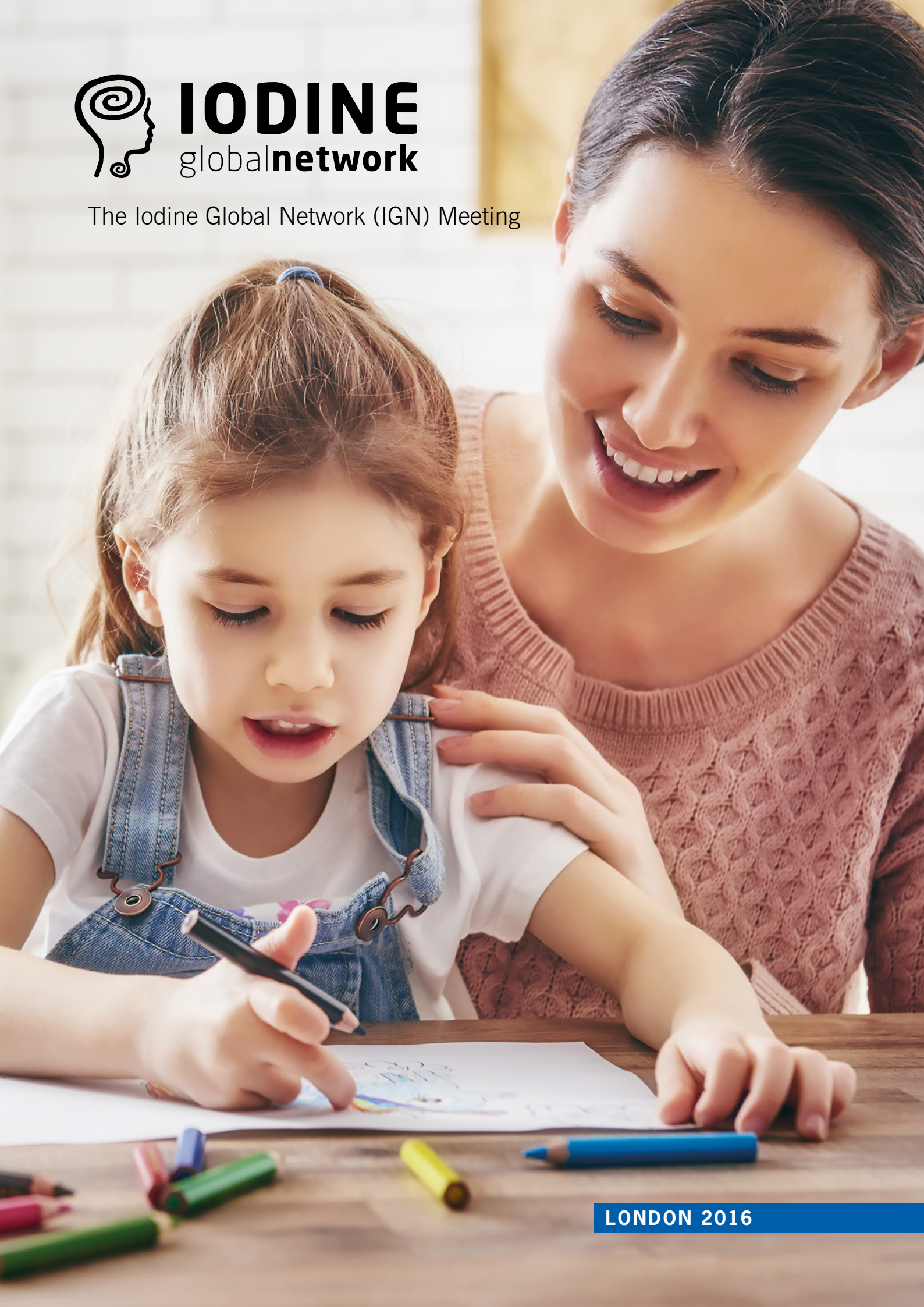
IODINE globalnetwork

The Iodine Global Network (IGN) Meeting



LONDON 2016

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The Iodine Global Network (IGN) Meeting

March 17, 2016.

Royal College of Obstetricians and Gynaecologists, London, UK.

Welcome and Introduction

Professor John Lazarus, Cardiff, Regional Coordinator IGN
West and Central Europe.

Iodine and the Thyroid

Dr Mark Vanderpump, Royal Free Hospital, London, National Coordinator, IGN, UK.

Iodine in Pregnancy

Professor Michael Zimmermann, Professor of Endocrinology, ETH Zurich, Switzerland. Chair, IGN.

Iodine in Pregnancy in the UK

Dr Sarah Bath, Guilford, MRC Fellow, University of Surrey, UK.

Guidelines on Thyroid Disease and Pregnancy – An Obstetric Viewpoint

Mr Michael Marsh, Kings College Hospital, London, UK,
Consultant Obstetrician.

Iodine Supplementation - an overview

Professor Kate Jolly, Professor of Public Health, University of Birmingham, UK.

Iodine Nutrition in UK – Is there enough for pregnancy?

Professor Margaret Rayman, Professor of Nutrition,
University of Surrey, UK.

Salt iodination – The Danish experience

Professor Peter Laurberg, Professor of Endocrinology,
Aalborg University, Denmark.

Professor Laurberg unexpectedly passed away on June 20, 2016.

EUthyroid – The way forward for iodine in Europe

Dr Tim Korevaar, Erasmus University, Rotterdam, The Netherlands.

Improving the Health of the Population – What do we need to do now?

Professor Simon Smail, Emeritus Professor of Medical Education,
Cardiff University, UK.

Conclusions

Jonathan Gorstein, CEO Iodine Global Network, Seattle, US and
Clinical Associate Professor, Department of Global Health, University of Washington, Seattle, US.

Lay summary

The importance of iodine and its essential role in the body is not widely known. However, iodine is vital because without it we would be unable to produce thyroid hormones, which are crucial for healthy growth and development.

This report reflects discussions at the UK meeting of the Iodine Global Network (IGN) held on March 17, 2016, and provides an overview of some of the key issues addressed. The symposium focused on the role of iodine in pregnancy, the issue of mild-to-moderate iodine deficiency in the UK, and how pregnant women with normal thyroid function living in this environment unknowingly place their children at risk of neurodevelopmental disorders and learning disabilities.

The IGN emphasises the importance of having sufficient iodine levels, both before and during pregnancy, as well as during breast-feeding. This report outlines a number of the key published studies that add to a growing evidence base about the mild-to-moderate iodine deficiency status in the UK population, as well as studies that look at cognitive development in children born to mothers who were iodine deficient during pregnancy. There is also discussion of possible solutions to remedy this situation – of note, salt iodisation; or iodine supplementation, prior to and during early pregnancy and breast-feeding.

According to the World Health Organization (WHO), the UK is one of the top ten most iodine deficient countries in the world. Various UK-based studies all show that pregnant women and women of child-bearing age have urinary iodine levels of less than 150µg/L which is below the level recommended by the WHO.

Ideally, a randomized controlled trial (RCT) is required to investigate iodine deficiency in pregnant mothers and cognitive outcomes in their children. But among UK pregnant women, no such trial has ever taken place. However, there is good observational evidence from the Avon Longitudinal Study of Parents and Children (ALSPAC) that shows children born to mothers with low iodine levels during pregnancy had children with verbal intelligence quotient (IQ), and reading scores in the lowest 25% at the age of nine years.

Aside from these potential interventions to boost iodine levels, experts refer to where iodine can be found as a source of nutrition in the standard UK diet. Primarily, iodine is sourced through dairy produce and fish. However, studies show that the iodine levels vary widely in both foodstuffs, and milk, in particular, can be very misleading. Organic milk has far less iodine content than conventional milk. There is also a big difference between oily and white fish, the latter having more iodine.

"The IGN urges the UK Government to provide the necessary support to determine conclusively the iodine status of the UK population, especially in pregnant women."

Despite the existing evidence, and WHO recommendations stating that in countries without access to iodised salt, iodine supplements should be made available, the last guidelines from the UK Government on iodine status were issued in 1991. But more evidence is required and so too is political will to promote a policy change to protect unborn children from the deleterious health effects of low iodine. The IGN urges the UK Government to provide the necessary support to determine conclusively the iodine status of the UK population, especially in pregnant women. Depending on that outcome, the optimal solution and recommendations should be made to alleviate the situation.

I. Iodine – a brief overview

Speaker: Mark Vanderpump, MD

Iodine – what is it and why is it important?

People need iodine for the production of thyroid hormones and to meet this need, it has to be sourced externally either from the diet or as a supplement. The major source of iodine in most industrialised countries is bread, milk and fish.

If there is a lack of iodine then this can lead to impaired growth and neurodevelopment. Of particular concern is the risk associated with iodine deficiency in pregnant women who experience increased demand for iodine because they have to provide it to their growing foetus as well as themselves during the first few months.

Iodine deficiency can cause a range of neuro-developmental issues in the foetus, the newborn, older children and adults.

Thyroid hormone target tissues

Thyroid hormones act everywhere

Basal metabolic rate
Growth and development
Temperature regulation
Fat production
Blood vessels
Skin
Hair
Bone marrow
Kidney
Lung

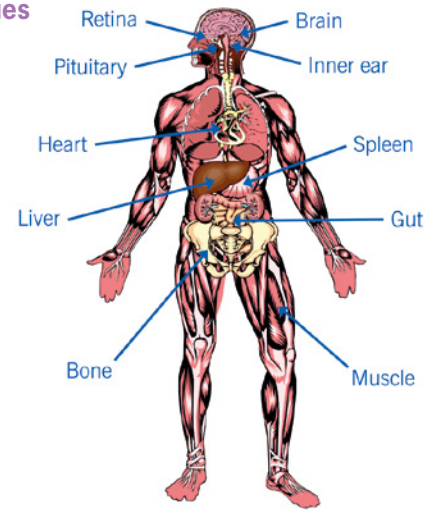


Figure 1: *Diagram of the human body showing of tissues that are targeted by thyroid hormone*

Disorders of iodine deficiency

- Mild perturbations of thyroid function in the pregnant mother and foetus can affect neurodevelopment and have a potential impact in older children
- In the foetus, deficiency is associated with abortion, stillbirth, congenital anomalies, perinatal mortality, endemic cretinism, irreversible brain damage (in severe deficiency)
- A newborn and child can suffer from goitre, hypothyroidism, mental retardation and delayed physical development
- Adults can suffer from goitre, hypothyroidism, impaired mental function, spontaneous hyperthyroidism, iodine-induced hyperthyroidism

Derbyshire Neck – 1769

Derbyshire, UK

Vanderpump highlighted that even during the mid-18th century there was documented recognition of the implications of goitre and iodine deficiency in maternal health, with women of child-bearing age being the main victims of the disease:

"There is one disease to which the inhabitants of Derbyshire are so much subject, that it has taken its name from its great prevalence in this situation."

Some thought it was hereditary, others that it was caused by living "on the bleak sides of hills." They all agreed that women, particularly "child-bearing poor women" were the main victims of "this very unfortunate female disease."

(Pilkington 1789 The Present State of Derbyshire)

Epidemiology of iodine

Global

A large study (4000 participants) from the Northern Himalayas where goitre was highly prevalent (92% of the population) showed that the consumption of iodised oil shrank goitre. No cretins or deaf mutes were born despite a previous incidence of 20-25%[1]. Similar results were observed in a placebo-controlled trial in Papua New Guinea (n=160,000) in which iodised oil injections were given pre-conception or during early pregnancy and were found to reduce cretinism and improve motor/cognitive function in their children.[2]

UK

Not long after World War II, iodine intake increased largely due to a change in farming practices at the time. Farmers used iodine-rich artificial cattle feeds and this led to a dramatic drop in the prevalence of goitre. At this time, UK governments encouraged compulsory milk consumption in schools and the iodine content of milk alone was sufficient to meet the recommended daily requirement for adults of 150μg/l. However the provision of free milk for primary school children was removed in the 1970s.

Documentation of a number of early UK-based surveys on the prevalence of goitre exist going back to the early 20th century: 1924 survey of 375,000 schoolchildren in England and Wales found visible goitre in 30% of the population; a 1948 MRC survey found visible goitre in 50% of women in Oxford, 43% of girls in Dorset, 26% of children in St Albans, and 2% in Essex, while a repeat MRC survey in 1958 found a reduction in goitre prevalence in girls in Oxford from 40% to 27%.

In the 2000s, various small studies showed approximately 50% of pregnant women in small surveys (Middlesbrough, Dundee, Cardiff, Guildford) had a median urinary iodine concentration (UIC) of 66μg/L, representing mild to moderate iodine deficiency.

In 2006, a survey provided evidence of iodine deficiency in pregnant women in Ireland, and also found that table salt preparations available in UK supermarkets showed sufficient iodine levels in only two brands.[3]

UK Iodine Status – a national survey of teenage schoolgirls

In 2011, a national survey of UIC in UK schoolgirls found a median UIC of only 80 μg/L. Consumption of milk was also found to be falling in these young women, many of whom will have pregnancies in coming years. The authors concluded that UK schoolgirls were iodine deficient, and highlighted an urgent need for more research and recommendations on iodine supplementation.[4]

Iodisation of salt

The WHO recommends salt iodisation as one solution in countries with iodine deficiency, but this needs to be considered in the context of a key public health message to reduce salt intake for other health reasons. In a 2007 statement on salt reduction, WHO noted that increasing iodine intake via salt does not entail increased consumption.

- Salt iodisation is safe, equitable, self-financing and extremely cost-effective
- Most salt in the UK diet is in processed food
- Mandatory bread salt iodisation in New Zealand and Australia has increased iodine intake
- Oral potassium iodide supplements are likely to benefit most susceptible groups e.g. women pre-pregnancy or in early pregnancy

UK in top ten iodine deficient countries internationally

In 2011, the WHO provided a table indicating the top ten iodine deficient countries worldwide (based on UIC of less than100 µg/L).[5] The UK came seventh, rated between Angola and Mozambique.

Most countries that have iodine deficiency in Europe have mild to moderate deficiency. The implication of this is that children born to women may have psycho-neurological deficits and delayed mental function.

II. The importance of iodine in pregnancy

Speaker: Michael Zimmerman, MD and Tim Korevaar, MD

WHO recommendation on managing iodine deficiency

The WHO recommends a UIC of 150 µg/L during pregnancy. [6]

With respect to salt iodisation, the WHO recommends that it should be used to eliminate iodine deficiency in the general population. It also recommends that in countries with poor access to iodised salt, for example in the UK, then 'the most vulnerable groups, pregnant and lactating women, should be supplemented with iodine.'

ALSPAC – a large birth cohort study

The most comprehensive and reliable study related to iodine deficiency, published in 2013, found that women with low iodine levels during the first trimester of pregnancy, had children with verbal intelligence quotient (IQ), and reading scores in the lowest 25% at the age of nine years. The authors of this well-received study concluded that "Iodine deficiency in pregnant women in the UK should be treated as an important public health issue that needs attention."[7]

Iodine and thyroid hormone in the healthy and iodine-deficient pregnancy

In an iodine-sufficient woman, the thyroid gland's store of iodine is substantial (15-20 mg iodine) and during pregnancy, the mother draws on this supply providing thyroid hormone production for around the first three months for herself and her baby.

If the mother lives in an area of iodine deficiency, the iodine store can drop dramatically (to around 1-2 mg) and the dietary source of iodine becomes very important. During a healthy pregnancy UIC falls and thyroid volume may increase slightly; thyroxine crosses the placenta so the foetus has sufficient thyroid hormone levels and experiences normal brain development. In an iodine-deficient pregnancy, thyroxine continues to cross the placenta unless there is severe deficiency when there is depletion of the mother's iodine store, a decrease in triiodothyronine and thyroxine synthesis, a lowering of foetal thyroid status resulting in potential brain damage.

"There's no doubt that in areas of severe iodine deficiency, we need to do everything we can to ensure pregnant women have adequate iodine provision."

Michael Zimmerman
Professor of Endocrinology, ETH Zurich, Switzerland.

Iodine and thyroid status have multiple effects on the developing brain including myelination (insulation of nerve cells), synaptic development, maturation, and blood vessel supply, all of which are most notable in the region of the brain called the hippocampus. In contrast, if the baby's brain develops in an environment of iodine deficiency, studies show insufficient development in this particular area of the brain.

Studies on salt iodisation and iodine supplementation

Salt iodisation in iodine deficient regions

WHO recommends that iodised table salt is the primary source of additional dietary iodine in areas of deficiency.[8] This recommendation has not been popular in the UK, with the government claiming it is at odds with the message to reduce salt intake for other health reasons, although WHO and others have stated that this is not the case. Ironically, iodised salt is manufactured in the UK, but is mainly produced for export and is not widely available to the public.

Evidence relating to the effect of salt iodisation on iodine deficiency disorders has been examined in the following papers:

- In 2014, a WHO systematic review showed that salt iodisation in areas of moderate to severe iodine deficiency is associated with a reduced risk of low IQ.[9]
- In the 2007 International Child Development Group key strategy aimed at avoiding loss of potential in children, it was noted that salt iodisation is the most cost effective way to deliver iodine and improve cognitive development in children.

"There's no doubt that in areas of severe iodine deficiency, we need to do everything we can to ensure pregnant women have adequate iodine provision," said Dr Zimmerman.

Supplementation in women with mild iodine deficiency

In areas of mild deficiency, (40-80 μg/L UIC), six studies that provided supplements (150-250 μg/day) showed this measure to overcome iodine deficiency was safe, but no changes in maternal or newborn thyroid hormones were found, and long-term clinical outcomes were not assessed.

A randomised study in mildly iodine-deficient pregnant women in Cardiff, UK, and Turin, Italy, who were provided with 100 μg/day of iodine contained in levothyroxine (effectively a supplement) showed no difference in the IQ of their children at age three years.[10]

In summary, other non-randomised studies looking at iodine status and pregnant offspring development found four studies that showed benefit, four that showed no benefit, and one that showed a potential harm. However, most of these studies have limitations.

As yet there has been no interventional randomised study that has investigated the effects if pregnant women in areas of mild-to moderate iodine deficiency (median UIC >50 μg/L) take supplements.

Can too much iodine in pregnancy be harmful?

Clearly, it is also important to consider any adverse effects of supplementation. Total iodine consumption should be considered when supplementation may be in addition to other iodine fortification strategies on a population-wide level. Currently, few good quality data exist, but the following was highlighted during the IGN meeting:

- A study from China shows that there was a slightly increased risk of thyroid disorders in women who had 250-499 μg/L UIC daily, particularly if they had high urinary iodine of greater than 500 μg/L. The study suggests that very high intakes may incur some harm.[11]

Dr Zimmerman concluded that in regions with mild iodine deficiency it remains uncertain whether supplements are needed. There is also a concern that women will not take supplements until the end of the first trimester missing the critical period of foetal brain development. In his opinion, a population-wide intervention of salt iodisation would cover the increased requirements in pregnant women.

EUthyroid – Maternal iodine and offspring neurodevelopment

Speaker Tim Korevaar, MD

The EUthyroid project is a collaboration between 27 countries across Europe. It is EU-funded research project with the goal of harmonising and sustainably improving the iodine intake in Europe.

Dr Korevaar pointed out the importance of the programme in taking a harmonising approach to ensure iodine intake of European citizens is sufficient to prevent health problems. The project aims to provide evidence for a cost effective, harmonised approach to prevention of iodine deficiency in Europe.

The key objectives of the EUthyroid project are to:

- Develop a European map of iodine status
- Build the capacity of national studies to perform harmonised studies
- Establish thyroglobulin as an iodine status marker
- Provide evidence for effectiveness of prevention of iodine deficiency disorders
- Disseminate Euthyroid outcomes

Dr Korevaar reiterated the well-known effect of severe iodine deficiency on offspring neurodevelopment. He added that there might be other associations that were as yet unknown and that potential underlying mechanisms also needed to be explored. In order to answer some of these questions, EUthyroid aims to foster a collaboration between three different population-based cohorts with ALSPAC in the UK, INMA in Spain and Generation R in the Netherlands. These cohorts will provide data on neurocognitive function, samples for iodine measurements during pregnancy, and data on differences in population iodine status.

The combination of cohorts will increase the sample size to around 5000 mother-child pairs, use repeated measurements, and harmonise and integrate data in a central database to perform an individual participant-based meta-analysis.

The primary endpoint will be the offspring IQ level, while secondary endpoints will be the incidence of attention deficit hyperactivity disorder (ADHD), autistic traits, and observations on language development.

More information on EUThyroid can be found here: **euthyroid.eu**

III. Iodine as a form of nutrition:

Speakers: Sarah Bath, PhD, and Margaret Rayman, PhD, Peter Laurberg, MD, PhD

Variability in the iodine content of milk: organic versus non-organic

Given most people in the UK obtain their iodine from milk and dairy products, it is important to note that milk is highly variable in iodine content. Iodine content varies by season with winter milk having a higher iodine concentration than summer milk at 400 µg/L versus 200 µg/L in summer. In winter, cows receive fortified feed but in summer, they feed on grass. Research also suggests that organic milk has 35-40% lower iodine content than non-organic milk. As mentioned earlier, iodine can be added to table salt but this is difficult to source in the UK. A recent meta-analysis found conventional milk to be 74% higher in iodine.[14]

Where to find iodine in the diet

The richest sources of dietary iodine are fish (especially white fish) and dairy products. Seaweed is a concentrated source of iodine, but it can be so concentrated that it can be harmful if eaten too often. The amounts of iodine in fish and dairy vary according to the iodine content of the soil, farming practice, fish species and season.

A 2001 study showed that fish has by far the highest concentration of iodine but that this food source only makes up a relatively low contribution to the overall intake of iodine, with milk and dairy providing the largest source in the UK diet.[12 13]

The contribution of milk to overall iodine intake in the UK increased from the 1930s and this largely eradicated the deficiency seen in the past. In the UK compared to other European countries, for example Switzerland or the Netherlands, milk makes a far higher contribution to iodine intake, although milk intake among young women is decreasing.

It is also notable that alternatives to cows milk are becoming popular e.g. rice or soy drinks and these are not fortified with iodine and individuals drinking milk alternatives may risk iodine deficiency.

Awareness of iodine importance

The awareness of why we need iodine in our diets is poor in the UK. A 2015 survey[15] among pregnant women and those who had recently given birth in Glasgow found that:

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

Of particular concern is that around 50% of UK pregnancies are unplanned so by the time a woman is aware of her situation the critical early stage of pregnancy has been missed; if iodine stores have not be maximised prior to pregnancy, this may compromise thyroid hormone production.

In the UK, many people source health information from the NHS Choices website. However, the NHS iodine page[16] makes no mention of the role of iodine in pregnancy, milk is not listed as a source of iodine, and a supplement of up to 500 µg/day is suggested as safe which many experts would consider too high. The NHS pregnancy pages do not discuss iodine, but milk and fish are recommended although not in the context of iodine.

Iodine nutrition in UK - is there enough for pregnancy and in women of child-bearing age?

In an adult woman, iodine intake should be 150 µg/day, rising to 250 µg/day in pregnancy and breast-feeding (WHO recommendations).

In the UK, the government set their recommendations about iodine requirements in 1991. Despite more recent WHO recommendations, the UK Scientific Advisory Committee on Nutrition (SACN) has not updated the UK recommendations accordingly. The Committee has reviewed the data, but say that there is currently insufficient evidence to revise the guidelines in pregnancy. There is also no recommendation in the UK to take an iodine supplement both pre- and during pregnancy, and it is assumed that the diet supplies enough.

Dietary iodine during pregnancy

With respect to the diet, the UK pregnancy recommendations relevant to iodine include eating two to three portions of dairy products daily and a specific recommendation for fish of 1-2 portions per week, one of which to be oily with no more than two portions of oily fish per week.[17]

Dr Bath stressed that dietary recommendations needed to be far more specific than they are currently due to the wide variability in iodine content, not only in milk but also in fish.

In studies of UK pregnant women, Dr Bath has shown that iodine status and milk intake are positively correlated. In two cohorts of pregnant women, from Surrey and Oxford, iodine status was higher in those who reported greater milk intake. [18] [19]

Iodine supplementation

There is no recommendation to take a supplement in the UK and there is no such supplement available. Most, but not all, prenatal multi-nutrient supplements contain iodine the amount of which varies. It is important to stress that kelp and seaweed supplements should not be used as an iodine source as the iodine content can be excessive.

Iodine storage in the thyroid gland

In aiming to meet iodine requirements in pregnancy, it is important to remember that iodine is also stored by the thyroid gland and for this

reason iodine consumption is important pre-pregnancy as well as during pregnancy. If necessary, these stores can make up for some of the shortfall during pregnancy, if stores have been maximised beforehand.

In conclusion, Dr Bath highlighted that in the UK, pregnant women and those planning a pregnancy need to have specific information on dietary sources of iodine, including appropriate supplements. There is information on dietary sources of iodine on the UK Iodine Group website,[14] and in the BDA iodine factsheet.[17 20]

Salt iodisation – The Danish Experience.

Denmark is one of the world's leading forces in improving iodine nutrition. In the late 90s, more than 90% of the population had moderate iodine deficiency, and the government initiated a mandatory programme of iodisation of salt for the household and for commercial bread production in 2000.

With respect to hypothyroidism, previous to the iodisation program this was dominated by the elderly but after it, hypothyroidism became even balanced between people under and over 60s, but absolute figures were low, reported Dr Laurberg.

Overall, the Danish iodisation programme has lead to a 40% increase in hyperthyroidism, much less goitre and subclinical hypothyroidism due to large decreases in people around the age of 40 years, but there has been a moderate increase in hyperthyroidism in those aged 20-40 years. "Iodine levels should be brought to the level where debilitating diseases are prevented but it should not be brought higher than necessary," added Dr Laurberg.

The Danish government chose to iodise salt used in bread because bread intake in Denmark is evenly distributed among the population. Prior to the iodisation project the median UIC of iodine was between 45 and 60 μg/L (mild to moderate deficiency). After bread salt iodisation, it rose to a UIC of 100.

In pregnant Danish women, iodine levels were found to be too low in women who did not take iodine-containing supplements (iron or folate with iodine included) but Danish researchers realised it was futile to ask these women to take iodine supplements because they did not take supplements already advised. For this reason, they believed salt iodisation that raised the iodine level in the general population was preferable. "In this population, taking supplements would probably do no harm."

IV. Iodine deficiency in pregnancy

Speakers: Margaret Rayman, PhD and Michael Marsh, MD

Iodine is essential for the production of thyroid hormones, which play an important role in the developing foetal brain. The foetal central nervous system is sensitive to the maternal thyroid status, and critical amounts of thyroid hormones must be transported across the placenta to the foetus to ensure healthy development of the brain. If sufficient thyroid hormones are not produced then the developing child may suffer cognitive deficits and learning disability due to compromised iodine intake or thyroid disease.

During pregnancy and breast-feeding, women are at increased risk of iodine deficiency. This is due to the need for increased thyroid hormone synthesis for the mother's needs as well as transfer of iodine and thyroid hormone to the foetus, that cannot make its own thyroid hormones during the first few months. However, despite the established need for greater amounts of iodine during pregnancy, many women suffer from iodine deficiency.

Studies showing iodine deficiency in UK women of child-bearing age

Evidence of mild-to-moderate iodine deficiency has been provided by a growing number of studies. Recent UK studies have shown iodine deficiency in:

- Two studies in women of childbearing age[4 18]
- Six studies in pregnant women[7 21 22 23 24 25]

"There was a considerable deficit between the iodine status of these pregnant women and the recommended level for pregnancy"

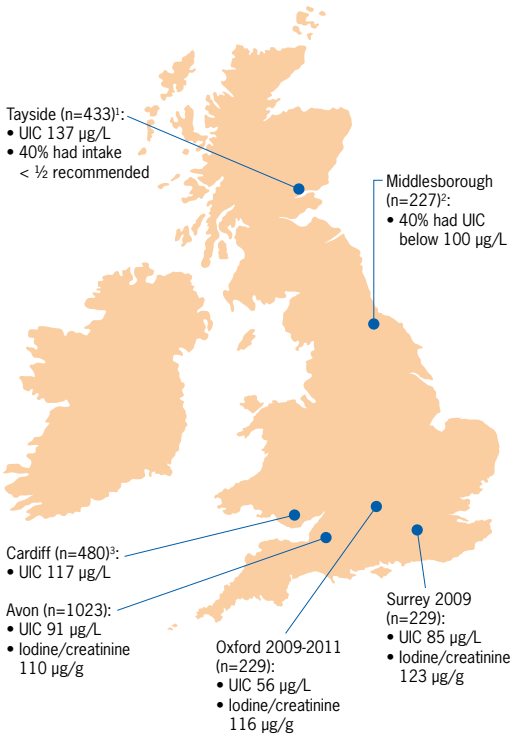
Professor Margaret Rayman

ALSPAC (Avon Longitudinal Study of Parents and Children)

This longitudinal study, carried out in the South West (Avon) of the UK, assessed the UIC of 14,541 pregnant women. Spot urine samples were collected in the years 1991-1992 and iodine was measured in the stored samples in 2012. According to the WHO, UIC should be above 150 µg/L/day but the median UIC in the pregnant ALSPAC participants was 91.1 µg/L.

UK schoolgirls study

Urinary iodine levels were systematically assessed in schoolgirls aged 14-15 years attending secondary school in nine UK centres. The median urinary iodine (UIC) levels in UK schoolgirls was 80·1 µg/L. These findings suggested that the UK school girls were iodine deficient, and highlighted an urgent need for a comprehensive investigation of UK iodine status and implementation of evidence-based recommendations for iodine supplementation (Iodine status of UK schoolgirls: a cross-sectional survey.)[4]



1. Barnett et al. 2002; 2. Kibirige MS et al. 2004; 3. Pearce et al 2010.

"There was a considerable deficit between the iodine status of these pregnant women and the recommended level for pregnancy", said Professor Rayman, presenting the data. In the early 1990s, none of these women was taking supplements or eating seaweed, according to their diet diaries.

This analysis shows that pregnant women, at least in this cohort, did not obtain adequate (WHO recommended) iodine nutrition from their diet.

Pregnant women in Surrey, UK (2009)

More recent data are available from a study that determined iodine levels in pregnant women from Surrey, UK. In this study 100 pregnant women recruited at 12 weeks of gestation in summer 2009 were measured for iodine and creatinine levels, and they answered questionnaires that asked whether they had used a supplement. [18]

The results showed that median UIC was 85.3 μg/L and iodine:creatinine ratio was 122 μg/g, classifying the group as mildly-to-moderately iodine deficient.. Notably, supplement users had significantly better iodine status.

"We have no reason at all to be complacent. In fact, just the opposite is true. The worse the iodine deficiency, the worse the effect on cognition"

Margaret Rayman
Professor of Nutrition, University of Surrey, UK.

Pregnant women in Oxford, UK (2009-2011)

This study comprised 230 pregnant women recruited from 2009-2011 at 12 weeks.[19]

of pregnancy. The women were recruited to a trial called the Selenium in Pregnancy Intervention Trial (SPRINT). Iodine status was not affected by selenium supplementation so it was possible to measure iodine levels in these women. Spot urinary iodine and creatinine were measured as well as some thyroid parameters. Only 3% of women took supplements containing iodine.

The results showed an overall median UIC of 56.8 μg/L and iodine:creatinine ratio of 116 μg/g, classifying the group as mildly-to-moderately iodine deficient throughout gestation.

Implications of the studies from Surrey and Oxford

Commenting on these two studies (Surrey and Oxford), Professor Rayman said that the level of deficiency in these studies was similar to that seen in the ALSPAC study. "In the ALSPAC study, children born to

women with similar iodine deficiency to that in these more recent studies was associated with poorer brain development as shown by significantly lower verbal IQ at age eight and reading comprehension at age nine."

"We have no reason at all to be complacent. In fact, just the opposite is true," she asserted. It was also found that the degree of iodine deficiency made a difference to the various IQ levels monitored. "The worse the iodine deficiency, the worse the effect on cognition," said Professor Rayman.

Professor Rayman also asserted that: "It seems to us that UK public health authorities and the NHS are currently failing pregnant women because women in the UK are unaware that deficiency of iodine in the UK is very common and has adverse consequences for their children's brain development. Ideally they need to enter pregnancy with good iodine stores and they need to know how they can achieve this. Also they need to know that a supplement after pregnancy is confirmed may be less effective."

She added that the UK needed to conduct an RCT of iodine in pregnancy because of the potential adverse effects of mild-to-moderate deficiency on child brain development. "We do not have a programme of salt iodisation. If women are told to supplement in pregnancy, there is some evidence of adverse effects on neurocognitive development if supplements of 150 μg/day or greater are begun when pregnancy has started. Supplementation should be started as early as possible in pregnancy but with a dose of not more than 140 μg/day, and certainly no later than the first trimester."

The Obstetrician's viewpoint – new guidelines in pregnancy

Michael Marsh, MD

To date, thyroid disease in pregnancy, some of which is associated with iodine deficiency, has not featured in management guidelines, and UK guidelines for management of thyroid disease before and during pregnancy are lacking. However, this is currently changing with the production of the UK's Royal College of Obstetrics and Gynaecology (RCOG) Greentop Guidelines for Thyroid disease in Pregnancy.

These guidelines are notable because it is the first time the RCOG has recognised the importance of thyroid disease in pregnancy, which is widely considered to be a significant step forward. Discussing the guidelines at the IGN meeting, obstetric consultant, Mr Marsh acknowledged that iodine deficiency in pregnancy is important and that the guidelines will emphasise this point.

V. Political will and international recommendations

Speakers: Kate Jolly, MD, PhD and Simon Smail, MD, CBE

Cost effectiveness of iodine supplementation

Speaker: Kate Jolly, Professor of Public Health & Primary Care at the University of Birmingham, UK

As with most health-related interventions in the UK and elsewhere, the health-economic case needs consideration.

Professor Jolly discussed a study that looked at the costs & benefits of iodine supplementation for pregnant women.

The study compared the costs and benefits of a strategy of iodine supplementation for pregnant women in a mild to moderately iodine deficient population against no iodine supplementation. Women took iodine supplements from early pregnancy until cessation of exclusive breastfeeding and outcomes-related assumptions included data from economic studies that linked IQ and income, as well as clinical data (e.g., ALSPAC) relating to iodine deficiency in pregnant women and the effect on their children's IQ.

The researchers, lead by Professor Jolly, found that from a NHS perspective there was a saving of £199 per/women supplemented & 1.22 IQ points gained. From a societal perspective, there was a saving of £4476/woman & 1.22 IQ points gained.[27]

Encouraging mothers to have a healthy pregnancy, for the benefit of mother and baby, as well as future generations, is usually a key tenet of any government's public health agenda. By way of example, the UK government advises pregnant women to take folic acid, and vitamin D, alongside eating a nutritious and balanced diet. However, it currently falls short of giving up-to-date advice on sufficient iodine status during pregnancy.

The evidence pertaining to mild-to-moderate iodine deficiency in UK women of child-bearing age and pregnant mothers is accumulating and hard to ignore. This raises the question of whether the UK government should be taking a stronger lead in encouraging pregnant women and those planning a pregnancy to increase their iodine intake. Of note, the last UK government advice on iodine intake was given in 1991.

Discussing how to work constructively at the interface between health improvement, which includes providing advice on nutritional status, and politics, Professor Simon Smail pointed out that the big challenges for public health are inevitably linked to politics and in particular, the difficulties associated with the definition and negotiation of the costs and benefits of reforms. Not least in this respect is the issue of iodine deficiency in pregnancy.

The Scientific Advisory Committee on Nutrition (SACN)

The SACN advises Public Health England (PHE) and other government agencies and departments on nutrition and related health issues.

After a review of the existing evidence in relation to iodine status and pregnancy in 2014 the SACN[26] stated: "This scoping paper highlights that the issue of iodine intake is of considerable public health significance, although the Committee is cautious in drawing conclusions on current evidence due to the limitations of the available data ……The Committee will keep a watching brief on the arising evidence to inform future research"

However, Professor Smail asserted that to date, the SACN had not made any further statements despite mounting evidence suggesting that the issue of iodine deficiency is gathering momentum, and despite the WHO advice on the matter (see international recommendations in section III).

"When I read the existing evidence about iodine deficiency, I was amazed at how reactionary they were being," he said, adding that, "but they are only advisors; they [SACN] don't take any action themselves, they advise PHE and other government agencies."

Concerning Wales, where Professor Smail is Vice Chair of Public Health Wales, he remarked that Public Health Wales is beginning to take a lead in health policy development. He highlighted that a key priority area was in working across sectors to improve the health of our children in their early years (from conception for a 1000 days), and in influencing policy to protect and improve health and reduce inequalities.

"We currently have a particular interest in epigenetics and I'd be interested to know more about brain development of children who were exposed to suboptimal iodine nutrition. Is there an epigenetic effect that should be factored in?" said Professor Smail.

Reflecting on the role of government in delivering policy to meet the health needs of the population, Professor Smail added that, "if you follow the true path of the evidence and think about outcomes then there are ways of taking this message about the need to improve the iodine status of the population to government agencies for action. Lobbying and campaigning strategies have been shown to be effective in other health-related policy arenas, for example in reducing smoking prevalence."

International recommendations

- The WHO and the Endocrine Society (US) guidance recommends a target daily intake of 250 mcg of iodine a day during pregnancy.
- The Endocrine Society suggests being mindful of local iodine fortification strategies and that supplements should contain between 150–200 mcg of iodine.
- The Spanish Endocrine Society and American Academy of Pediatrics endorse iodine supplementation but in pregnancy, breast-feeding, lactating or in women considering pregnancy, no strength is recommended.[28]

Closing remarks

Speaker: Jonathan Gorstein, PhD

After thanking the speakers for a productive series of presentations and stimulating discussions, Dr Gorstein noted that it was somewhat ironic that the UK Government supports international development programmes that include addressing nutritional challenges overseas but it is unable to support some of these same needs in its own country, he remarked.

Globally there has been "amazing progress" towards the elimination of iodine deficiency. Primarily, this has been due to the enactment of universal iodisation programmes (USI) in many countries across the world, including both developing and industrialised ones, leading to a virtual elimination of clinical manifestations of iodine deficiency.

The IGN promotes universal salt iodisation as the primary strategy to improve iodine intake and prevent deficiency, but acknowledges that there may be settings in which other implementations are required, including supplementation. Universal salt iodisation includes the addition of adequate iodine to both table salt and salt found in processed foods.

"In some countries, such as Australia, New Zealand, and Denmark, the mandatory use of iodised salt in bread has helped to establish a strong foundation of adequate iodine intake," he added.

However, if iodisation of table salt or its addition to processed foods is too challenging, then the UK Government might consider supplementation in the most at-risk groups, that is women planning to get pregnant, in early pregnancy or breast-feeding.

Effective programmes and structures require first and foremost good advocacy, and we need to be able to advocate the key messages and the importance of iodine nutrition, said Dr Gorstein. He pointed out that there are cost effective interventions that when appropriately implemented can alleviate iodine deficiency.

It is also necessary to generate robust evidence and data that can be used to inform effective policies and appropriate programme recommendations, without which the translational value of these data can be lost. Strong and clear communication of these data will effect change.

"The UK can follow some of the lessons learnt from the developing world by recognising that iodine deficiency is an impediment to cognitive development."

Jonathan Gorstein
Executive Director, Iodine Global Network, Seattle, US.

Much of the work of the IGN focuses on Africa and Asia where micronutrient malnutrition is pervasive, but uniquely with iodine, this problem is prevalent in both industrialised and developing countries.

"What we are actually seeing is that some of the greatest progress in alleviating iodine deficiency is in the developing world not the developed world," remarked Dr Gorstein. "The UK can follow some of the lessons learnt from the developing world by recognising that iodine deficiency is an impediment to cognitive development. Not doing anything about this is handicapping our countries from being able to progress and enabling our children to reach their full potential and participate in society."

Elimination of iodine deficiency needs to be sustained through ongoing effective action, persistence and communication to policy-makers. There is also a need to generate further evidence to further clarify the iodine deficiency status in the UK.

At present, the IGN recommends that in countries like the UK, which are iodine deficient and lack any routine iodine fortification programmes, iodine supplementation both three months prior to pregnancy and during pregnancy is required for the short-term. However, this needs to be accompanied by parallel efforts to improve the availability and supply of iodised salt in the food system, as this is the most viable and sustainable long-term measure to prevent iodine deficiency.

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