European Journal of Clinical Nutrition (2004) 58, 979–984

0954-3007/04 $30.00
www.nature.com/ejcn

REVIEW

Iodine supplementation of pregnant women in Europe: a review and recommendations

M Zimmermann[1]* and F Delange[2]

[1]*Laboratory for Human Nutrition, Swiss Federal Institute of Technology, Zürich, Switzerland; and* [2]*International Council for Control of Iodine Deficiency Disorders, Brussels, Belgium*

Objective: Nearly two-thirds of the population of Western and Central Europe live in countries that are iodine deficient. Damage to reproductive function and to the development of the fetus and newborn is the most important consequence of iodine deficiency. The objective of this review was to examine the iodine status of pregnant women in Europe and the potential need for iodine supplementation.
Design: A MEDLINE/PubMed search and compilation of all published studies since 1990 of iodine nutrition and iodine supplementation of pregnant women in Europe, as well as an Internet-based search and review on availability and legislation of iodine supplements in the European Union.
Results: Although the data suggest most women in Europe are iodine deficient during pregnancy, less than 50% receive supplementation with iodine. Mild-to-moderate iodine deficiency during pregnancy adversely affects thyroid function of the mother and newborn and mental development of the offspring and these adverse effects can be prevented or minimized by supplementation. There are no published data on the effect of iodine supplementation on long-term maternal and child outcomes. The iodine content of prenatal supplements in Europe varies widely; many commonly used products contain no iodine. The European Union is developing legislation to establish permissible levels for iodine in food supplements.
Conclusions: In most European countries, pregnant women and women planning a pregnancy should receive an iodine-containing supplement ($\approx$150 μg/day). Kelp and seaweed-based products, because of unacceptable variability in their iodine content, should be avoided. Prenatal supplement manufacturers should be encouraged to include adequate iodine in their products. Professional organizations should influence evolving EU legislation to ensure optimal doses for iodine in prenatal vitamin–mineral supplements.
Sponsorship: International Council for Control of Iodine Deficiency Disorders.
European Journal of Clinical Nutrition (2004) **58,** 979–984. doi:10.1038/sj.ejcn.1601933

Keywords: women; pregnancy; Europe; iodine; deficiency; supplementation

Introduction

Nearly two-thirds of the 600 million people in Western and Central Europe live in regions of mild-to-severe iodine deficiency (Delange, 2002; Vitti *et al*, 2003). Damage to reproductive function and to the development of the fetus and newborn is the most important consequence of iodine deficiency (Dunn & Delange, 2001). The fetal brain is particularly vulnerable to maternal hypothyroidism in iodine deficiency, and iodine deficiency is the leading cause worldwide of preventable mental retardation (Bleichrodt & Born, 1994). Even mild or subclinical maternal hypothyroidism during pregnancy can impair mental development of the newborn (Haddow *et al*, 1999; Glinoer & Delange, 2000). This paper discusses: (a) the iodine nutrition of pregnant women and women of child-bearing age in Europe; (b) the use of iodine-containing supplements by these groups; (c) trials of iodine supplementation in pregnancy; and (d) the availability and regulation of iodine-containing supplements in Europe.

*Correspondence: M Zimmermann, Laboratory for Human Nutrition, Institute of Food Science and Nutrition, Swiss Federal Institute of Technology Zürich, Seestrasse 72/Postfach 474, CH- 8803 Rüschlikon, Switzerland.
E-mail: michael.zimmermann@ilw.agrl.ethz.ch
Guarantor: M Zimmermann.
Contributors: Both MZ and FD gathered and analyzed the published data and each contributed to the interpretation and discussion. The main preparation of the manuscript was done by MZ with revisions and editing by FD.
Received 9 September 2003; revised 29 October 2003; accepted 13 November 2003

Iodine status of pregnant women

In national surveys of women of child-bearing age in European countries, median iodine intakes are approximately half of recommended levels. The recommended daily iodine intake during pregnancy from the World Health Organization/United Nations Children's Fund/International Council for Control of Iodine Deficiency Disorders (WHO/UNICEF/ICCIDD) is 200 μg (WHO/UNICEF/ICCIDD, 2001), while the United States Institute of Medicine (IOM) suggests a Recommended Dietary Allowance (RDA) during pregnancy of 220 μg (IOM, 2001). The Verbundstudie Ernahrungserhebung und Risikofaktoren–Analytik (VERA) study in Germany reported a median (range) iodine intake of 100 (33–284) μg/day in 19–24-y-old women (Bergmann *et al*, 1997). Rasmussen *et al* (2002) found the median iodine intake in 18–22-y-old Danish women in Aalborg and Copenhagen to be 85 and 116 μg/day, respectively. Even in the Netherlands, considered iodine sufficient, the National Food Consumption Survey found the mean (s.d.) iodine intake of 20–49-y-old women was 149 (36) μg/day (Brussaard *et al*, 1997).

Recent studies reporting low urinary iodine (UI) in pregnant women in Europe reinforce the dietary intake data (Table 1). UI excretion is an accurate indicator of dietary iodine intake as >90% of ingested iodine is excreted in the urine and UI is highly sensitive to recent changes in iodine intake (IOM, 2001). For population estimates, daily iodine intake can be extrapolated from UI by assuming 90% of ingested iodine is found in urine and a 24-h urine volume of 1.5 l (IOM, 2001). Using this estimation, a UI of ≈140 μg/l would correspond to a daily intake of 200 μg iodine. During pregnancy this extrapolation may be less valid due to an increase in renal iodine clearance (Aboul-Khair *et al*, 1964). In Sweden and Switzerland, two iodine-sufficient countries, UI concentrations indicate adequate dietary iodine intake during pregnancy, while in eight iodine-deficient countries (with the exception of Ireland), UI concentrations indicate that iodine intakes are clearly inadequate. Studies of thyroid size in pregnancy measured by ultrasonography also indicate iodine nutrition is suboptimal in much of Europe. In countries affected by mild or moderate iodine deficiency (Ireland, Germany, Belgium, Italy, Denmark), thyroid volume increases 14–30% during pregnancy, while in iodine-sufficient countries (Finland, the Netherlands), there is no increase in thyroid volume during pregnancy (Berghout & Wiersinga, 1998; Glinoer, 2003).

Prevalence of iodine supplementation during pregnancy and its impact on status

Studies suggest only 13–50% of pregnant women in Europe receive iodine-containing supplements. In Switzerland, although 70% of pregnant women receive a prenatal supplement, only 13% receive a supplement containing iodine; the median UI in women taking iodine-containing supplements is 194 *vs* 130 μg/l in nonsupplemented women (Hess *et al*, 2001). In Denmark, although most pregnant women take prenatal supplements, only approx. one-third contain iodine (Nohr *et al*, 1993). In Germany, only 21% of

Table 1 Urinary iodine in pregnant women in Europe (1990–2002)

Country	n	*S/C*[a]	*Trimester*[b]	*Urinary iodine*	*Source*
Iodine-sufficient countries					
Sweden	32	S	1	180 μg/day	Elnagar *et al* (1998)
	32	S	2	170 μg/day	
	32	S	3	145 μg/day	
Switzerland	511	C	2,3	138 μg/l	Hess *et al* (2001)
Iodine-deficient countries					
Belgium	230	C	1	58 μg/l	Glinoer *et al* (1990)
	265	C	2	58 μg/l	
	370	C	3	53 μg/l	
Denmark	26	S	2	51 μg/l	Pedersen *et al* (1993)
	26	S	3	40 μg/l	
	98	C	5 d PP	35 μg/l	Nohr *et al* (1993)
France	306	S	1	50 μg/l	Caron *et al* (1997)
	224	S	3	54 μg/l	
Germany	89	S	1	53 μg/g cr	Liesenkötter *et al* (1996)
	89	S	11 d PP	50 μg/g cr	
Hungary	119	C	1,2,3	57 μg/g cr	Mezosi *et al* (2000)
Ireland	38	S	1	150 μg/l	Smyth *et al* (1997) and Smyth (1999)
	38	S	2	120 μg/l	
	38	S	3	115 μg/l	
	84	C	40 d PP	74 μg/l	
Italy	67	C	1,2	74 μg/g cr	Antonangeli *et al* (2002)
Turkey	90	C	1,2,3	91 μg/day	Mocan *et al* (1995)

[a]S/C, sequential (S) or cross-sectional study (C).
[b]Timing of urinary iodine determination. PP, postpartum. Adapted from Glinoer (2003).

pregnant women receive iodine supplements (German Ministry of Health, 1998). In both countries, median daily urinary iodine excretion is significantly higher in pregnant women supplementing with iodine than those not supplementing: 58 *vs* 35 μg/day in Denmark, and 85 *vs* 59 μg/day in Germany. In Hungary, ~50% of pregnant women receive a supplement containing iodine. In those taking supplements containing ≥150 μg l/day, the median UI was 115–130 μg/g cr, compared to 57–68 μg/g cr in women not supplementing (Mezosi *et al*, 2000). In a cross-sectional study in Denmark, iodine supplement use (150 μg/day) and thyroid function were assessed in pregnant women and their newborns ($n = 144$) (Nohr & Laurberg, 2000). At term, the median UI in supplemented mothers was 60 μg/l, compared to 35 μg/l in nonsupplemented mothers. In the supplement group, thyroglobulin (Tg) in both maternal and cord blood was significantly lower, and free T4 significantly higher, compared to the nonsupplement group. Although maternal TSH was lower in the supplement group, cord TSH was 27% higher in the supplement group ($P < 0.05$) (Nohr & Laurberg, 2000), suggesting that, in iodine-deficient areas, the fetal thyroid may be particularly sensitive to the inhibitory effect of iodine.

Trials of iodine supplementation

Six randomized, controlled trials of iodine supplementation in pregnancy have been published, involving 450 women with mild–moderate iodine deficiency (Table 2). Romano *et al* (1991) gave 120–180 μg iodine as iodized salt or control daily beginning in the first trimester to healthy pregnant women ($n = 35$; median UI 31–37 μg/l). In the treated group, median UI increased three-fold and thyroid volume did not change. In the controls, there was no change in UI, but a 16% increase in thyroid volume. Treatment had no effect on maternal TSH. Pedersen *et al* (1993) randomized pregnant women ($n = 54$) to receive either 200 μg iodine/day as KI solution or no supplement from 17 weeks to term. Median UI increased from 55 to 90–110 μg/l in treated group. Maternal thyroid volume increased 16% in the treated group *vs* 30% in controls ($P < 0.05$). Maternal Tg and TSH, and cord Tg were significantly lower in the treated group. No significant differences were found between groups comparing maternal or cord T4, T3, and FT4. In a double-blind, placebo-controlled trial, Glinoer *et al* (1995) supplemented pregnant women ($n = 120$; median UI 36 μg/l; biochemical criteria of excess thyroid stimulation) with 100 μg iodine/day or control from ~14 weeks to term. Treatment had no significant effect on maternal or cord T3, FT4, and T3/T4 ratio. The treated women had significantly higher UI, smaller thyroid volumes, and lower TSH and Tg levels, compared to controls. Newborns of the treated group also had significantly higher UI, smaller thyroid volumes and lower Tg levels compared to controls. There was a nonsignificant 14% increase in cord serum TSH in the treated group.

Table 2 Randomized, controlled trials of iodine supplementation in pregnancy: effect on urinary iodine concentration

Iodine dose (μg/day)	*Urinary iodine*		*Source*
	Pretreatment	*Post-treatment*	
50	65 μg/g cr	128 μg/g cr	Antonangeli *et al* (2002)
100	36 μg/l	80–90 μg/l	Glinoer *et al* (1995)
120–180	37 μg/day	100 μg/day	Romano *et al* (1991)
150	50 μg/l	105 μg/l	Nohr *et al* (2000)
200	55 μg/l	90–110 μg/l	Pedersen *et al* (1993)
200	91 μg/g cr	230 μg/g cr	Antonangeli *et al* (2002)
230	53 μg/g cr	104 μg/g cr	Liesenkötter *et al* (1996)

Liesenkötter *et al* (1996) reported results from a quasi-random, controlled trial of 230 μg iodine/day from 11 weeks to term in pregnant women ($n = 108$; median UI 53 μg/g cr; goiter rate 42.5%). Median UI increased to 104 μg/g cr in treated group, and median thyroid volume was significantly lower in the newborns of the treated women compared to controls (0.7 *vs* 1.5 ml, respectively, $P < 0.005$). Treatment had no significant effect on maternal TSH, T3, T4, thyroid volume, or Tg, and had no effect on newborn TSH. In a placebo-controlled, double-blind trial, Nohr *et al* (2000) gave a multinutrient supplement containing 150 μg iodine/day or control to pregnant women positive for antithyroid peroxidase antibodies (TPO-Ab) ($n = 66$) from 11 weeks to term. Median UI was significantly higher in the treated women at term, but there were no differences in maternal TSH, FT4 or Tg between groups. There was no difference in the prevalence of antithyroglobulin antibodies (Tg-Ab) or TPO-Ab, and no differences in prevalence or severity of postpartum thyroid dysfunction (PPTD; defined as an abnormal TSH in the postpartum period) between groups. However, 12/20 (60%) of treated women developed PPTD compared to 11/24 (46%) of controls, and failure to detect a significant difference in PPTD prevalence may have been due to a type II error. In a prospective, randomized, open-label trial, Antonangeli *et al* (2002) supplemented pregnant women ($n = 67$; median UI 74 μg/g cr) with 50 μg or 200 μg iodine/day from 18–26 to 29–33 weeks. Median UI was significantly higher in the 200 μg group than in the 50 μg group (230 *vs* 128 μg/g cr). However, there were no differences in maternal FT4, FT3, TSH, Tg or thyroid volume between groups, and no differences in TPO-Ab, Tg-Ab or prevalence of PPTD.

In summary, what do these trials tell us about the dose, safety and efficacy of iodine supplementation in mild–moderately iodine-deficient pregnant women? In all six trials, supplementation resulted in a significant increase in maternal UI. Iodine doses varied between 50 and 230 μg/day, and the data indicate no clear dose–response relationship for UI (Table 2), TSH, Tg, thyroid hormones, or thyroid volume. Iodine supplements during pregnancy appear to be generally safe; there was no increase in maternal thyroid autoimmunity, or in the prevalence or severity of PPTD in the trials.

However, sample sizes were small, and more data, particularly from TPO-Ab+ women, would be valuable. For the newborn, most data suggest supplementation is safe, although the studies of Nohr *et al* (2000) and Glinoer *et al* (1995) reported higher newborn TSH levels with supplementation. Iodine supplementation is efficacious, both for the mother and newborn. Low intakes of iodine during pregnancy cause maternal and fetal thyroid stress, characterized by increased thyroid size and Tg release in both mother and newborn. In three of the five trials that measured maternal thyroid volume, supplementation was associated with significantly reduced maternal thyroid size. The studies also suggest an increase in newborn thyroid volume and Tg can be prevented or minimized by supplementation. Although less consistent, the data also suggest maternal TSH is generally lower (within the normal reference range) with supplementation. Supplementation has little or no impact on maternal and newborn total or free thyroid hormone levels. There are no clinical data on the effect of supplementation on birth weight or prematurity, and no data on long-term outcomes, such as maternal goiter, thyroid autoimmunity, or child development.

Availability and regulation of iodine-containing supplements

The labeled iodine content of multivitamin/minerals marketed as prenatal supplements in Europe varies widely. Many commonly used products contain no iodine (eg Eunova®, GlaxoSmithKline; Elevit Pronatal®, Roche; Stuart Prenatal®, Stuart), while others contain 200 μg (eg Femibion Folic Acid plus®, Merck; Orthonatal®, Orthomo, NeoVin®, Milupa) or even 300 μg (Pre-Natal®, Twin Labs). The actual iodine content in supplements is determined not only by the original amount added, but also by the stability of the compound, the time elapsed since manufacture, and the conditions under which the product is stored. Lee *et al* (1994) reported on the variability of iodine content in multinutrient supplements ($n=42$) available in the UK. The median iodine content (range) of the manufacturer's recommended daily supplement regimen was 104 (11–171) μg/day. The mean measured iodine content (as a percent of declared content) was 79 (8–197)%, and 16% of the supplements contained <60% of their declared iodine content. The iodine content of kelp supplements, a popular supplemental form, was highly variable. The median iodine content (range) of the manufacturer's recommended daily supplement regimen was 1005 (210–3840) μg/day. The mean measured content (as a percent of declared content) was 137 (45–914)%. For half of the kelp supplements, the manufacturer's recommended daily dose was greater than 1100 μg/day, the recommended Safe Upper Limit for pregnancy (IOM, 2001). In addition, bioavailability of iodine from supplements has not been tested. Bioavailability can be influenced by the physical form of the product, for example, tablets *vs* gelatin capsule, the substance used in coating and thickness of coat, the amount of pressure used to form the tablet, the disintegration and dissolution of the tablet, and other nutrients or substances present which may interfere with bioavailability (Park *et al*, 1991). There are no published data assessing iodine bioavailability from vitamin/mineral supplements.

Until recently, there was no specific European Union regulation of multivitamin/mineral supplements. They were classified as foods, and had to comply with relevant EU food legislation and individual member state's internal legislation. This resulted in wide variation across Europe in legislation, compounds allowed and permissible levels. To remedy this, the EU Parliament approved a Common Position 'On the approximation of the laws of member states relating to food supplements'(C5-0640/2001) in 2002. Its goals are to harmonize divergent national rules on sales of food supplements that contain vitamins and minerals, and to ensure food supplements are safe and properly labeled (EU Website, 2003). Its provisions apply to all food supplements except those licensed as medicines (EU Council Directive 65/65/EEC) and those covered under 'foods for particular nutritional uses'(Council Directive 89/398/EEC). Provisions of the Common Position state that the label of the supplement must contain clear instructions for daily dosage, and a warning about possible health risk from excess use. Purity criteria are those specified by EU legislation for foods. Any language suggesting a varied diet does not provide necessary amounts of essential nutrients is prohibited, with the exception of 'when the need for supplementation of specific population groups is established by generally accepted scientific data'. It could be argued this exception would apply to iodine in iodine-deficient regions of Europe. Provisions specific for iodine state: (a) supplements may contain iodine; (b) the amount present should be labeled in μg; (c) the only iodine compounds permitted are potassium iodide, sodium iodide, potassium iodate, and sodium iodate. This legislation entered into force in July 2002, and EU Member States needed to enact the necessary regulations to comply with this Directive by July 2003. Permissible maximum and minimum levels for iodine in supplements will be set by the EU Standing Committee on Food no later than 2007. Regulation of nonvitamin/mineral supplements containing iodine (eg kelp tablets) is due in a second report of the Commission in 2007, and until then individual member states' laws apply.

Conclusions

Iodine status of pregnant women is clearly suboptimal in many regions in Europe, and iodine-containing supplements have a beneficial impact on the iodine and thyroid status of both the mother and newborn. Pregnant women in these regions, if not adequately covered by iodized salt, should be supplemented with iodine in the form of potassium iodide tablets or iodine-containing prenatal multivitamin preparations. Another option is oral iodized oil; it is safe and its single dose is easier to administer, but it may not provide constant blood iodine levels (Delange, 1996). Adequate iodine before conception is best, and women who are planning a pregnancy should consider iodine supplementation if iodized salt is not available. The fetus is particularly vulnerable to damage from iodine deficiency early in pregnancy (Pharoah *et al*, 1971; Xue-Yi *et al*, 1994; Delange, 2001), and if supplementation begins only at the first prenatal care visit, this critical period may be missed. Because certain groups of women—the poor and less educated—are less likely to benefit from campaigns that encourage iodine supplementation, continued efforts for universal salt iodization remain a priority. More research to determine the optimal dose of supplemental iodine, the bioavailability of iodine from multinutrient preparations, and efficacy in terms of long-term clinical outcomes would be valuable.

Recommendations

Clinicians in European countries harboring iodine deficiency should consider recommending an iodine-containing supplement ($\approx 150\,\mu g$/day) for pregnant women and for those women planning a pregnancy. Kelp and seaweed-based products, because of unacceptable variability in their iodine content, should be avoided. Professional organizations, such as the European Thyroid Association and the European Office of ICCIDD should encourage prenatal supplement manufacturers to include adequate iodine ($\approx 150\,\mu g$/day) in their products. These organizations should also take a lead advocacy role to ensure the EU Standing Committee on Food establishes optimal minimum and maximum doses for iodine in food supplements.

References

Aboul-Khair SA, Crooks J, Turnbull AC & Hytten FE (1964): The physiological changes in thyroid function during pregnancy. *Clin. Sci.* **27**, 195–207.

Antonangeli L, Maccherini D, Cavaliere R, Di Giulio C, Reinhardt B, Pinchera A & Aghini-Lombardi F (2002): Comparison of two different doses of iodide in the prevention of gestational goiter in marginal iodine deficiency: a longitudinal study. *Eur. J. Endocrinol.* **147**, 29–34.

Berghout A & Wiersinga W (1998): Thyroid size and thyroid function during pregnancy: an analysis. *Eur. J. Endocrinol.* **138**, 536–542.

Bergmann R, Huch R, Bergmann KE & Dudenhausen JW (1997): Nutrition and prevention during pregnancy (in German). *Vitaminspur.* **12**, 173–178.

Bleichrodt N & Born MP (1994): A metaanalysis of research on iodine and its relationship to cognitive development. In *The Damaged Brain of Iodine Deficiency* ed. JB Stanbury, pp 195–200. New York: Cognizant Communication.

Brussaard JH, Brants HA, Hulshof KF, Kistemaker C & Lowik MR (1997): Iodine intake and urinary excretion among adults in the Netherlands. *Eur. J. Clin. Nutr.* **51** (Suppl 3), S59–62.

Cao XY, Jiang XM, Dou ZH, Rakeman MA, Zhang ML, O'Donnell K, Ma T, Amette K, DeLong N & DeLong GR (1994): Timing of vulnerability of the brain to iodine deficiency in endemic cretinism. *N. Engl. J. Med.* **331**, 1739–1744.

Caron P, Hoff M, Bazzi S, Dufor A, Faure G, Ghandour I, Lauzu P, Lucas Y, Maraval D, Mignot F, Ressigeac P, Vertongen F & Grange V (1997): Urinary iodine excretion during normal pregnancy in healthy women living in the southwest of France: correlation with maternal thyroid parameters. *Thyroid* **7**, 749–754.

Delange F (1996): Administration of iodized oil during pregnancy: a summary of the published evidence. *Bull. WHO* **74**, 101–108.

Delange F (2001): Iodine deficiency as a cause of brain damage. *Postgrad. Med. J.* **77**, 217–220.

Delange F (2002): Iodine deficiency in Europe. *Thyroid Int.* **5**, 3–18.

Dunn JT & Delange F (2001): Damaged reproduction: the most important consequence of iodine deficiency. *J. Clin. Endocrinol. Metab.* **86**, 2360–2363.

Elnagar B, Eltom A, Wide L, Gebre-Medhin M & Karlsson FA (1998): Iodine status, thyroid function and pregnancy: study of Swedish and Sudanese women. *Eur. J. Nutr.* **52**, 351–355.

European Union website at: http://europa.eu.int/comm/food/fs/sfp/df/df_fs_en.html (accessed August 2003).

German Ministry of Health (1998): Iodine Monitoring 1996. In *Vol. 110, Series of the German Ministry of Health* (in German). Nomos: Baden-Baden.

Glinoer D (2003): The maternal handling of iodine and metabolism of thyroid hormone during pregnancy. In *Thyroid and Brain* eds G Morreale de Escobar, JJM de Vijlder, S Butz & V Hostalek pp 97–112. Stuttgart: Schattauer.

Glinoer D, de Nayer P, Bourdoux P, Lemone M, Robyn C, van Steirteghem A, Kinthaert J & Lejeune B (1990): Regulation of maternal thyroid during pregnancy. *J. Clin. Endocrinol. Metab.* **71**, 276–287.

Glinoer D, de Nayer P, Delange F, Lemone M, Toppet V, Spehl M, Grun JP, Kinthaert J & Lejeune B (1995): A randomized trial for the treatment of mild iodine deficiency during pregnancy: maternal and neonatal effects. *J. Clin. Endocrinol. Metab.* **80**, 258–269.

Glinoer D & Delange F (2000): The potential repercussions of maternal, fetal and neonatal hypothyroxinemia on the progeny. *Thyroid* **10**, 871–887.

Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, O'Heir CE, Mitchell ML, Hermos RJ, Waisbren SE, Faix JD & Klein RZ (1999): Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N. Engl. J. Med.* **341**, 549–555.

Hess SY, Zimmermann MB, Torresani T, Burgi H & Hurrell RF (2001): Monitoring the adequacy of salt iodization in Switzerland: a national study of school children and pregnant women. *Eur. J. Clin. Nutr.* **55**, 162–166.

Institute of Medicine (IOM), Food and Nutrition Board (2001): Iodine. In *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc* pp 258–289. Washington, DC: National Academy Press.

Lee SM, Lewis J, Buss DH, Holcombe GD & Lawrance PR (1994): Iodine in British foods and diets. *Br. J. Nutr.* **72**, 435–446.

Liesenkötter KP, Gopel W, Bogner U, Stach B & Grüters A (1996): Earliest prevention of endemic goiter by iodine supplementation during pregnancy. *Eur. J. Endocrinol.* **134**, 443–448.

Mezosi E, Molnar I, Jakab A, Balogh E, Karanyi Z, Pakozdy Z, Nagy P, Gyory F, Szabo J, Bajnok L, Leovey A, Kakuk G & Nagy EV (2000): Prevalence of iodine deficiency and goitre during pregnancy in east Hungary. *Eur. J. Endocrinol.* **143**, 479–483.

Mocan MZ, Erem C, Telatar M & Mocan H (1995): Urinary iodine levels in pregnant women with and without goiter in the Eastern Black Sea part of Turkey. *Trace Element Electrolyte* **12**, 195–197.

Nohr SB, Jorgensen A, Pedersen KM & Laurberg P (2000): Postpartum thyroid dysfunction in pregnant thyroid peroxidase antibody-positive women living in an area with mild to moderate iodine deficiency: is iodine supplementation safe? *J. Clin. Endocrinol. Metab.* **85**, 3191–3198.

Nohr SB & Laurberg P (2000): Opposite variations in maternal and neonatal thyroid function induced by iodine supplementation during pregnancy. *J. Clin. Endocrinol. Metab.* **85**, 623–627.

Nohr SB, Laurberg P, Borlum KG, Pedersen KM, Johannesen PL, Damm P, Fuglsang E & Johansen A (1993): Iodine deficiency in pregnancy in Denmark. Regional variations and frequency of individual iodine supplementation. *Acta Obstet. Gynecol. Scand.* **72**, 350–353.

Park YK, Kim I & Yetley EA (1991): Characteristics of vitamin and mineral supplement products in the United States. *Am. J. Clin. Nutr.* **54**, 750–759.

Pedersen KM, Laurberg P, Iversen E, Knudsen PR, Gregersen HE, Rasmussen OS, Larsen KR, Eriksen GM & Johannesen PL (1993): Amelioration of some pregnancy-associated variations in thyroid function by iodine supplementation. *J. Clin. Endocrinol. Metab.* **77**, 1078–1083.

Pharoah POD, Buttfield IH & Hetzel BS (1971): Neurological damage to the fetus resulting from severe iodine deficiency during pregnancy. *Lancet* **i**, 308–310.

Rasmussen LB, Ovesen L, Bulow I, Jorgensen T, Knudsen N, Laurberg P & Pertild H (2002): Dietary iodine intake and urinary iodine excretion in a Danish population: effect of geography, supplements and food choice. *Br. J. Nutr.* **87**, 61–69.

Romano R, Jannini EA, Pepe M, Grimaldi A, Olivieri M, Spennati P, Cappa F & D'Armiento M (1991): The effects of iodoprophylaxis on thyroid size during pregnancy. *Am. J. Obstet. Gynecol.* **164**, 482–485.

Smyth PPA (1999): Variation in iodine handling during normal pregnancy. *Thyroid* **9**, 637–642.

Smyth PPA, Hetherto AMT, Smith DF, Radcliff M & O'Herlihy C (1997): Maternal iodine status and thyroid volume during pregnancy: correlation with neonatal iodine intake. *J. Clin. Endocrinol. Metab.* **82**, 2840–2843.

Vitti P, Delange F, Pinchera A, Zimmermann M & Dunn JT (2003): Europe is iodine deficient. *Lancet* **361**, 1226.

WHO/UNICEF/ICCIDD (2001): *Assessment of Iodine Deficiency Disorders and Monitoring their Elimination* WHO/NHD/01.1. Geneva: World Health Organization.