has Hasimoto’s thyroiditis
- Diet still extremely restricted
- Started on Fruitivits and Thyroxine stopped as symptoms resolved
Case Study 3

- 9½ year old male
- immediate and delayed allergy reactions to dairy, eggs, soya, wheat, peas and mushrooms – avoids fish
- Goitre diagnosed 04/2013 age 5
  - Antibody negative
  - Thought to be iodine deficient hypothyroidism
- Currently reintroducing fish, then wheat then baked milk
- Weight 25\textsuperscript{th} C height 50\textsuperscript{th} C
- Thyroxine and Fruitivits
  - Symptoms starting to resolve
Review of patients on multiple exclusion diets

- Dietetic review of all patients with multiple allergies
- If no reintroduction of iodine containing foods then started on multivitamin and mineral supplement containing iodine
- Increased knowledge and awareness in the team of iodine deficiency
- Dietary analysis and testing inaccurate
- Questions raised of should all patients on milk/egg/wheat/fish free diets be started on a supplement containing iodine?
<table>
<thead>
<tr>
<th>Milk alternative</th>
<th>Iodine content µg per 100ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aptamil Pepti</td>
<td>12</td>
</tr>
<tr>
<td>Althera</td>
<td>11</td>
</tr>
<tr>
<td>Nutramigen LGG</td>
<td>14.3</td>
</tr>
<tr>
<td>Similac Alimentum</td>
<td>10</td>
</tr>
<tr>
<td>Neocate LCP</td>
<td>13.8</td>
</tr>
<tr>
<td>Alfamino</td>
<td>11</td>
</tr>
<tr>
<td>Puramino</td>
<td>10.1</td>
</tr>
<tr>
<td>Neocate Active</td>
<td>7.0</td>
</tr>
<tr>
<td>*Neocate Junior</td>
<td>15</td>
</tr>
<tr>
<td>Alpro Soya Junior</td>
<td>24.5</td>
</tr>
<tr>
<td>Made without dairy M&amp; S Soya</td>
<td>22.5</td>
</tr>
<tr>
<td>Made without dairy M&amp; S Oat</td>
<td>28.9</td>
</tr>
<tr>
<td>Made without dairy M&amp; S Rice</td>
<td>30.7</td>
</tr>
</tbody>
</table>
Where’s the Evidence

**SACN statement on iodine and health, Feb 2014**

- Comprehensive document that provides guidance on iodine availability, absorption and risk of deficiency
- Japanese studies (Miyal *et al*, 2008 and Nagataki *et al* 1967) show even populations with high daily intakes of marine fish and seaweed still have low UIE
- Iodine deficiency with or without other nutritional deficiencies most common cause of Goitre.
- **National Diet and Nutrition Survey (NDNS), Bates *et al* 2012** indicates ~1/5 of non pregnant girls ages 11-18 years in the general population are at risk of low intakes
- **SACN Subgroup on Maternal and Child Health (SMCN)** insufficient evidence but the pre pregnancy iodine status of the women could be crucial
Where’s the Evidence

Avon Longitudinal Study of Parents and Children (ALSPAC), 2013. (14500 participants)

- 1040 1st trimester women enrolled
- Had UIC measured and samples frozen
- Mother-child pairs by measuring UIC
- Assessed association between maternal iodine status and child IQ at age 8 years and reading ability at age 9 years.
- Children of women with lower iodine levels more likely to have scores in lowest quartile for verbal IQ, reading accuracy and reading comprehension.
- Scores worsened the lower the iodine levels were.
- Preventable cause with adverse childhood outcomes.
- Urgent review of UK iodine situation.
Where’s the Evidence

A practical approach to vitamin and mineral supplementation in food allergic children, R. Meyer, 2015

- 110 children reviewed with non IgE mediated food allergies
- Observational study 4 weeks to 16 years of age
- Those on hypoallergenic milks less likely to be deficient
- 71% had prescribable supplements suggested by dietitian/physician
- 60% with supplements had low vitamin D
- Low Zinc, calcium, and selenium common
- Iodine not reviewed
- Raises the question of routine vitamin and mineral supplementation with multiple restrictive diets
Where’s the Evidence

Dietary restriction causing iodine-deficient goitre, Cheetham et al, 2015

- Case review by the Newcastle team
  - 4 year old boy mix of IgE and non IgE mediated food allergies
  - Chronic urticaria/atopic dermatitis/asthma/ seasonal allergic rhinitis
  - Highly restrictive diet – avoids milk/wheat/egg/cod fish/shell fish/peanuts and tree nuts.

- Goitre and hypothyroidism
  - Resolved with adequate supplementation of iodine

- Highlights the importance of comprehensive nutritional assessment in all children with food restrictions.
Where does that leave us with iodine deficiency?

- Appropriate supplements
  - GP prescribing – multivitamin and mineral supplements expensive
  - Iodine solutions – difficult preparation required
  - Careful not to overdose with excess iodine intake
- How to monitor levels of iodine
  - 24 hours urine sample more accurate but not practical
- Selenium and Iodine work together in the thyroid
  - deficiency of selenium affects utilisation of iodine
- Severe iron deficiency
  - If not treated affects iodine utilisation/absorption
Is it the restricted diets that have contributed to these 3 cases?
Did mum already have iodine deficiency during pregnancy/breast feeding followed by a restrictive diet?
NDNS (2012) indicates milk consumption has fallen since previous surveys.
  - Mainly teenage girls at risk of low iodine intakes; 1/5 11-18 year old females at risk of deficiency
WHO, 2009 suggests the UK population as a whole are now iodine deficient.
ALSPAC 2013 and Gordon et al 2009
  - concluded mild maternal iodine deficiency could prevent offspring from attaining their full intellectual potential
Standard Practice following this

- Awareness
- Urinary testing and dietary analysis unhelpful
- Prevention rather than treatment in those on restrictive diets
- Suitable multivitamin and mineral supplement containing iodine to be started
- Encourage infant formula if age appropriate
- Consider Hypoallergenic formula age 1-10years if appropriate
- Alpro Soya Junior now fortified with Iodine and Iron
- Prevent mum from restricting diet unnecessarily
- Education on supplementation for mums
  - Prenatal/postnatal/lactation
Prescription complete supplements

- Paediatric Seravit – SHS
  - Tub of powder
  - Ages suitable for; 0-14 years
- Fruitvits – Vitaflor
  - Sachets of powder
  - Ages suitable for; 1-6 years
- Phlexy-Vits
  - Sachets and tablets
  - Ages suitable for; 11 years upwards

*check iodine content of shop bought complete vitamin and mineral supplements
Summary

- Iodine deficiency is on the rise
- The government need to be making it a public health concern
- Very difficult to measure due to the variations in diet
- Raises the question that children's behavioral and intellectual progress could be linked with deficiency
- Full dietary history from mum and child essential
- Adequate supplementation needed
- Children on Milk/Fish/Egg/Wheat free diets need regular Dietetic Input to liberalise diet
References

- SACN Statement on Iodine and Health, Feb 2014
KEEP CALM AND ASK A DIETITIAN