Iodine in Pregnancy and Lactation

Elizabeth N. Pearce, M.D., M.Sc.
Overview

- Dietary iodine requirements & status assessment
- Consequences of iodine deficiency
- Consequences of iodine excess
- Current U.S. iodine nutrition status
- Sources of dietary Iodine
- Supplement recommendations
Increased demand for thyroid hormone (↑ 50%), requires an additional 50-100 μg iodine:
- Thyrotropic regulation by hCG
- Estrogen-mediated TBG increase

**Increased Maternal Dietary Iodine Requirements in Pregnancy**

- Placental Type 3 deiodinase
- Iodide transferred to the fetus
- Increased renal iodine clearance (↑ 30-50%)
Increased Dietary Iodine Requirements in Lactation

• Normal lactating breast ducts concentrate iodide (via sodium iodide symporter), secreting it into milk
  Tazebay et al Nat Med 2000; 6:859-60

• Only source of iodine nutrition for breastfed infants
## Recommended Daily Dietary Iodine Intakes

<table>
<thead>
<tr>
<th>Age Group</th>
<th>U.S. Institute of Medicine (µg/day)</th>
<th>WHO, UNICEF, ICCIDD (µg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 months (AI)</td>
<td>110</td>
<td>0-5 years 90</td>
</tr>
<tr>
<td>7-12 months (AI)</td>
<td>130</td>
<td>6-12 years 120</td>
</tr>
<tr>
<td>1-8 years</td>
<td>90</td>
<td>&gt;12 years 150</td>
</tr>
<tr>
<td>9-13 years</td>
<td>120</td>
<td>Pregnancy 250</td>
</tr>
<tr>
<td>&gt;13 years</td>
<td>150</td>
<td>Lactation 250</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>220</td>
<td></td>
</tr>
<tr>
<td>Lactation</td>
<td>290</td>
<td></td>
</tr>
</tbody>
</table>

- U.S. Institute of Medicine 2006
## Urinary Iodine Values and Iodine Nutrition in Pregnancy and Lactation

<table>
<thead>
<tr>
<th>Population group</th>
<th>Median Urinary Iodine Concentration (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Optimal</td>
</tr>
<tr>
<td>Non-pregnant adults</td>
<td>100-199</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>150-249</td>
</tr>
<tr>
<td>Lactating Women</td>
<td>≥100</td>
</tr>
</tbody>
</table>

WHO Public Health Nutr 2007
Diurnal Urinary Iodine Concentration Variation

Als C et al J Clin Endocrinol Metab 2000;85:1367-9
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- Consequences of iodine deficiency
- Consequences of iodine excess
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- Sources of dietary iodine
- Supplement recommendations
# Spectrum of IDD

<table>
<thead>
<tr>
<th>Category</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FETUS</strong></td>
<td>Abortionss, Stillbirths, Congenital anomalies, Increased perinatal mortality, Increased infant mortality, Neurological cretinism: <em>mental deficiency, deaf mutism, spastic Diplegia squint</em>, Myxoedematous cretinism: <em>mental deficiency, dwarfism, hypothyroidism</em> Psychomotor defects</td>
</tr>
<tr>
<td><strong>NEONATE</strong></td>
<td>Neonatal hypothyroidism</td>
</tr>
<tr>
<td><strong>CHILD &amp; ADOLESCENT</strong></td>
<td>Retarded mental and physical development</td>
</tr>
<tr>
<td><strong>ADULT</strong></td>
<td>Goitre and its complications, Iodine-induced hyperthyroidism (IIH)</td>
</tr>
<tr>
<td><strong>ALL AGES</strong></td>
<td>Goitre, Hypothyroidism, Impaired mental function, Increased susceptibility to nuclear radiation</td>
</tr>
</tbody>
</table>
Maternal Iodine Supplementation and Child IQ Difference

7.4 point IQ difference in supplemented vs. unsupplemented groups

Child IQ in Relation to First-Trimester Maternal Urinary Iodine: ALSPAC

Maternal Iodine and Child Neurodevelopment: Cohort Studies

- Maternal UIC <150 µg/L associated with lower child spelling, grammar, reading age 9
- Lower maternal iodine intakes associated with child language delays age 3, ADHD symptoms age 8
- Low maternal UIC associated with poorer receptive/expressive language age 6, 12, 18 months

Abel MH et al. *J Nutr* 2017;147(7):1314-1324
Markhus MW et al. *Nutrients* 2018;10(9)
Iodine supplementation in Mild-to-Moderate Iodine Deficiency: Systematic Review

• Controlled trials assessing child neurodevelopment are lacking

• Gestational iodine supplements reduced maternal thyroid volume and, in some studies, improved thyroid function

Taylor PN et al. *Eur J Endocrinol* 2014;170:R1-15
RCT: Effect of Iodine Supplementation in Pregnancy on Child Neurodevelopment

- Bangalore, India and Bangkok, Thailand
- n=832; mean 10.7 weeks gestation at baseline
- Baseline MUIC 132 µg/L
- 200 µg I/day vs. placebo

Neurodevelopmental outcomes age 5-6

Costs and benefits of iodine supplementation for pregnant women in a mildly to moderately iodine-deficient population: a modelling analysis

Mark Monahan, Kristien Boelaert, Kate Jolly, Shiao Chan, Pelham Barton, Tracy E Roberts

Findings Our systematic search identified 1361 published articles, of which eight were assessed to calculate the monetary value of an IQ point. A discounted lifetime value of an additional IQ point based on earnings was estimated to be £3297 (study estimates range from £1319 to £11967) for the offspring cohort. Iodine supplementation was cost saving from both a health service perspective (saving £199 per pregnant woman [sensitivity analysis range –£42 to £229]) and societal perspective (saving £4476 per pregnant woman [sensitivity analysis range £540 to £4495]), with a net gain of 1.22 IQ points in each analysis. Base case results were robust to sensitivity analyses.
Overview

• Dietary iodine requirements & status assessment
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• Consequences of iodine excess
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• Sources of dietary Iodine
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Iodine-Induced Hypothyroidism

• Failure of homeostatic mechanism (escape from the Wolff-Chaikoff effect)
• Susceptible individuals
  – Thyroid autoimmunity
  – Fetus
Congenital Hypothyroidism From Excess Prenatal Maternal Iodine Ingestion

TSH: >100 419 217

Subclinical Hypothyroidism And UIC In Pregnant Women

n = 7,190 women at 4-8 weeks gestation

Median UIC 152.5 µg/L

Subclinical hypothyroidism: TSH >5.22 mIU/L with normal FT4

X Shi et al. J Clin Endocrinol Metab 2015;100:1630-8
## Tolerable Upper Limits for Iodine Exposure

<table>
<thead>
<tr>
<th>Age Group</th>
<th>µg/day (U.S. Institute of Medicine)</th>
<th>µg/day (WHO, UNICEF, ICCIDD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12 months</td>
<td>unknown</td>
<td>Infants 180</td>
</tr>
<tr>
<td>1-3 years</td>
<td>200</td>
<td>Pregnancy 500</td>
</tr>
<tr>
<td>4-8 years</td>
<td>300</td>
<td>Lactation 500</td>
</tr>
<tr>
<td>9-13 years</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>14-18 years</td>
<td>900</td>
<td></td>
</tr>
<tr>
<td>19-50 years</td>
<td>1,100</td>
<td></td>
</tr>
</tbody>
</table>

- U.S. Institute of Medicine 2006
Overview

• Dietary iodine requirements
• Assessment of iodine sufficiency
• Consequences of IDD
• Consequences of iodine excess
• Current U.S. iodine nutrition status
• Sources of dietary Iodine
• Supplement recommendations
U.S. Goiter Belt (pre-1920s)

- 26 - 70% of children had goiter
Median U.S. Urinary Iodine Concentration
NHANES 1971-2004

<table>
<thead>
<tr>
<th>Year</th>
<th>Median Urine Iodine Concentration (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1971-74</td>
<td>320</td>
</tr>
<tr>
<td>1988-94</td>
<td>145</td>
</tr>
<tr>
<td>2001-02</td>
<td>168</td>
</tr>
<tr>
<td>2003-04</td>
<td>160</td>
</tr>
<tr>
<td>2007-08</td>
<td>164</td>
</tr>
<tr>
<td>2009-10</td>
<td>144</td>
</tr>
</tbody>
</table>

% of U.S. Population with Urinary Iodine <50μg/L: NHANES I and NHANES III

Hollowell, JCEM 1998; 83:3401-8
Median UIC In Pregnant US Women

<table>
<thead>
<tr>
<th>Year</th>
<th>Median UIC (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHANES I</td>
<td>327</td>
</tr>
<tr>
<td>NHANES III</td>
<td>141</td>
</tr>
<tr>
<td>2001-2006</td>
<td>153</td>
</tr>
<tr>
<td>2005-2010</td>
<td>129</td>
</tr>
<tr>
<td>2007-2014</td>
<td>144</td>
</tr>
</tbody>
</table>

Hollowell JG et al. *J Clin Endocrinol Metab* 1998; 83:3401-8
Perrine CG et al. *Thyroid* 2019;29(1):153-154
Overview

• Dietary iodine requirements & status assessment
• Consequences of iodine deficiency
• Consequences of iodine excess
• Current U.S. iodine nutrition status
• **Sources of dietary Iodine**
• Supplement recommendations
Median Iodine Content of Adult* Diets
2008-2012 FDA Total Diet Study

% Daily Iodine Intake

Dairy
Meat, Fish, Poultry
Grain
Fruit, Veg
Mixture
Sweets
Beverages
Egg

*Women age 25-30
Mixtures: meat/poultry//fish/grain/veg

Salt in the U.S. diet

- ~77% of salt in U.S diet from restaurant/processed food, usually not iodized
- ~11% table salt added at the table or in cooking, 53% of table salt in U.S. is iodized at 60-100 ppm
- ~50% of reproductive age women never/rarely use table salt

Bread Iodine Content

- Iodate dough conditioners used starting 1940s. Use ↓ 1970s-1990s.
- Boston-area supermarkets 2001-2002:
  - 20 brands measured
  - 3 breads >313 μg l/slice
  - Others 2.2-54 μg l/slice (mean 10 μg/slice)

Pearce et al J Clin Endocrinol Metab 2004; 89:3421-4
Mean Iodine Content of New England Cows’ Milk by Season

Winter          Summer

116       91

n = 18 brands  p < 0.0005

Pearce et al J Clin Endocrinol Metab 2004; 89:3421-4
Iodine Sources in U.S. Cows’ Milk

- Cattle feed
  - Cows’ milk iodine content increased 300-500% 1965-1980 due to increased I in cattle feed
  - Organic iodine ethylenediamine dihydriodide (EDDI) content of cattle feed limited 1986 to 10mg/cow/day

- Iodophor disinfectant in teat dip/udder wash
  - Up to 1% available iodine

Pearce et al J Clin Endocrinol Metab 2004; 89:3421-4
The Example of Australia...

- Late 1980s: median urinary iodine values 200 μg/L
- <10% of the population uses iodized salt
- Iodophor cleaners eliminated by the dairy industry
- 1999: median urinary iodine value 64 μg/L in healthy volunteers

Guntun et al. MJA 1999; 171:467-70
Li et al. Asia Pac J Clin Nutr 2001; 10:200
Median Urinary Iodine Levels in U.S. Vegetarians and Vegans

Optimal iodine intake (WHO) (µg/L)

<table>
<thead>
<tr>
<th></th>
<th>Vegans n=62</th>
<th>Vegetarians n=78</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>78.5</td>
<td>147</td>
</tr>
<tr>
<td>Median U.S.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>urinary iodine</td>
<td></td>
<td>164</td>
</tr>
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Overview

• Dietary iodine requirements & status assessment
• Consequences of iodine deficiency
• Consequences of iodine excess
• Current global and U.S. iodine nutrition status
• Sources of dietary Iodine
• Supplement recommendations
Women who are planning to be pregnant or are pregnant or breastfeeding should supplement their diet with a daily oral supplement that contains 150 µg of iodine.

• De Groot L et al. *J Clin Endocrinol Metab* 2012;97:2543-65
• AAP Council on Environmental Health. *Pediatrics* 2014;133:1163-6
• JH Lazarus et al. *Eur Thyroid J* 2014;3:76-94.
Percentage of Reproductive-Age U.S. Women Reporting Supplement Use Within 30 Days

Based on NHANES 2011-2014

Gupta PM et al. *Nutrients* 2018;10(7)

Percentage of Women Reporting Supplement Use

- **Non-pregnant women**: 45.3%
- **Pregnant women**: 72.2%
- **Lactating women**: 75%

Supplement Use by Pregnancy Status

- **Any Supplement**
  - Non-pregnant women: 14.8%
  - Pregnant women: 17.8%
  - Lactating women: 19%

- **Supplement with iodine**
  - Non-pregnant women: 8%
  - Pregnant women: 10.2%
  - Lactating women: 18.2%

Sample Sizes

- Non-pregnant women: n = 2155
- Pregnant women: n = 122
- Lactating women: n = 61
Proportion of U.S. Prenatal Multivitamins Containing Iodine

Lee SY et al. *Thyroid* 2017;27(8):1101-2
Conclusions

• Iodine status can be determined at the population, but not individual, level

• Pregnant women/fetuses are particularly vulnerable to iodine deficiency disorders and to iodine excess

• Mild iodine deficiency has re-emerged among pregnant U.S. women
  – Recommend iodine-containing prenatal multivitamin 150 µg/day