European Journal of Clinical Nutrition (1997) 51, Suppl. 1, S9–S12

Bioavailability of iodine

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Descriptors: iodine, bioavailability, absorption methods, goitrogens

Physiology and relevance

The healthy human body contains 15–20 mg iodine of which about 70–80% is in the thyroid gland most concentrated in the iodinated glycoprotein, thyroglobulin (Hetzel, 1993). The only known role of iodine is for the synthesis of the thyroid hormones, thyroxine or tetraiodothyronine (T4) and tri-iodothyronine (T3), which help regulate a wide range of physiological processes including metabolic rate, calorigenesis, thermoregulation, growth and development of most organs, and protein synthesis. Iodine occurs in foods mainly as inorganic iodide, which is readily and almost completely absorbed from the gastrointestinal tract (Keating and Albert, 1949). Other food components do not appear to influence inorganic iodide absorption as they do with iron and zinc. Iodate and protein-bound iodine in animal foods are reduced to iodide for absorption. Only about half of the ingested protein-bound iodine is absorbed (Keating and Albert, 1949). Iodide is transported in the body bound to plasma proteins, the necessary amount is removed by the thyroid for hormonal synthesis, and the remainder is excreted by the kidney. Faecal excretion consists mainly of endogenous organic iodine (van Middlesworth, 1960). At normal intakes, urinary iodine is 85–90% of daily intake and is a good indicator of iodine intake and status (Lamberg, 1993). There is no general homoeostatic mechanism to conserve iodine by increasing absorption or reducing excretion.

A very active iodide trapping mechanism transports plasma iodide into the thyroid against a high gradient. The iodide is first oxidised to iodine and then incorporated into the tyrosine residues of thyroglobulin. These tyrosine residues then undergo covalent crosslinking to form iodinated tyrosine dimers (Brody, 1994). Both reactions are catalysed by thyroperoxidase, a haem protein. Iodinated thyroglobulin then enters the thyroid cells by pinocytosis and the iodinated tyrosine dimers are released by proteolysis mainly as T4 which enters the blood stream by simple diffusion. Most of the T3 in the blood stream results from the deiodination of T4 in the liver and kidney under the action of the selenium dependent enzyme 5-deiodinase. In the plasma, the hormones are mostly bound to albumin and globulin proteins. The thyroid secretion is under the control of the pituitary gland through the thyroid stimulating hormone (TSH). When plasma T4 falls, TSH secretion is increased and thyroid activity including iodide uptake increases.

To ensure an adequate supply of thyroid hormones, the thyroid must trap about 60 μg iodine per day (Underwood, 1977) and to provide a margin of safety, a daily allowance of 150 μg is recommended for adolescents and adults (National Research Council, 1989). Dietary iodine deficiency results in decreased plasma levels of T4 and T3 and a compensatory increase in TSH secretion. In an attempt to increase iodine uptake with limited intake, TSH increases thyroid cell size and cell number and the gland enlarges to form a goitre. When this reaches a prevalence of 10% it is called endemic goitre. Women and adolescent girls seem especially affected. Apart from goitre, there are other effects on growth and development, particularly of the brain, and these are classed together as iodine deficiency disorders (IDD) which can be classified by the different effects on the fetus, neonates, children and adults (Hetzel *et al*, 1990). Iodine deficiency of the fetus is the most serious and leads to a greater incidence of stillbirths, spontaneous abortions, congenital abnormalities and cretinism. Endemic cretinism, primarily due to a failure of brain development, occurs when iodine intake falls below 25 μg/d and affects up to 10% of populations in severely iodine deficient areas of India (Kochchupillai and Pandav, 1987), Indonesia (Djokomoeljanto *et al*, 1983) and China (Ma *et al*, 1982). The most common form, neurological cretinism, is characterized by mental deficiency, deaf mutism and spastic deplegia, in contrast to the less common hypothyroid type characterised by thyroid failure and dwarfism. The neurological effects are not reversed by administration of iodine or thyroid hormones. In the neonate, iodine deficiency leads to increased perinatal and infant mortality (Thilly, 1981), whereas in adults and children it is normally associated with goitre, reaching a maximum in adolescence, but it also leads to hypothyroidism with a lower metabolic rate and impaired mental function. Children living in iodine deficient areas also have impaired psychomotor development, school performance and lower IQs (Vermiglio *et al*, 1990, Bleichrodt *et al*, 1987). According to recent estimations, 200 million people in the world have goitre and almost six million suffer from the mental and neurological effects of cretinism (World Health Organization, 1990). Endemic goitre affects all parts of the world. In large areas of South America (Ecuador, Peru, Bolivia), Africa (Zaire, Cameroon, Burundi) and Asia (India, Nepal) there is a high prevalence of goitre and cretinism (Lamberg, 1993). IDD was also common in Europe prior to the 20th century, but with more varied diets and salt fortification it has been brought under control in most countries, except Bulgaria, Germany, Greece, Italy, Poland, Roumania, Spain and Turkey, where it can still be classed as moderate to severe (Delange *et al*, 1993) with cretinism still present in mountainous areas of Spain and Sicily (Lamberg, 1993). The eradication of IDD world wide is a major priority for international health and nutrition (Hetzel 1993; Delange *et al*, 1993).

Factors controlling bioavailability

Bioavailable iodine is that which is absorbed from the food and utilized to produce thyroid hormones. As virtually all inorganic iodide is absorbed, and as under normal intakes 85–90% of that absorbed is excreted directly in the urine (Lamberg, 1993), inorganic iodide bioavailability should be around 10–15%. With a 100 μg iodide dose, about 20% is taken up by the thyroid (Keating and Albert, 1949). The major factor controlling the amount of bioavailable iodine in the diet is iodine intake itself, which depends on the level in the soil, access to seafoods, and access to fortified foods such as salt. Food components do not appear to greatly influence iodine absorption but can reduce its utilization for the production of thyroid hormones, Such components are termed goitrogens and are considered to be important only when iodine intake is low (Hetzel, 1993). In addition, other nutrient deficiencies can influence thyroid hormone production. Selenium deficiency, for instance, prevents the conversion of T4 to T3 in the liver (Arthur *et al*, 1993).

Iodine intake

Most of the iodine on earth now resides in the sea as it has been leached from surface soil by glaciation, snow and rain. The mountainous areas of the world, such as the Himalayas, Andes and Alpes, are most deficient in iodine. Foods grown in these areas are low in iodine, as is the water, and iodine intake is insufficient. Iodine intake can be increased by food fortification and the favoured method is iodinization of salt with sodium iodide. In this form the absorption of iodide is almost complete (Delange and Burgi, 1989; Nath *et al*, 1992) and many successful salt fortification programmes which correct IDD have been reported (Dunn *et al*, 1986).

Goitrogens

Potentially goitrogenic substances or their precursors are widespread in our food supply especially in plants of the Brassica species such as cabbage, Brussels sprouts and turnip, but also in staple food such as cassava and millet. Grazing livestock can transfer goitrogens to milk (Wright, 1958). Consumption of Brassica goitrogens by man, however, is considered insufficient to be an important factor in the aetiology of goitre (Clements, 1960). A great many compounds have been studied for their goitrogenic effect in thyroid slices, in animals, and in man so as to identify goitrogens, to determine their relative potency, and to define their mechanism of action (for reviews see Clements, 1960; Greer, 1962; Langer and Greer, 1977; Gaitan, 1990). The major goitrogens in plant foods are sulphur-containing glucosides (glucosinolates) (Fenwick and Heaney, 1983). There are two major types: those that yield thiocyanates which block the transport of iodine into the thyroid gland, and those that yield oxazolidine-2-thiones, which inhibit the iodinization of thyroglobulin and the coupling of the iodotyrosine residues.

Thyocyanates occur as glycosides in radish, cabba cauliflower and other vegetables of the Brassica fam Isocyanates, such as mustard oil, and cyanogenic gly sides, such as linamarin in cassava, can be metabolize thyocyanate after ingestion. The thyocyanate ion ha molecular volume and charge similar to that of iod and competes with iodide for uptake into the thyr Cassava consumption has been linked to the aetiology goitre in Zaire (Thilly *et al*, 1993). Many glucosinolate plants are metabolized to oxazolidine-2-thiones (Fenw and Heaney, 1983). The most studied is goitrin (5-vinyl thio-oxazolindine) which was first isolated from yell turnip by Astwood *et al*, (1949) and which inhibits activity of thyroperoxidase in the oxidation of iodine a the formation to tyrosine dimers. Its activity is o partially overcome by extra iodine. It also occurs in seeds of various Brassica and goitrin in milk has be linked to goitre observed in Finland (Gaitan, 1990).

Other less well-established goitrogens include pheno compounds and substances in groundnuts and soybea Phenolic compounds present in millet (Gaitan *et al*, 198 or as pollutants such as resorcinol in drinking wa (Gaitan, 1990), are reported to inhibit thyroperoxida Goitre has been reported in babies fed soy baby foo (van Wyk *et al*, 1959) and a peptide has been isolated fr soy flour which inhibitis both iodine uptake and iodiniz tion of thyroglobulin in the rat (Konijn *et al*, 1973). addition, soy also seems to increase endogenous faec losses of organic iodine (van Middlesworth, 1960).

Iodine bioavailability from foods

There are virtually no data on the bioavailability of iodi from foods since the early human balance studies of v Fellenberg (1926) which demonstrated high iodine absor tion from most foods (ca. 90%) except water cress. T iodine absorption from water cress was subsequent reported to be 100% using plants intrinsically labell with radioiodine (Mailer *et al*, 1964). Although ear human studies using radioiodine showed that inorgan iodide was almost completely absorbed in test subject absorption of protein-bound iodide was less good (Keatin and Albert, 1949). Absorption was 41% from casein, 69 from thyroxine and 89% from thyroglobulin. A more rece study also indicates that food iodide may not always b completely absorbed. Katamine *et al* (1987) showed th whereas 100% of the 1000–5000 μg iodine dose fed to me as eggs or a seaweed (kombu) was excreted in the urin within 48 h, only 10% of the iodine ingested in anothe seaweed (hijiki) and 1% from the food colour erythrosin was recovered. These values were supported by rat balanc studies. As prolonged cooking of hijiki increased th urinary iodine excretion in men to 53% of dose, poo release of iodine from the plant structure during digestio was proposed as the factor inhibiting absorption.

Nutrient interactions

Other micronutrients are necessary for the utilization o iodine for thyroid hormone synthesis, and deficiencies i these micronutrients could decrease iodine bioavailability Selenium is part of the deiodidase enzyme which convert T4 to T3 in the liver and selenium deficiency increase thyroid size in iodine deficient animals (Beckett *et al*, 1993). Vitamin A affects thyroid hormones at several levels (Inglebleck and Visscher, 1979; Higueret *et al*, 1989) and thyroperoxidase is a haem enzyme requiring iron. In iron deficiency, thyroid metabolism is impaired with an inability to control body temperature (Beard *et al*, 1990). Widespread iron and vitamin A deficiencies occur in developing countries, and often in iodine deficient regions.

Critical assessment of methodology

As with other nutrients, balance techniques are imprecise. With iodine, they are further complicated because of analytical difficulties in measuring the trace quantities in the diet and by possible contamination with atmospheric iodine (Dworkin and Simeck, 1965). The relative potency, and the mechanism of action, of various goitrogens have been usefully evaluated using in vitro enzymic assays, by animal tests and in man, often using radioiodine techniques. It is clear that the magnitude of response to a particular goitrogen in the rat may be very different to the response in man (Clements, 1960). The ideal method to measure iodine bioavailability in man would be to use radioiodine and to quantify urinary and faecal excretion as well as thyroid uptake. In this way absorption as well as utilization could be quantified. Iodine has only one stable isotope and stable isotope tracer studies are therefore not possible. Although there is some radioiodine data in man on the effect of extracted plant substances on the utilization of iodine by the thyroid, there have been no systematic studies measuring iodine bioavailability from different plant and animal tissues. Urinary excretion in human subjects consuming a relatively high dose of food iodine was used by Katamine *et al* (1987) to measure iodine bioavailability. This method could give a useful indication of iodine absorption if the food were assumed to have no effect on the thyroid utilization of iodine or, if absorption was assumed to be 100%, it would indicate the potential goitrogenic effect.

Conclusions/Recommendations

Iodine bioavailability from foods would appear to be relatively high and deficiency results mainly from low intake. From a public health viewpoint, therefore, the best way to prevent iodine deficiency is to increase iodine intake by fortifying food such as salt with inorganic iodide which is almost completely absorbed. Such strategies have successfully reduced the incidence of IDD. Although much useful data exists on the goitrogenic effect of various substances extracted from plant foods, and their influence on iodine utilization by the thyroid, these studies have usually been made from a pharmaceutical perspective, and their influence in diets is assumed to be important only at marginal iodine intake. Studies on the bioavailability of iodine in man from plant foods and animal tissues do not exist and are now needed together with a quantification of the effect of foods containing known goitrogens (for example cassava, millet and various Brassica vegetables) on iodine utilization. Based on early data, the bioavailability of iodine from protein-bound iodine in animal tissues may be as low as 50%. The radioiodine technique with an extrinsic tag or with intrinsically labelled foods would seem ideal for this purpose. It is also necessary to further investigate the influence of other micronutrients on iodine utilization. The influence of selenium deficiency on thyroid hormone synthesis has been recently reported but vitamin A, and especially iron, are also important for thyroid function and are widely deficient in many of the same developing countries that have low iodine intakes.

References

Arthur JR, Nicol F, Beckett GJ (1993). Selenium deficiency, thyroid hormone metabolism and thyroid hormone deiodinases. *Am J Clin Nutr*. **57**(Suppl): 236S–239S.

Astwood EB, Greet MA, Ettlinger MG (1949). L-5-vinyl-2-thio-oxazolidone, an antithyroid compound from yellow turnip and from Brassica seeds.. *J Biol Chem*. **181**: 121–130.

Beard JL, Borel MJ, Derr J (1990) Impaired thermoregulation and thyroid function in iron-deficiency anemia. *Am J Clin Nutr*. **52**: 813–819.

Beckett GJ *et al* (1993). Effects of combined iodine and selenium deficiency on thyroid hormone metabolism in rats.. *Am J Clin Nutr*. **57**(Suppl): 240S–243S.

Bleichrodt N *et al*. (1987): Development disorders associated with severe iodine deficiency. In: Hetzel BS, Dunn JT, Stanbury JB (eds). *The Prevention and Control of Iodine Deficiency Disorders*. Elsevier, Amsterdam, pp 65–84.

Brody T (1994): *Nutritional Biochemistry*. Academic Press, San Diego/New York, pp 519–527.

Clements FW (1960). Naturally occurring goitrogens. *BR Med Bull*. **16**: 133–137.

Delange F, Dunn JT, Glinoer D (1993): General comments conclusions, and final recommendations. In: Delange F, Dunn JT, Glinoer D (eds). *Iodine Deficiency in Europe A Continuing Concern*. Plenum Press, New York/London, pp 473–478.

Delange F, Burgi H. (1989). Iodine deficiency disorders in Europe. *Bull. WHO*. **67**: 317–325.

Djokomoeljanfo R, Tarwotjo I, Maspaitella F (1983): Goitre control programme in Indonesia. In: Uri N, Torizuka K, Nagataki S, Miyai K (eds). *Current Problems in Thyroid Research*. Excerpta Medica, Amsterdam, pp 394–397.

Dunn JT, Pretell EA, Daza CH, Viteri, FE (1986). Towards the eradication of endemic goitre, cretinism and iodine deficiency. Scientific Publication No 502, PAHO, Washington.

Dworkin HJ, Simeck CM (1965). Efficiency of molecular iodine removal from air. *J Clin Endocr*. **25**: 1505–1510.

Fenwick GR, Heaney RK (1983). Glucosinolates and their breakdown products in cruciferous crops, food and feedingstuffs. *Food Chem*. **11**: 249–271.

Gaitan E *et al* (1989). Antithyroid and goitrogenic effects of millet: Role of C-Glycosylflavones. *J Clin Endocrinol Metab*. **68**(4): 707–714.

Gaitan E (1990). Goitrogens in food and water. *Annu Rev Nutr*. **10**: 21–39.

Greer MA (1962). The natural occurrence of goitrogenic agents. *Recent Prog Horm Res*. **18**: 187–219.

Hetzel BS, Potter BJ, Dulberg EM. (1990): The iodine deficiency disorders: nature, pathogenesis and epidemiology. In: Bourne GH (ed). *World Review of Nutrition and Dietetics* vol 62: S Karger, Basel, pp 59–119.

Hetzel BS (1993): Iodine-deficiency disorders. In: Garrow JS, James WPT (eds). *Human Nutrition and Dietetics*. Churchill Livingstone, Edinburgh, pp 534–555.

Higueret P, Pailler I, Garcin H (1989). Vitamin A deficiency and triidothyronine action at the cellular level in the rat. *J Endocrinol*. **121**: 75–79.

Ingenbleek Y, De Visscher M (1979). Hormonal and nutritional status: Critical conditions for endemic goitre epidemiology? *Metabolism*. **28**: 9–19.

Katamine *et al* (1987). Differences in bioavailability of iodine mong iodine-rich foods and food colors. *Nutr Rep Int*. **35**: 289–297.

Keating FR Jr, Albert A (1949). The metabolism of iodine in man as disclosed with the use of radioiodine. *Recent Prog Horm Res*. **4**: 429–481.

Kochupillai N, Pandav CS (1987): Neonatal chemical hypothyrodiism in iodine deficient environments. In: Hetzel BS, Dunn JT, Stanbury BJ (eds). *The Prevention and Control of Iodine Deficiency Disorders*. Elsevier, Amsterdam, pp 85–93.

Konijn AM, Gershon B, Guggenheim K (1973) Further purification and mode of action of goitrogenic material from soybean flour. *J Nutr*. **103**: 378–383.

Lamberg BA (1993) Iodine deficiency disorders and endemic goitre. *Eur J Clin Nutr*. **47**: 1–8.

Langer P, Greer MA (1977): *Antithyroid Substances and Naturally Occurring Goitrogens*. S Karger, Basel.

Ma T *et al* (1982). The present status of endemic goitre and endemic cretinism in China. *Food Nutr Bull*. **4**: 13–19.

Mailer CM, Harrison MT, Wayne EJ (1964). Absorption of iodine from ingested watercress. *Nature*. **201**: 403–404.

Nath SK *et al* (1992). Urinary excretion of iodide and fluoride from supplemented food grade salt. *Internt J Vit Nutr Res*. **62**: 66–72.

National Research Council (1989): Recommended Dietary Allowances, 10th edn, National Academy Press, Washington, DC.

Thilly CH (1981). Goitre et crétinisme endémiques: role étiologique de la consommation de manioc et stratégie d'éradication. *Bull Belgian Acad Med*. **136**: 389–412.

Thilly CH *et al* (1993). The epidemiology of iodine-deficiency disorders in relation to goitrogenic factors and thyroid-stimulating-hormone regulation. *Am J Clin Nutr*. **57**(Suppl): 267S–275S.

Underwood EJ (1977): Iodine. In: *Trace Elements in Human and Animal Nutrition*, 4th edn. Academic Press, New York, pp 271–331.

van Middlesworth L (1960). Re-evaluation of certain aspects of iodine metabolism. *Recent Prog Horm Res*. **16**: 405–438.

van Wyk JJ, Arnold MB, Wynn J, Pepper F (1959). Effects of soy- product on thyroid function in humans. *Pediatrics*. **24**: 752–760.

Vermiglio F *et al* (1990). Defective neuromotor and cognitive abili iodine-deficient schoolchildren of an endemic goitre region in Sici *Clin Endocrinol Metab*. **70**: 379–384.

von Fellenberg T (1926). Das Vorkommen, der Kreislauf und der S wechsel des Jods. *Ergebn Physiol*. **25**: 176–363.

WHO (1990): Report to the 43rd World Health Assembly, Geneva.

Wright E (1958). Giotrogens of milk produced on kale. *Nature*. **181**: 1 1603.