Iodine

Iodine	µg/d	Women	Men	Children 2-5 y	Children 6-9 y	Children 10--13y
Recommended intake	RI	150	150	90	120	150
Average requirement	AR	100	100			
Lower intake level	LI	70	70			
Upper intake level	UL	600	600			

Introduction

Iodine deficiency is considered to be one of the most common nutritional disorders in the world and the most common cause of goitre (1, 2). In Sweden and Finland iodine deficiency goitre was common during the first decades of the 1900s. The introduction of iodine fortification of salt resulted in a sharp decrease in the prevalence (3). In 2000, mandatory iodisation of table salt and bread salt was introduced in Denmark as a response to studies showing low iodine status and goitre in certain population groups (4, 5). In 2004-2005 the urinary iodine excretion had increased significantly in all age groups compared with before mandatory iodine fortification (6).

Dietary sources and intake

In plants, iodine predominantly occurs in inorganic form and the content varies with the iodine content in the environment. The iodine content in sea-plants is higher than in plants grown on land. In certain seaweed species, the iodine content can be up to 4.5 g/kg dry weight. The iodine content of milk and milk products varies considerably depending on feed and use of iodine-containing disinfectants in connection with milking. The iodine content is generally higher in winter than in summer milk (7). The iodine in drinking water varies considerably between regions and can locally be a significant iodine source (8,9). Fish, especially marine fish and shellfish, generally have high iodine content. Eggs can also be an important iodine source.

Iodised table salt is available in Denmark, Sweden, Finland and Norway and contributes to iodine intake. The levels vary from 5-50 µg/g salt. Denmark also fortifies salt used in bread (3,4,6). Iodised salt is not commonly used in Iceland (10). In Norway iodisation of cow fodder has been more important for the iodine intake than iodised table salt (7,11).
The dietary supply of iodine is difficult to assess in dietary surveys, since data for iodised table salt and drinking water are commonly lacking (see Chapter XX Intake of Vitamins and minerals in Nordic countries). An overview of studies on iodine nutrition in the Nordic

countries (intake and iodine excretion), published in the years 2000 to 2010, is given in a literature review published in 2012 (12).

Physiology and metabolism

Iodine is essential for a number of animal and plant species. Only vertebrates have developed a thyroid gland to cater for synthesis, storage and secretion of the iodine-containing hormones, thyroxine (T4) and the biologically active form triiodothyronine T3 (13). The utilisation of iodine in the thyroid gland occurs via: 1) active uptake of iodide (iodide concentration is approx. 30 times higher in the gland than in plasma), 2) incorporation of iodine in thyroglobulin and iodine tyrosine, and 3) secretion of the iodine thyronines triiodothyronine and thyroxine. The thyroid-stimulating hormone (TSH) from the pituitary gland regulates the formation of the thyroid hormones.

The thyroid hormones increase metabolism in body cells. The mechanism of action is not completely known, but protein synthesis increases, e.g. with respect to those enzymes necessary for an increased metabolic activity. The thyroid hormones also increase the size and number of mitochondria - a sign of increased ATP-production.

Dietary iodine is generally efficiently absorbed as iodide, although some sources of iodine, such as certain seaweed and protein-bound iodine, may be absorbed less efficiently (14,15). About 90 % of the iodine in a mixed diet, providing about 200 µg/d, is excreted in the urine (14). Iodine absorption and utilisation may be affected by goitrogens, mainly sulphur-containing glucosides (glucosinolates). These are dietary constituents that may inhibit the uptake of iodine into the thyroid gland, e.g. thiocyanates, or interact with hormone production (goitrins) (15). They occur in e.g. Brassica species such as cabbage, Brussels sprouts, turnip, and rapeseeds. Generally the levels of glucosinolates in the current Nordic diet are too low to have an impact on iodine status. Iodide is mainly excreted through the kidneys (iodine clearance approximately 40 mL/min). Faecal losses vary, but are in general only 10-20 µg/d. Small amounts are lost through the skin.

The iodine concentration in breast milk varies with the iodine intake (16). Reported levels in breast milk from Danish mothers, before the introduction of salt iodination, were about 30 µg/L (17). No data is available on iodine content of breast milk from Danish mothers after the introduction of iodised salt. Older data from Finland reported average levels of 25 µg/L in breast milk from goitrous areas compared to 53 µg/L in non-goitrous areas (16). In Sweden, breast milk samples have been reported to contain 50-90 µg/L (16). Smoking is associated with lower iodine concentrations in breast milk, possibly due to impaired iodine uptake in the mammary gland (18).

The recommended indicator for measuring iodine status is the population median urinary iodine concentration (UIC). Other potential indicators of iodine status and thyroid function, such as thyroid volume (TV), thyroid stimulating hormone (TSH), T3, T4 and serum thyroglobulin concentration have also been used (19-21). Iodine intake is regarded as adequate when the median UIC is 100-199 µg/L in the population studied (19). Population iodine sufficiency during pregnancy is defined by median urinary iodine concentrations of 150 -249 µg/L (21).

Iodine deficiency primarily occurs as non-toxic goitre, i.e. an enlarged thyroid gland with a normal production of thyroid hormones. A non-toxic goitre can gradually develop to a toxic goitre with an increased secretion of hormones and an increased metabolism.

(thyrotoxicosis). In hyperthyroidism the thyroid gland can be enlarged (toxic goitre) either in a diffuse form (Basedow's or Graves' disease) or with focal changes (nodular goitre). In more severe iodine deficiency cretinism can occur, which is characterised by impaired growth, mental disturbances and disturbances in speech and acuity (deaf mutism) as well as hypothyroidism (myxoedema) among adults (2, 19, 22).

Overall, the current iodine status in the Nordic countries is not well documented. However, according to WHO data, based on UIC, the iodine nutrition status in Denmark, Iceland, Finland and Sweden is sufficient and deficient in Norway (23). The prevalence of goitre due to iodine deficiency is generally low in the Nordic countries.

Requirement and recommended intake

Adults and children

The recommendations in NNR 2004 (20) for adults and children are kept unchanged, since there is no new data supporting changes (12). The iodine requirement to prevent goitre (increased thyroid gland size) is estimated to be 50-75 µg/d or approximately 1 µg/kg body weight and day (24,25). The average requirement is estimated to be 100 µg/d for both adult women and men. At this level the iodine concentration in the thyroid gland reaches a plateau. Iodine turnover in euthyroid subjects is at a similar level (26). The recommended intake is set to 150 µg/d for adults and adolescents and includes a safety margin for any goitrogenic substances in foods.

The recommended intakes for infants and children are based on data on goitre prevalence and urinary iodine excretion in European children (27) and extrapolations from adults based on energy and growth requirements.
The lower limit of intake for adults is estimated at 70 µg/d. It is lower for children.

Pregnancy and lactation

In pregnancy and lactation an extra daily supply is needed to cover the needs of the foetus and to provide sufficient iodine in the breast milk.

The WHO/UNICEF/ICCIDD reference value for pregnant and lactating women is 250µg/day (21). In the 4th edition of NNR an extra 25µg/day was recommended during pregnancy (RDI set to175µg/day) and an extra 50µg/day during lactation (RDI set to 200µg/day) to provide sufficient iodine in the breast milk (20). Results from the Norwegian MoBa study (28) suggest that an iodine intake of 175µg/day would result in a median UIC within the optimal range (150-249 µg/day) defined by the World Health Organization (21). The recommendations from NNR 2004 are therefore kept unchanged. However, there is need for more data on the level of iodine intake that ensures maternal and newborn euthyroidism, not least in the Nordic countries (12).

Reasoning behind the recommendation

The recommended daily intake for adults in NNR 2004 was based on data the iodine requirement to prevent goitre (increased thyroid gland size). The recommended intakes for infants and children were based on data on goitre prevalence and urinary iodine excretion in European children (27) and extrapolations from adults based on energy and growth requirements. The recommended daily intake for pregnant and lactating women in 2004 was based on extra daily supply is needed to cover the needs of the foetus and to provide sufficient iodine in the breast milk. Iodine deficiency is known to affect thyroid function of

the mother and the neonate as well as the mental development of the child (21). The reference values are kept unchanged compared to NNR 2004 (20), since there are no new scientific data to justify any major changes (12).

Upper intake levels and toxicity

An iodine intake in excess of 2 mg/d can in rare cases cause sensitivity reactions such as rhinitis, nasal congestion, swollen salivary glands, headache and acne-like skin changes (29).

High iodine intakes can also cause disturbances in the thyroid function. Symptoms include inflammation in the thyroid gland (auto-immune thyroiditis), goitre, and hypo- or hyperthyroidism (29). A high iodine intake from e.g. drugs, certain types of seaweed or supplements in amounts corresponding below 1 mg up to 10 mg iodine per day has resulted in increased incidence of iodine goitre, in certain cases with hyperthyroidism or myxoedema (29-33). Very high iodine excretion (up to 1700 µg per 24 h) has been reported in subjects consuming seaweed preparations (34).

There is a substantial inter-individual variation with respect to the dose of iodine that can cause adverse effects. This complicates the assessment of an upper safe limit of intake. Persons with a normal thyroid function can in general tolerate prolonged consumption of iodine up to 1 mg/d (29). The Scientific Committee for Food has proposed 600 µg/d of iodine as the safe upper level (UL) for adults (35). The UL is based on elevations in TSH levels after iodine intake and an enhanced response in TSH levels to TRH stimulation. The effects are of a biochemical nature and are not associated with any clinical adverse effects. The UL includes an uncertainty factor and is also considered acceptable for pregnant and lactating women. In children UIC $\geq$ 500 µg/L was found to be associated with increasing thyroid volume in 6-12 yr children while UIC 300-500 µg/L was not (36). The authors did however not rule out adverse possible adverse effects of UIC in the range of 300-500 µg/day not detected in the study (36).

References

1. FAO/WHO. Vitamin and Mineral Requirements in Human Nutrition, 2nd ed. Geneva: World Health Organization, 2005. Available from: http://whqlibdoc.who.int/publications/2004/9241546123.pdf

2. WHO (World Health Organizaton). Iodine deficiency in Europe. A continuing public health problem, 2007.

3. Sjöberg K-H. Berikat koksalt som jodkälla (Fortified table salt as iodine source). Vår Föda 1980;32:338-44.

4. Rasmussen LB, Andersen G, Haraldsdóttir J, Kristiansen E, Molsted K, Laurberg P, Overvad K, Perrild, H, Ovesen L. Jod - er der behov for berigelse af kosten? Jodindtagelsen i Danmark og betydningen for forekomsten af struma og

stofskiftesygdomme. Publikation nr. 230. Søborg: Levnedsmiddelstyrelsen, 1995. Iodine. Do we need an enrichment program in Denmark. Int J Food Sci Nutr 1996;47:377-81.

5. Knudsen B, Bülow I, Jørgensen T, Laurberg P, Ovesen L, Perrild H. Goitre prevalence and thyroid abnormalities at ultrasonography: a comparative epidemiological study in two regions with slightly different iodine status. Clin Endocrin 2000; 53: 479-85.

6. Rasmussen LB, Carlé A, Jørgensen T, et al. Iodine intake before and after mandatory iodization in Denmark: results from the Danish Investigation of Iodine Intake and Thyroid Diseases (DanThyr) study. Br J Nutr 2008;100:166-173.

7. Dahl L, Opsahl JA, Meltzer HM, Julshamn K. Iodine concentration in Norwegian milk and dairy products. British Journal of Nutrition 2003;90:679-85.

8. Sjöström G. Jodhalten i svenska vatten. Nord Hyg Tidskr 1956;27:265-82.

9. Rasmussen LB, Ovesen L, Bulow I, Jorgensen T, Knudsen N, Laurberg P, Perrild H. Dietary intake and urinary iodine excretion in a Danish population: effect of geography, supplements and food choice. Br J Nutr 2002;87:61-69.

10. Gunnarsdottir I, Gustavsdottir AG, Steingrimsdottir L, Maage A, Johannesson AJ, Thorsdottir I. Iodine status of pregnant women in a population changing from high to lower fish and milk consumption. Public Health Nutr. 2012 May 21:1-5. [Epub ahead of print]

11. Pedersen JI, Frølich W, Johansson L, Nordgård H, Trygg K. Behovet for tilsetning av næringsstoffer til matvarer i Norge. Scand J Nutr 1995;39:84-87.

12. Gunnarsdottir I, Dahl L.Iodine intake in human nutrition: a systematic literature review. Food Nutr Res. 2012;56. doi: 10.3402/fnr.v56i0.19731. Epub 2012 Oct 9.

13. Stanbury JB. Iodine deficiency and the iodine deficiency disorders. In: Present knowledge in nutrition, 7th ed. Washington, D.C.: ILSI Press: 1996: 378-83.

14. Jahreis G, Hausmann W, Kiessling G, Franke K, Leiterer M. Bioavailability of iodine from normal diets rich in dairy products - results of balance studies in women. Exp Clin Endocrinol Diabetes 2001;109:163-7.

15. Hurrell RF. Bioavailability of iodine. Eur J Clin Nutr 1997; 51(Suppl. 1): S9-S12.

16. Dorea JG. Iodine nutrition and breast feeding. J Trace Elem Med Biol 2002;16:207-20.

17. Nøhr SB, Laurberg P, Børlum K-G, Pedersen KM, Johannesen PL, Damm P, et al. Iodine status in neonates in Denmark: regional variations and dependency on maternal iodine supplementation. Acta Pædiatr 1994;83:578-82.

18. Laurberg P, Nohr SB, Pedersen KM, Fuglsang E. Iodine nutrition in breast-fed infants is impaired by maternal smoking. J Clin Endocrinol Metab. 2004;89:181-7.

19. WHO/UNICEF/ICCIDD. Assessment of the iodine deficiency disorders and monitoring their elimination. A Guide for Program Managers. Geneva: World Health Organization WHO, 2008.

20. Nordic Nutrition Recommendations 2004. Integrating nutrition and physical activity. 4th ed. Nordic Council of Ministers. Arhus, Denmark, 2005.

21. WHO/UNICEF. Reaching optimal iodine nutrition in pregnant and lactating women and young children. Joint Statement of the World Health Organization and the United Nations Children's Fund. Geneva, Switzerland: World Health Organization WHO, 2007.

22. Zimmerman MB (2009) Iodine deficiency in pregnancy and the effects of maternal iodine supplementation on the offspring: a review. Am J Clin Nutr 89, 668S–672S.

23. Zimmermann MB, Andersson M. Prevalence of iodine deficiency in Europe in 2010. Ann Endocrinol (Paris) 2011;72:164-6. Epub 2011 Apr 20.

24. National Research Council. Recommended dietary allowances. 10th ed. Washington D.C.: National Academy Press, 1989.

25. Commission of the European Communities. Reports of the Scientific Committee for Food: Nutrient and energy intakes for the European Community (Thirty-first series of Food Science and Techniques). Luxembourg: Office for Official Publications of the European Communities, 1993.

26. Food and Nutrition Board. Dietary reference intakes for vitamin A, vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zink. Institute of Medicine, National Academic Press, Washington:2000

27. Delange F, Benker G, Caron P, Eber O, Ott W, Peter F, Podoba J, Simescu M, Szybinsky Z, Vertongen F, Vitti P, Wiersinga W, Zamrazil V. Thyroid volume and urinary iodine in European schoolchildren: standardization of values for assessment of iodine deficiency. Eur J Endocrinol 1997;136:180-7.

28. Brantsaeter AL, Haugen M, Hagve TA, Aksnes L, Rasmussen SE, Julshamn K, et al. Self-reported dietary supplement use is confirmed by biological markers in the Norwegian Mother and Child Cohort Study (MoBa) Ann Nutr Metab. 2007;51:146–54.

29. Alexander J, Borch-Iohnsen B, Frey H, Kumpulainen J, Meltzer HM, Grawé KP, et al. Risk Evaluation of Essential Trace Elements - essential versus toxic levels of intake. Oskarsson A. editor. København: Nordic Council of Ministers Nord 1995:18.

30. Coakley JC, Francis I, Gold H, Mathur K, Conelly JF. Transient primary hypothyroidism in the newborn: Experience of the Victorian Neonatal Thyroid Screening Programme. Aust Pediatr J 1989;25:25-30.

31. Lamberg BA. Jodin terveydellinen merkitys (Betydelsen av jod för hälsan). Kivennäis- ja hivenaineet. Valtion Neuvottelukunnan Julkaisuja N:o 3:43-50, Helsinki 1975.

32. Skare S, Frey HMM. Iodine induced thyrotoxicosis in apparently normal thyroid glands. Acta Endocrinol 1980;94:332-6.

33. Jørgensen H, Svinland O. Hyper- og hypotyreose etter bruk av jodholdige ”naturprodukter” og jodholdige vitamin- og mineraltilskudd (Hyper- and hypothyreosis after use of iodine containing ”health products” and iodine containing vitamin and mineral supplements). Tidsskr Nor Lægeforen 1991;111:3153-5.

34. Rauma A-L, Törmöla M-L, Nenonen M, Hänninen O. Iodine status in vegans consuming a living food diet. Nutr Res 1994; 14: 1789-95.

35. Scientific Committee on Food. Opinion of the Scientific Committee on Food on the tolerable upper intake level of iodine (expressed on 26 September 2002). SCF/CS/NUT/UPPLEV/26 Final. 7 October 2002. European Commission. Health and Consumer Protection Directorate General.

36. Zimmermann MB, Ito Y, Hess SY, Fujieda K, Molinari L. High thyroid volume in children with excess dietary iodine intakes. Am J Clin Nutr 2005;81:840-844.