

# International Iodine Deficiency

By L. Preston Mercer

Professor of Biochemistry, University of South Florida

## Abstract

Iodine is an essential trace element. However, thirty-five percent of the world's population is estimated to live in areas of iodine deficiency. Iodine's only known function is in the synthesis of thyroid hormones, so severe dietary deficiency results in impaired thyroid hormone synthesis and/or thyroid enlargement (goiter). Population effects of severe iodine deficiency, termed iodine deficiency disorders (IDD's), include endemic goiter, hypothyroidism, cretinism, decreased fertility rate, increased infant mortality, and mental retardation. Iodine deficiency is the most common preventable cause of mental retardation in the world. Deficiency occurs primarily in mountainous regions such as the Himalayas, the European Alps, and the Andes, where iodine has been washed away by glaciations and flooding. Iodine deficiency also occurs in lowland regions far from the oceans, such as central Africa and Eastern Europe. Those who consume only locally produced foods in these areas are at risk for IDD. Internationally, nearly 2 billion people worldwide, living in 53 countries, are at risk for IDD - of these, 655 million are known to have goiter and 11.2 million cretinism. Universal salt iodization provides the most effective and affordable means to prevent IDD throughout the world – but this effort requires coordination of political, legislative, public health management and educational agencies for maximum effect.

## Introduction

Iodine ( $I_2$ ), an essential nutrient, is a nonmetallic element belonging to the halogen family, converted to iodide in the gut, efficiently absorbed in the digestive tract and carried into circulation by serum proteins. Most iodide is actively trapped by the thyroid and is present in the human body in minute amounts (15-20 mg in adults). The only confirmed function of iodine is as an essential substrate for the synthesis of thyroid hormones, tetraiodothyronine (thyroxin or  $T_4$ ) and triiodothyronine ( $T_3$ ) (Hetzl, 1989). In target tissues, such as the liver and the brain,  $T_3$ , the physiologically active thyroid hormone, can bind to thyroid receptors in the nuclei of cells and regulate gene expression.  $T_4$ , the most abundant circulating thyroid hormone, can be converted to  $T_3$  by enzymes known as deiodinases in target tissues. In this manner, thyroid hormones regulate a number of physiologic processes, including growth, development, metabolism, and reproductive function

The recommended intake of iodine is 150  $\mu\text{g}$  per day and the thyroid has to trap about 60  $\mu\text{g}$  per day to maintain an adequate pool (Fisher, 1985). The excretion of ingested dietary iodine in the feces has been reported to be 30% (Follis, 1964) and is dependent on the type of

food eaten. 150 µg per day is sufficient to prevent clinical manifestation of iodine deficiency disorders for at least several months even if iodine would become absent from the diet (Table 1) (Dunn, 1993, Stanbury, 1998). Goiter becomes almost universal in a population with an iodine intake less than 10 µg per day (Fisher, 1985). Collectively, health problems arising from a lack of iodine are known as iodine deficiency disorders (IDD's).

Thyroglobulin is a protein found in the colloid of follicular cells that binds the thyroid hormones. Thyroglobulin functions as an iodine store and in healthy adults [8-15 mg] is 160-300 times the minimum daily requirement to maintain an euthyroid state (Dunn, 1993, Stanbury, 1998).

A fall in the level of T<sub>4</sub> increases thyroid stimulating hormone (TSH) output from the pituitary, enhancing uptake of iodide, and increased turnover associated with hyperplasia of the cells of the thyroid follicles. The reserves of colloid containing thyroglobulin are gradually used up so that the gland has a much more cellular appearance than normal. The size of the gland increases with the formation of a goiter - enlargement is regarded as significant in the human when the size of the lateral lobes is greater than the terminal phalanx of the thumb of the person examined (Table 2). Measurements that are more precise can now be made using ultrasound (Fisher, 1985).

Endemic goiter is caused by iodine deficiency as well as other multiple factors resulting in variations in the prevalence observed between areas, where iodine intake is scarcely below normal. From a public health point of view, it has been suggested that endemic goiter can be defined as a prevalence of goiter of at least grade 1B of 5% or more in pre-and adolescent individuals or of 30% or more of grade 1A among adults (Ulhaq, 1996). At this level, public health intervention seems to be called for (Table 3).

**Deficiencies:** Iodine deficiency impairs growth and neurological development, which can damage the brain. Thyroid hormones play an important role in cellular metabolism and early growth and development of most organs, especially of the brain (Koutras, 1989, Taurog, 1991). The effects of iodine deficiency include goiter, stillbirth and miscarriage, neonatal and juvenile thyroid deficiency, dwarfism, mental defects, deaf mutism, spastic weakness, impaired movement and paralysis (Fisher, 1985). Depending on its severity and stage of development at which it occurs, deficiency can produce mild intellectual impairment and/or severe mental retardation. Consequently, a deficit in iodine and/or in thyroid hormones will result not only in the slowing down of metabolic activities but also in irreversible alterations in brain development (Davis, 1991). Cretinism, in which many of these abnormalities occur, represents the extreme of early iodine deficiency. Much more widespread is an intellectual blunting that may afflict as many as 50 million of the estimated 2 billion "at-risk" people living in iodine deficient regions, making iodine deficiency *the most common preventable cause of mental retardation in the world*. Because of decreased production of thyroid hormones, iodine deficiency causes compensatory hypertrophy of the thyroid gland as it attempts to make more thyroid hormone, resulting in a goiter - a disfiguring condition that is common in high risk areas.

**Dietary recommendations:** The physiological requirement of iodine for humans is difficult to assess and has given rise to much controversy. Intake must be at least equal to the amount of hormonal iodine degraded at the level of the tissues and not recovered by the thyroid gland. In adults and adolescents, this amount is 50 to 150  $\mu\text{g}$  iodine/day (Bürigi, 1991). Therefore, the US National Research Council, US Food and Drug Administration (FDA) recommended dietary allowance (RDA) and WHO recommendations are a dietary allowance of iodine of 150  $\mu\text{g}$  for adolescents and adults. The recommendation is 175  $\mu\text{g}/\text{day}$

and 200 µg/day for pregnant and lactating women, respectively; 70-100 µg/day for children aged 1-10 years, 50 µg/day for infants aged 6-12 months and 40 µg/day for infants 6 months of age or younger. Normal dietary iodine intake is 100-150 µg /d. In areas where iodine is not added to the water supply or food products meant for humans or domesticated animals, the primary sources of dietary iodine are saltwater fish, seaweed, and trace amounts in grains.

The figure of 150 µg/day in adults is based on the following assumptions and observations, and in order to provide an extra margin of safety and to meet increased demand that may be imposed by naturally-occurring goitrogens under certain condition. The daily iodine requirement for prevention of iodine deficient goiter in adults is approximately 1 µg/Kg body weight that is 50 to 100 µg/day. The figure of 100 to 150 µg/day in adults corresponds to the daily urinary excretion of iodide and to the iodine content of food in non-endemic areas. The iodine intake needed to prevent the plasma iodide level from falling below the critical limit of 1 µg/L, likely to initiate the onset of goiter, is 120 µg/day.

**Food sources:** Iodine present in the earth has been gradually leached away from the soil surface by glaciations, snow and air and carried out by wind, rivers, and floods into the sea and oceans, where the concentration of iodide in deep sea water is about 50- 60 µg/L (AOAC, 1990). Evaporation from the ocean into the atmosphere occurs, where it is then concentrated in rain and falls back to the earth replenishing the soil. It is estimated that every year about 400 tons of iodine escape from the oceans (High Institute of Public Health, 1993).

Iodine content of food and water depends primarily on the supply of iodine in the soil. Iodine deficiency persists in the soil indefinitely and the iodine content of plants grown in such soils may be as low as 10 µg/kg compared to 1000 µg/kg dry weight in plants in a non-iodine-deficient soil. As a result, human and animal populations, which are totally dependent

on food grown in iodine-replete soil, become iodine deficient. This accounts for severe iodine deficiency in vast populations in Asia living within systems of subsistence agriculture.

Glaciated, mountainous or heavy rainfall areas are likely to be low in iodine placing human and animal populations at risk. Thus, individuals can not usually improve iodine intake by diversifying their diet. Some foods contain goitrogenous substances that interfere with iodine absorption. Many goitrogens are generally members of the brassica family. These include: broccoli, cauliflower, brussel sprouts, cabbage, mustard, kale, turnips, and rape seed (canola oil). Other goitrogens include: soy, pine nuts, millet and peanuts. This is of public health concern only where these foods are regularly consumed in large amounts and dietary iodine is low.

**Prevention of IDD:** Several vehicles have been used for fortification with iodine including salt, bread, candy, milk, sugar, and water. Sources of salt are limited and are frequently the only commodity for which a community is not self-sufficient, thereby offering an excellent opportunity for intervention. Finally, the iodination technology is straightforward and can be adapted to many local conditions, at a low cost. Universal salt iodization provides the most effective and affordable means to prevent IDD throughout the world; as of 2002, approximately two out of three households, or 66% in the developing world now consume adequately iodized salt, a significant improvement upon the 1990 estimate of less than one in five.

For example, since there is little naturel iodine in the soil and water in inland areas, the Midwest US was once known as the "Goiter Belt." In 1921, for example, almost half the schoolchildren in Michigan had signs of goiter (surveyed 66,000 students). However, in 1924 Michigan began supplementing table salt with sodium iodide. Salt was chosen because it is used by almost everyone. And by 1951 only <1% of the state's population had goiter. Today,

many countries require the iodination of salt (it is optional in the United States), and goiter has been all but eradicated in developed countries.

Typically, the iodine concentration is from 30 to 100  $\mu\text{g}$  per g of salt, levels that take into consideration anticipated losses during transport and storage. At salt intakes of 5-20 g per day, this fortification range is sufficient to meet requirements in most countries. Iodization costs between 2-7 US cents per kg of salt. Other iodizable vehicles include water, grain and dairy products. Iodized oil supplements may be periodically administered in remote areas where salt iodization is not feasible, possibly a single oral dose at the time of oral polio vaccine. Damage to the fetus resulting from maternal iodine deficiency is irreversible. Most goiters can be cured or reduced in size with iodine therapy.

**Clinical:** Affected patients come from geographic regions where IDD is endemic. Patients with IDD most commonly present with goiter. Children present with diffuse goiters, while adults present with nodular goiters. If a goiter is large enough, patients may complain of compressive symptoms such as hoarseness, shortness of breath, cough, or dysphagia. Individuals with severe iodine deficiency may also have hypothyroidism and may complain of fatigue, weight gain, cold intolerance, dry skin, constipation, or depression. Cretinism is the most extreme manifestation of IDD. Cretinism can be divided into neurologic and myxedematous subtypes. These subtypes have considerable clinical overlap. Both conditions can be prevented by adequate maternal and childhood iodine intake. Neurologic cretinism is thought to be caused by severe IDD with hypothyroidism in the mother during pregnancy and is characterized by mental retardation, abnormal gait, and deaf-mutism but not by goiter or hypothyroidism in the child. Myxedematous cretinism is considered a result of iodine deficiency and hypothyroidism in the fetus during late pregnancy or in the neonatal period, resulting in mental retardation, short stature, goiter, and hypothyroidism.

**Iodine analysis in urine:** Urinary analysis for IDD is a common and acceptable method that reflects dietary iodine intake and median urinary levels tends to be representative of a population's iodine intake. Most methods of urinary analysis involve the spectrophotometric measurement of iodine in the Sandell-Kolthoff reaction (Sullivan, 2000). This method is similar to that proposed by PAMM (Program Against Micronutrient Malnutrition), where both are based on the Sandell-Kolthoff method that utilizes the fact that iodine catalyses the reduction of ceric (IV) ions to cerous (III) ions by arsenic in acidic conditions. The only difference is that the alkaline ashing of samples have been replaced by digestion with ammonium persulfate, which is less explosive and safer to work with, as well as cheaper (Sandell, 1937).

**Correction of an iodine deficiency:** This should be instituted based on the recommendations of the FDA and the WHO. In an adult, 100-150  $\mu\text{g}$  /d is sufficient for normal thyroid function. Routine laboratory tests of thyroid function are not as helpful as the urinary iodine concentration in assessing a population. Long-term dietary iodine replacement at levels recommended by the FDA and WHO may decrease the size of iodine-deficient goiters in very young children and pregnant women and is indicated for all patients with iodine deficiency. Generally, long-standing IDD goiters respond with only small amounts of shrinkage after iodine supplementation. Patients do not routinely require specific therapy unless the goiter is large enough to cause compressive symptoms (eg, tracheal obstruction, thoracic inlet occlusion, hoarseness).

Using highly concentrated pharmaceutical agents such as a saturated solution of potassium iodide (SSKI), ie, 35,000-50,000  $\mu\text{g}$  /drop, is impractical and potentially dangerous. Replacement of iodine is most easily achieved by requesting that the patient use

iodized salt in their cooking and at the table. Other alternative food sources include milk, egg yolks, and saltwater fish.

In developing countries, eradication of iodine deficiency has been accomplished by adding iodine drops to well water or injecting people with iodized oil. Exogenous L-thyroxine (L-T4) can also be used to decrease goiter size but generally is not effective in adults and older children. Supplemental L-T4, when added to the T3 and T4 secretion by the autonomous nodules in the endemic goiter, may cause thyrotoxicosis. Long-term L-T4 therapy that results in the suppression of the TSH level to below-normal levels may have deleterious effects on cardiac and bone health; therefore, L-T4 therapy is no longer routinely administered to patients with goiter.

Radioactive iodine (I-131) has been used, primarily in Europe, to decrease thyroid volume in patients with euthyroid goiters (40-60% volume reduction). In the United States, I-131 is the most common treatment for toxic multinodular goiters associated with hyperthyroidism.

**Iodine analysis in salt:** Recently, the board of the International Council for the Control of Iodine Deficiency Disorders proposed guidelines towards IDD elimination - that all salt for human and animal consumption in all regions where IDD is known or suspected is iodized at the factory. The board stressed that representative salt samples obtained regularly from retail outlets or preferably from homes, have reasonable levels usually 30-100 mg/kg (30-100 ppm) iodine content sufficient to ensure an average daily intake of at least 1.18  $\mu\text{M}$  (150  $\mu\text{g}$ ) of iodine per day. The actual requirement at the household level will vary from 20 to 50 mg/kg (20-50 ppm) depending on the quality of salt (warm moist vs. cool dry) and daily consumption of salt.



The two chemical compounds in general use are potassium iodate ( $\text{KIO}_3$ ) and potassium iodide (KI).  $\text{KIO}_3$  has 59.5% iodine, while KI contains 76.5% iodine. KI is considerably more soluble in water and less expensive than  $\text{KIO}_3$ ; but it is less stable under conditions of moisture, exposure to sunlight or heat, or in the presence of impurities. For these reasons, most countries use  $\text{KIO}_3$  for salt iodination, exception includes the U.S.A, Switzerland, Canada, and Ecuador.  $\text{KIO}_3$  is particularly recommended for countries where the salt is less refined.

In Pakistan, 62% of the iodized salts available to the consumer at retail points were found to contain inadequate supply of iodine (Ulhaq, 1996). Ulhaq et al. emphasized therefore the importance of regular monitoring of the iodine content of salt at the plant, retail and consumer levels. Since 1922 Switzerland in a political compromise iodinated salt at a level of 3.75 mg/kg (3.75 p.p.m) to eliminate IDD. In 1962 and 1980, iodination was raised to 7.5 mg/kg and 15 mg/kg (7.5 and 15 ppm) respectively (Bürigi, 1991). Retrospective analysis of the Swiss data showed that seven years after iodized salt was introduced the number of admission to special schools for deaf (but intellectually normal) children dropped by more than half. Salt iodination programs are therefore successful when iodine intake requirements for the populace are met. This required level results in the absence of any anomalies of the thyroid gland and is sufficient to reverse the effects of low salt iodination and enable recovery from the various types of goiter as observed from this study.

The iodine content of salt can be determined by a standard iodometric titration. The test detects the presence of iodate over the range of recommended levels of iodination (6-130 mg of potassium iodate per kg of salt). Available commercial salt claimed by the manufacturer to be iodized at a level of 50-80 mg/kg (50-80 ppm) potassium iodate has been analyzed in the laboratory for iodine content. High iodine losses from salt, amounting to

50%, have been reported due to excessive or long-term exposure to moisture, light, heat and contaminants (Chopra, 1991). On the average, iodine losses from salt have been reported to amount to 20% from production site to households; with another additional 20% losses taking place during cooking, before consumption. The commercial salt analyzed (Hassanien, 2003)) revealed that only 20 % complied with the manufacturer's label as being iodinated with potassium iodate at levels of 50-80 mg/kg (50-80 ppm). Large individual variability between batches of iodinated commercial salt was found to vary from -95 to + 150% of the claimed iodine level. Salt iodination requires careful supervision to ensure that promised iodine levels are being delivered and consumed.

**Toxicity:** A wide range of iodine intake is tolerated by individuals. For this reason, long term consumption of iodine through iodized salt is considered safe. Chronic, excessive iodine intakes may occasionally lead to goiter and hypothyroidism. A small increase in thyrotoxicosis (<0.1%) may occur from increasing the iodine intake of a population which has had a low intake for many generations.

**Patient Education:** Importantly, the public must understand the importance of using iodized salt, especially in the United States, where iodization of salt is not mandated by law. Several areas of the world, including the United States and the Netherlands, in which iodine deficiency had been eradicated by voluntary methods, have recently shown a significant decrease in iodine intake compared to previous years.

**Saturation kinetics analysis:** Optimal salt iodination can be computed by applying the four-parameter saturation kinetics model (SKM) proposed by Mercer (Mercer, 1980), based on the enzyme kinetics equation of n kinetic order (Michaelis-Menten Equation that describes allosteric enzyme kinetics). This equation describes accurately the response to a

range of nutrient intakes is related to enzyme-related processes. This is consistent with the concept that a nutritional response is composed of a series of enzymatic reactions.

Optimal salt iodination can be computed by applying the SKM according to the following equation:

$$r = \frac{b(K.5)^n + R_{max}I^n}{(K.5)^n + I^n} \quad \text{Equation (1)}$$

Where

$r$  = physiological response

$I$  = dietary concentration or nutrient intake

$R_{max}$  = maximum theoretical response

$K.5$  = concentration or intake for  $1/2 (R_{max} + b)$

$n$  = apparent kinetic order

$b$  = intercept on  $r$  axis

Observed data pairs ( $I, r$ ) are fitted by standard non-linear curve fitting techniques and the four derived parameters are calculated ( $b, n, K.5, R_{max}$ ). These parameters can then be used to generate a theoretical response curve for varying levels of nutrient intake (in this case, iodized salt). Equation 2 is a mathematical derivative of equation 1 and, since equation 1 is continuous in its derivatives, a slope curve can be generated using equation 2.

$$\text{slope} = \frac{nI^{n-1}(R_{\max}-b)(K.5)^n}{[(K.5)^n + I^n]^2} \quad \text{Equation (2)}$$

One can then calculate a point on the nutrient-response curve associated with 95% slope reduction. The slope reduction approach was chosen since a 95% reduction in slope indicates that 95% of the potential of the nutrient for producing the response has been utilized. Mathematical analysis can be carried out using the software program Systat, Version 11 (Systat, Inc, Point Richmond, CA).

**Optimum level of iodine in salt preparation** The application of the saturation kinetic model (SKM) to experimental data is illustrated in Figure (1). Urinary iodine excreted is depicted as a function of the iodine concentrations in the salt used for cooking. The fitted parameters are:  $b = 0.049 \pm 1.28 \mu\text{M/L}$ ;  $R_{\max} = 0.012 \pm 6.02 \mu\text{M/L}$ ;  $K.5 = 19.65 \pm 1.85 \text{ mg/kg}$ ; and  $n = 2.52 \pm 0.44$ . The parameters are interpreted in a manner analogous to enzyme kinetics. The saturation kinetic model indicated that for a maximum physiological response ( $R_{\max}$ ), the iodine intake requirement is 63.32 mg/kg salt iodination, corresponding to  $1.19 \times 10^{-4} \mu\text{M/L}$  of excreted urinary iodine.

Concentrations of iodine in casual urine is now widely accepted as the best and most cost-effective way of monitoring iodine deficiency in a community (Sandell, 1937, Groppel, 1988, WHO, 1996). Subjects with an iodide excretion below a certain cutoff point are considered to be at risk of a marginal iodine supply and therefore of goiter and other iodine deficiency disorders. The SKM parameters  $b$  and  $R_{\max}$  give the range of response, with  $b$  being the intercept on the response axis (response with no supplementation) and  $R_{\max}$  representing the plateau of response (maximum excretion).  $K.5$  is the supplementation level at half-maximal response and  $n$  is the apparent kinetic order.

With these parameters, it is possible to establish any point on the theoretical curve. Since 0.79  $\mu\text{M/L}$  urinary iodine excretions are considered the cutoff for IDD, it is possible to calculate that a salt iodination of 16.9 mg/kg would maintain a urinary iodine excretion of 0.79  $\mu\text{M/L}$ . However, 16.9 mg/kg falls below K.5, indicating a greater physiological capacity for iodine excretion, which is known empirically to be true.

Determining a requirement is arbitrary when confronted with a nutrient, which produces a plateau of biological response ( $R_{\text{max}}$ ) as shown in Figure 1. Standard break-point analysis puts the requirement too low. Another approach is to look at slope of response (Figure 1). Slope (response/intake) peaks at about 14 mg/kg salt iodination level. This is obviously too low for a supplementation level but represents the organisms' point of greatest response to the nutrient. In the past the point of 95% slope reduction has been selected; i.e., the intake level where the slope has been reduced by 95% and the capacity of the organism to respond been used within 5% of maximum. For urinary iodine excretion, this point is 63.32 mg/kg salt iodination, producing  $1.19 \times 10^{-4}$   $\mu\text{M/L}$  urinary iodine. To achieve 99% capacity would require over 102 mg/kg salt iodination, producing only  $1.22 \times 10^{-4}$   $\mu\text{M/L}$  urinary iodine, indicating the law of diminishing returns in physiological responses – a very small incremental response for a very large increase in iodination. Thus, the modeling approach allows one to choose a desired response level and correlate an intervention program with other pertinent data. This requirement level of 63.32 mg/kg determined for the specific  $R_{\text{max}}$  for this group of subjects may be specific to the population studied, the adaptation to the deficiency and/or the length of the experiment, but should however be close in approximation to that for other groups. Variability might also be due to factors such as age, gender and physical state, and determinants of body composition that might affect iodine requirement (1).

The four-parameter saturation kinetics model has several advantages: (a) being extremely robust (b) analyzing all data points even if it is hyperbolic in nature (c) makes no assumption that urinary iodine excretion by humans is constant and (d) facilitates the actual calculation of parameters from the data observed and the determination of required levels of nutrient intake to prevent deficiency. This contrasts with the model proposed by Furnee (1995) in which different oral preparations of iodized oil was administered to severely deficient school children and the urinary iodine excretion measured. Furnee's model assumed that iodine excretion by the body was constant and parameters were estimated after log-linear transformation of the data. The four-parameter model is more applicable than that proposed by Furnee, despite the fact that the study designs were different in both instances. Combining the four-parameter model with studies of salt iodination is important as policy interventions can be implemented if necessary to address any deficiencies in the main source of iodine within a population. The use of the four-parameter saturation kinetics model facilitates the accuracy of determining the appropriate intake levels for iodine required to ensure the production of the maximum physiological response.

Iodine excretion parameters, determined by the application of the saturation kinetics model, can be conveniently used to characterize iodine utilization and determine a reasonable, achievable level of iodination with predictable results (Mercer, 1989). Based on analysis using the saturation kinetics model, a salt iodination level of 63 mg/kg produces a urinary excretion of  $1.19 \times 10^{-4}$   $\mu\text{M/L}$ . This gives a convenient mechanism for providing adequate dietary iodine with a non-invasive index. There is an obvious need to maintain appropriate quality control in the production commercial iodized salt to ensure that required iodination levels are met as indicated by the data. Salt iodination is therefore an effective vehicle of delivery and can ensure that intake.

**E-resources for relevant agencies:**

<http://www.who.int/bulletin/releases/2002/05/en/>

<http://indorgs.virginia.edu/iccidd/aboutidd.htm>

<http://www.sph.emory.edu/PAMM/iodine.htm>

<http://www.iodinenetwork.net/>

<http://www.fao.org/>

[http://www.micronutrient.org/Salt\\_CD/4.0\\_useful/4.3\\_keybio/index.html](http://www.micronutrient.org/Salt_CD/4.0_useful/4.3_keybio/index.html)

<http://www.unsystem.org/scn/archives/rwns04/ch19.htm>

<http://kif.kiwanis.org/kif/grants/wsp.asp>

## References

- AOAC, Official Methods of Analysis 15, (1990) Washington D.C. , pp. 334, 335 and 870.
- Bürgi, H., Klinik, M., (1991) How Switzerland eliminated IDD with Iodized salt, IDD Newsletter 7 1-15.
- Chopra, I.J. (1991), Nature, Sources, and relative biological significance of circulating thyroid hormones, in: L.E. Braverman, R.D. Utiger (Eds.), A Fundamental and Clinical Text JB Lippincott Publishing, Philadelphia, PA, pp. 190-203.
- Davis, P.J, (1991) Cellular action of thyroid hormones, in: L.E. Braverman, R.D. Utiger (Eds.), The Thyroid: A Fundamental and Clinical Text, JB Lippincott Publishing, Philadelphia, PA, pp.190-203.
- Dunn, J.T., Crutchfield, H.E., Gutekunst, R., Dunn, A.D. (1993) Two simple methods for measuring iodine in urine, Thyroid 3 119-123.
- Fisher, D.A. (1985) Thyroid hormone effects on growth and development, in: Delange, Fisher, Malvaux (Eds.), Pediatrics Thyroidology, Basel S. Karger Publishing, pp. 75-89.
- Follis, R.H. (1964) Patterns of urinary iodine excretion in goitrous and non-goitrous area, Anal. J. Clin. Nutr. 14, 253-268.
- Furnee, C.A., Pfann , G.A., West, C.E., van der Haar, F., van der Heide, D., Haustvast, J., (1995) New model for describing urinary iodine excretion: its use for comparing different oral preparations of iodized oil, American Journal of Clinical Nutrition 61, 1257 – 1262.
- Groppe, B., (1988) Jodversorgung und Jod status des wiederkaues (Rind, Schaf ,Ziege) habilitations schrift Universitat Leipzig
- Hassanien, M.H., Hussein, L.A., Robinson, E.N. and Mercer, L.P., (2003) Human iodine requirements determined by the saturation kinetics model J. Nutr, Bioc., 14:280-287
- Hetzel, B.S. (1989) The story of iodine deficiency an international challenge in nutrition, Oxford University press, Oxford, pp.1-87.
- High Institute of Public Health, (1993), Report on assessment of the prevalence of iodine deficiency disorders in the New Valley governorate, Egypt.
- Koutras, D.A. , (1989) The ecology of iodine, in: J.B. Stanbury, B.S Hetzel (Eds.), Endemic Goiter and Endemic Cretinism, p.206.
- Mercer, L.P. (1980) Mathematical model in nutrition, Nutrition Reports International 21 No.2, 189-198.
- Mercer, L.P., May, H.E., Dodds, S.J., (1989) Mathematical modeling and the determination of nutritional requirements: sigmoidal and inhibited nutrient-response curves. J. Nutr. 119 1464-1471.
- Sandell, E.B, Kolthoff, I.M. (1937), Micro determination of iodine by a catalytic method, Mikro Chim Acta , pp.1-9.
- Stanbury, J.B. (1998) Iodine, in: M.E. Shils, V.R. Young (Eds.), Modern Nutrition in Health and Disease, Lea and Febiger Publishing, Philadelphia, PA, pp.252-262.



- Sullivan, K.M., May, S., Maberly, G., (2000) Urinary Iodine Assessment, A Manual on Survey and Laboratory Methods, PAMM, Unicef 15, 2nd ed.,
- Taurog, A. (1991) Hormone synthesis and thyroid iodine metabolism, in: L.E. Braverman, R.D. Utiger (Eds.), The Thyroid: A Fundamental and Clinical Text, JB Lippincott Publishing, Philadelphia, PA, pp. 51-97.
- Ulhaq, M., Ahmad, I., Salarzai, SM, (1996) Iodized salt in Peshawar, Pakistan: its iodine content price, and use by the people. IDD Newsletter 12, 1-12.
- WHO, UNICEF, ICCIDD, (1996), Recommended iodine level in salt and guide lines for monitoring their adequacy and effectiveness. WHO.

**Table 1**

**Urinary iodine and nutritional status**

Median Urinary Iodine Concentration (mcg/L)	Approximate Iodine Intake (mcg/day)	Iodine Nutritional Status
<20	<30	Severe deficiency
20-49	30-74	Moderate deficiency
50-99	75-149	Mild deficiency
100-199	150-299	Optimal
200-299	300-449	More than adequate
>299	>449	Possible excess

**Table 1 –WHO, Iodine status worldwide, 2004, p. 6.**

**Table 2**

**Classification of the goiter size according to the World Health Organization**

<b>Grade</b>	<b>Classification of Goiter size</b>
O	No Goiter
IA	Thyroid lobes larger than ends of thumbs.
IB	Thyroid, enlarged, visible with head tilted back
2	Thyroid enlarged, visible with neck in normal positions
3	Thyroid greatly enlarged, visible from about 10 meters.

**Table 2 – ICCIDD/UNICEF/WHO. A practical guide to the correction of iodine deficiency 1990. Manual No. 3.**

**Table 3**

**Iodine Deficiency Characteristics**

<b>Iodine Deficiency</b>	<b>None</b>	<b>Mild</b>	<b>Moderate</b>	<b>Severe</b>
Median urine iodine, mcg/dL	>100	50-99	20-49	<20
Goiter prevalence	<5%	5-20%	20-30%	>30%
Neonatal thyroid stimulating hormone (TSH), >5 IU/mL whole blood	<3%	3-20%	20-40%	>40%
Cretinism	0	0	+	+

**Table 3 World Health Organization (WHO)/United Nations Children's Fund (UNICEF)/International Council for Control of Iodine Deficiency Disorders (ICCIDD), 1997**

Figure 1 – Saturation kinetics response curve for morning urinary iodine as a function of salt iodine supplementation level. The solid curve is the theoretical response curve predicted by the model equation. The dotted curve is the slope of the response. Standard errors shown on values. The iodine supplementation requirement is calculated at the point of 95% slope reduction.

Figure 1

