

Recent Advances in Iodine Nutrition

Michael Donaldson, PhD

Summary

Though iodine is known for its importance for the thyroid, little has been publicized about its other roles. Iodine is needed in microgram amounts for the health of the thyroid. For the rest of the body iodine is needed in larger amounts, hundreds of micrograms or even milligram amounts; perhaps as much as 100 times as much as the RDA.

Iodine supports the health of many organs in the body. It is taken up by most every gland and, when taken in milligram quantities, is found in nearly every tissue of the body. The thyroid cannot function properly without an adequate supply of iodine, and much of the subclinical hypothyroidism in the USA is likely just a shortage of iodine. The immune system uses iodine to fight infections, so many chronic illnesses tax the body's iodine supply. The reproductive glands and tissues have high levels of iodine in them, if iodine is provided. This iodine is necessary for optimal function of the breasts, ovaries, endometrium, and prostate. Research has shown that milligram amounts of iodine can reverse fibrocystic breast disease. Iodine suppresses chemically-induced breast cancer in rats. Iodine balances estrogen levels, thus supporting ovary health. Sufficient iodine is needed for a stable rhythmic heart beat. Iodine, directly or indirectly, can normalize serum cholesterol levels and normalize blood pressure. Iodine attaches to insulin receptors and improves glucose metabolism, which is good news for people with diabetes. Iodine is essential for the development of the central nervous system; women need a good supply before becoming pregnant. Iodine may also play a role in bone health and lung function. Even the skin needs iodine. Iodine has been shown to help remove heavy metals from the body along with bromide.

Iodine can be obtained as a dietary supplement, as Iodoral or Iosol. Both of these supplements have a long history of safe use. For general health maintenance an intake of one to three milligrams of iodine, supplied as a mix of iodine and iodide, is likely to be healthful. For people with lower organ function and in greater need of optimization of body iodine stores intakes up to 50 mg per day can be done safely. If intakes of more than 10 mg per day are used continually it is highly recommended that a person has their thyroid function checked twice a year.

Introduction

In many ways the American population has not been well served by those who make food policies and dietary guidelines. Sometimes this is for selfish reasons, desiring personal gain at the expense of others. Sometimes there is genuine ignorance mixed in with an incredible lack of interest in new ideas or ways to bring health to the world's people.

Such is the case with iodine. There is some ignorance about how larger intakes can be beneficial to people while there is a "professional" skepticism gathered from medical

school and university days that high levels of iodine are “toxic.” But here at Hallelujah Acres we are always looking for ways to empower people to take care of their own bodies in a way that is safe and effective. After quite some time examining the evidence around iodine, its use in milligram amounts, and the benefits of iodine, we are ready to pass along our findings to you.

The human body has a requirement for iodine (discussed in detail below) that must be met from what we eat. Land vegetables, unfortunately, have very, very little iodine in them as there is very little iodine in the soil. If the soil is fertilized with kelp, or irrigated with iodine-rich water then garden produce can contain substantial amounts of iodine. Sea vegetables have the ability to concentrate iodine out of sea water, making them an excellent source of iodine. Dairy products, eggs, and iodized salt are generally where Americans get their iodine. Dairy products contain iodine because iodine is concentrated by all mammary glands.

In order to control goiter, David Marine conducted controlled studies with school children, supplying them with iodine in the 1930s. After these trials showed conclusively that iodine could prevent and reverse simple goiter the public was offered iodized salt as a way to prevent goiter. And so now we associate iodine with the prevention of goiter and proper thyroid function. And that is all that most of us know about the action of iodine. But some research has brought to light that iodine plays a much greater role in the body than just keeping the thyroid functioning properly. Much more.

Where is Iodine Found in the Body

The primary role of iodine is to make thyroid hormones. But there are several other roles that iodine also plays in the body. Iodine has the ability to attach to tyrosine and histidine amino acid residues on proteins throughout the body. Iodine also reacts with double carbon bonds in lipids, making it possible to form iodolipids. Iodine also functions as an antioxidant in the body, raising the serum total antioxidant capacity. So, you can see that iodine’s chemistry is much more than just the production of thyroid hormones.

The thyroid gland is the main iodine-concentrating gland of the body. It is widely stated that the body contains between 15 and 20 mg of iodine and that two-thirds of this iodine is found in the thyroid gland ⁽¹⁾. Under microgram intakes this is true, but under high intakes of iodine much of the rest of the body also contains iodine, up to 1,500 mg or so ⁽²⁾. This is one area of ignorance. Where does all of this iodine go?

Other organs are also able to take up iodine, too, by the same transport protein as the thyroid. Research has shown that the receptor for iodine uptake is in the thyroid gland, salivary gland, parotid gland, submandibular gland, pituitary gland, pancreas, testis, mammary gland, gastric mucosa, prostate, ovary, adrenal gland, heart, thymus, lung, ⁽³⁾ bladder, kidney, endometrium, ⁽⁴⁾ and also breast, ovary and colon ⁽⁵⁾ and the lacrimal gland ⁽⁶⁾. The ovaries hold the second highest concentration of iodine, after the thyroid. The breasts also have a high concentration of iodine. Most secretions in the body, whether gastric, nasal, tears, sweat, etc., have iodine in them if sufficient iodine is present in the body. The skin also contains quite a bit of iodine, though its exact role isn’t clear. Dr. Flechas tells that clinically the ability to sweat is related to iodine and extremely low

body iodine stores prevent sweating, opening the body to the spread of cancer ⁽⁷⁾. Many of the functions of iodine are separate from its role as part of thyroid hormones. Iodine has a major impact on the thyroid, but it will also have a direct impact on all of the other tissues of the body that utilize iodine.

Now we will look at different glands and systems of the body that are affected by iodine in more detail.

Thyroid

The thyroid utilizes iodine to make thyroxine, or T4 as it is commonly called, and triiodothyronine, or T3. Thyroxine contains 4 iodine atoms and triiodothyronine contains 3 iodine atoms. The thyroid secretes about 10% T3 and 90% T4 into the bloodstream. The organs of the body can convert the T4 into the more active T3 form via enzymes called deiodinases. Release of the thyroid hormones is controlled by thyroid releasing hormone, from the hypothalamus, which is sent to the pituitary, which secretes thyroid stimulating hormone, TSH, which causes the activity of the thyroid to increase and secrete more T3 and T4. Elevated levels of T3 in the blood downregulate the hormones from the hypothalamus and pituitary. High levels of iodine temporarily (26-40 hours) inhibit release of T3 and T4 from the thyroid (acute Wolff-Chaikoff effect), but then normal function of the thyroid continues as previously (escape from the Wolff-Chaikoff effect) after the thyroid down-regulates the number of sodium-iodide symporters in the cell membranes of the thyroid.

The thyroid hormones regulate your metabolic rate, and thus energy production, of the entire body. The effects are felt in every system and cell of the body. A glance at the symptoms of hypothyroidism (see Table 1) gives an idea of the wide range of effects.

Table 1. Signs and Symptoms of Hypothyroidism.

Brittle Nails	Hypotension
Cold hands and feet	Inability to concentrate
Cold intolerance	Infertility
Constipation	Irritability
Depression	Menstrual irregularities
Difficulty swallowing	Muscle cramps
Dry skin	Muscle weakness
Elevated cholesterol	Nervousness
Essential hypertension	Poor memory
Eyelid swelling	Puffy eyes
Fatigue	Slower heartbeat
Hair loss	Throat pain
Hoarseness	Weight gain

In infants and children these hormones are necessary for normal growth and development, both physically and mentally. Very severe hypothyroidism in the womb and in infancy leads to cretinism, a dwarfed and mentally retarded state that quickly becomes permanent.

Goiters used to be more common in the USA before the iodination of salt. Simple goiter is an enlargement of the thyroid due to the lack of iodine. The thyroid expands so that it can better capture iodine from a very scarce blood supply. Goiters can also be due to an autoimmune reaction as well, but even here a lack of iodine probably still plays a role.

Hypothyroidism can be caused by a multitude of factors, including a lack of iodine. The Hallelujah Diet takes care of most of the other factors, except for iodine. Hypothyroidism slows down your entire metabolism and causes many symptoms which vary in different people. Not everyone has all of the symptoms. Some of the common symptoms are given in Table 1, taken from Dr. Brownstein's book, *Iodine: Why You Need It, Why You Can't Live Without It* ⁽⁸⁾. Two of the most common symptoms are fatigue and being cold when everyone else is warm.

Fibromyalgia and Chronic Fatigue Syndrome may be a manifestation of a hypothyroid condition. It is no coincidence that hypothyroidism, fibromyalgia, and chronic fatigue syndrome are all much more common in women. There is a common link—women need more iodine than men. This is true not only during pregnancy and lactation, but for every women. Breast tissue requires iodine for maintenance of structure ⁽⁹⁾ and to keep cells exposed to hormone surges from multiplying out of bounds.

Since iodine is an integral part of the thyroid hormones, it is obvious that a lack of iodine is going to have a direct effect on the ability of the thyroid to produce these hormones. Even if a doctor prescribes replacement thyroid hormone, iodine is always still needed to fully support the function of the thyroid. The prescription hormone takes care of the symptom, but sufficient iodine will meet the underlying cause of many cases of subclinical hypothyroidism all.

Autoimmune disorders of the thyroid are also more common when people lack sufficient iodine. Both hyperthyroid and hypothyroid conditions can result from a lack of iodine, in combination with other factors. Dr. Brownstein mentioned that 92% of his patients with Hashimoto's or Grave's disease also were deficient in iodine ⁽⁸⁾. Further, symptoms improved dramatically when they took high amounts of iodine to build up their body's supply of iodine.

Breast

In Japan seaweed, a concentrated source of iodine, has a legendary history for protecting women's health. In Korea new mothers are traditionally fed seaweed soup ⁽¹⁰⁾. We are beginning to understand what these cultures have known for a long time. Lactating women actively take up the iodide ion by the same symporter protein that is in the thyroid. However, molecular iodine is also taken up by the breasts, and not just when a women is nursing. The concentration in the breast tissue is not as high as in the thyroid or ovaries, but because of their much larger size a substantial portion of iodine can be present in the breasts, if supplied to the body.

A link between thyroid function and breast disease was reported in the Western medical literature over 100 years ago. Since then there has been some controversy over this link, but some very clear results have now demonstrated that there is a connection that can be

ignored only to the peril of women's health. The hypothesis being put forward here is that a lack of iodine changes the architecture of the tissue of the breast by not being available to cause differentiation of cells or apoptosis of abnormal breast cells that respond to hormonal surges. The connection between breast disease, including cancer, and thyroid disease is a lack of iodine, which negatively affects both of them independently. There are four lines of evidence: (1) thyroid disease-breast cancer link, (2) iodine content in breast tumors and normal breast tissue, (3) animal models wherein iodine suppressed breast tumors, and (4) resolution of fibrocystic breast disease in women.

A recent study investigated the question of whether there was an increased risk for breast cancer for women who had already had thyroid cancer. Using the National Cancer Institute's large database they found that white premenopausal women had a 42% higher risk of developing breast cancer than expected if the two cancers were not related⁽¹¹⁾. Having breast cancer first did not lead to higher levels of thyroid cancer. Though the radioactive iodine treatment was detrimental to the breasts as well, there is more to the connection than that.

Smyth and coworkers⁽¹²⁾ looked at thyroid volumes in 200 patients with breast cancer, 354 with benign breast disease, and 124 healthy premenopausal women in a control comparison group. Mean thyroid volumes were 21.2 ± 1.4 ml in the breast cancer group, 14.5 ± 0.34 ml in the benign breast disease group, and 12.5 ± 0.38 ml in the healthy control group, all being significantly different from each of the other groups. The breast cancer group was also significantly different from age-matched controls. Smyth and coworkers had seen similar results in a previous study⁽¹³⁾, which is consistent with the hypothesis that a lack of iodine causes an enlarged thyroid and also leads to breast disease.

In a study from the University of Pisa in Italy researchers looked for thyroid disease in 102 consecutive breast cancer patients right after their surgery for breast cancer. The overall prevalence of thyroid disease in the breast cancer patients was 46%, compared to just 14% in their control group⁽¹⁴⁾. Nodular goiter (27%) and Hashimoto's thyroiditis (14%) accounted for most of the thyroid disease. Another study found a significantly higher incidence of thyroid antibodies in breast cancer patients (50%) compared to age-matched healthy controls⁽¹⁵⁾. Turken and coworkers examined 150 breast cancer patients (without known thyroid disease) and 100 age-matched control women for thyroid abnormalities. They, too, found an association between high levels of autoimmune thyroiditis (38% versus 17%, breast cancer vs. control group), nodular goiter (50% versus 26%), and breast cancer⁽¹⁶⁾. Thyroid disease is often associated with breast cancer. More direct evidence below shows the link is low iodine intake.

Interestingly, in all four of the studies just mentioned, values for thyroid function (T3, T4, TSH) were all normal in all groups, showing that these tests do not accurately catch early stages of thyroid disease. Normal levels of thyroid hormones are very important for the body, so the thyroid gland is designed to accommodate many levels of iodine intake, both very low and very high, before hormone levels are changed. Dr. David Derry suggests that the TSH test, which is the standard used by endocrinologists for monitoring thyroid

health, is useless since it doesn't correlate with symptoms of the patient ⁽¹⁷⁾. Possibly thyroid volume, measured ultrasonically, would be a better indicator of optimal thyroid function.

More direct evidence of iodine levels in breast tumors was seen in a study by Kilbane and coworkers ⁽¹⁸⁾. Total tissue iodine levels in 23 benign tumors was 80.9 ± 9.5 ng I/mg protein, compared to a value of 18.2 ± 4.2 ng I/mg protein in 19 breast cancers. Thyroid antibodies in the blood, an indication of autoimmune thyroid disease, was much more common in the breast control group than in the female age-matched control group. So, here there is a link between breast cancer, low iodine, and thyroid disease. Iodine induces apoptosis of abnormal cells, so low levels of iodine in tissue can allow abnormal cells to develop into tumors, if not caught by other defense mechanisms of the body.

A third line of evidence comes from animal studies. Indeed, animal studies by Japanese researchers have shown that Lugol's iodine solution ⁽¹⁹⁾ as well as Wakame seaweed ⁽²⁰⁾ and a water extract of Mekabu seaweed ⁽²¹⁾ all were able to suppress growth of mammary tumors in rats fed the carcinogen 7,12-dimethylbenz(a)anthracene. The water extract of Mekabu clearly induced apoptosis, or programmed cell death, in a human breast cancer cell lines as well ^(21, 22). Molecular work by Eskin's group has shown that iodine downregulates the estrogen receptors in breast cancer cells and changes the expression of genes involved in differentiation, cell cycle, hormone metabolism, and cancer growth ⁽²³⁾. Together these animal and *in vitro* studies show how iodine could be working at a molecular level and give plausibility to the iodine-breast cancer link.

In addition to breast cancer, Bernard Eskin published several studies showing that iodine was necessary just for normal breast tissue structure in higher vertebrates ⁽⁹⁾. When rats were given low iodine diets their breast tissue changed in ways very similar to what is seen in fibrocystic breast disease in women. Also, the rats' breasts were more susceptible to carcinogens and promoted lesions earlier and in greater abundance. This led Eskin's group to pursue clinical studies of women with fibrocystic breast disease, supplementing their diet with iodine.

Fibrocystic breast disease is associated with lumps in the breasts and cyclical breast pain. About 70 percent of reproductive-aged women regularly experience cyclical breast pain, and 10-30 percent of them have pain severe enough to interfere with normal activities ⁽²⁴⁻²⁶⁾. Fibrocystic breast disease, which is benign and not cancerous, increases the risk of breast cancer. The greater the changes in the tissue the higher the risk, almost double for proliferative changes and a four-fold increased risk for atypical hyperplasia ⁽²⁷⁾. In a study of 111 women with benign fibrocystic breast disease they were given iodine at different levels for 6 months. Their own ratings of pain fell significantly by 3 months in the 3 mg iodine/day and the 6 mg iodine/day groups, but not in the placebo or the 1.5 mg iodine/day. Physician assessments of breast pain, tenderness, and nodularity were also significantly less in the 3 and 6 mg iodine/day groups ⁽²⁸⁾. At least 3 mg of iodine per day were needed to get a response. William Ghent and Bernard Eskin together treated over 1,300 patients with fibrocystic breast disease using iodine in 3 different forms, with over 70% improvement in pain and objective evaluations using elemental iodine at 4 months ⁽²⁹⁾, and over 90% recovery after 16 months of treatment ⁽³⁰⁾. Treatment usually was in

the range of 3-6 mg of iodine, though some clinicians have also found higher amounts to work safely and faster.

So, iodine appears to be the primary link between thyroid health and breast health. Both organs independently require iodine and a shortage of it will cause disease in either one or both of them.

Ovaries

After the thyroid gland the ovaries contain the highest concentration of iodine. Dr. Flechas has seen that iodine reverses polycystic ovarian syndrome. Ghent and Eskin reported the reversal of ovarian cysts with iodine ⁽³⁰⁾, along with reversal of endometriosis and premenstrual syndrome. Iodine is necessary for normal ovarian function. Dr. Jonathan Wright reports that iodine elevates the amount of anti-carcinogenic estriol made and lowers the amount of estrone and estradiol, so that the three forms of estrogen are more balanced in favor of cancer prevention. ⁽³¹⁾

In the process of treating fibrocystic breast disease Ghent and Eskin also found that the elemental iodine was also an effective treatment for endometriosis, ovarian cysts, and premenstrual syndrome ⁽³⁰⁾. Iodine appears to normalize ovarian function and estrogen production to alleviate these female problems as well.

Prostate

Many glands in the body concentrate iodine from the blood. There is very little known about any connection between iodine deficiency and the prostate gland. Some researchers suspect a link similar to what is seen with breast health, and there is proof that the prostate gland expresses the sodium iodine symporter ⁽⁴⁾, albeit at a lower level, thus having a method of concentrating iodine. Iodine causes apoptosis of abnormal cells and functions as an antioxidant, both of which would favor better health of whatever organ takes up iodine.

Cardiovascular System

Iodine is critical to the heart and arterial system. Iodine (as well as omega 3 fats) is critical to the stabilization of the electrical pulses of the heart. Lack of iodine is related to atrial fibrillation. An iodine-containing drug called amiodarone is used to prevent atrial and ventricular fibrillation and releases about 9 mg of iodine per day ⁽³²⁾. It is a complex, toxic drug and is stored in the fatty tissues of the body, but part of its mechanism of action appears to be the iodine that is being released slowly by the drug.

Bruce West is a chiropractic doctor who has found iodine to be very helpful in helping patients with arrhythmia problems. He says, "The body needs adequate stores of iodine for the heart to beat smoothly. After close to a year now of using Iodine Fulfillment Therapy, I can attest to this fact. Most of the stubborn cases of cardiac arrhythmias and atrial fibrillation that we were unable to completely correct with our cardiac protocols have now been resolved with adequate supplies of iodine added to the protocol." ⁽³³⁾

The country of Finland is an excellent case study of cardiovascular disease and iodine, as reviewed by Stephen Cann⁽³⁴⁾. Endemic goiter was common in the early 1900s in people and in domestic animals, particularly in the eastern part of Finland away from the sea. Studies in the 1950s revealed that the major dietary difference between eastern and western Finland was iodine. The risk of death from coronary heart disease was 3.5 times higher for people with a goiter in Finland. Iodized salt was introduced in the 1963 for people and also for animals, with over 90% of household salt now being iodized. Iodine intake on the population level is about 300 µg/day, the highest level in Europe⁽³⁵⁾. Much of their iodine comes from dairy products and hen eggs. Selenium was also added as a crop fertilizer because their soil selenium levels were very low. (Selenium has a unique synergistic interaction with iodine discussed more below.) People were also encouraged to eat less saturated fats and to stop smoking.

And the results of these population interventions with iodine and selenium? Goiter has virtually disappeared. Serum cholesterol levels and blood pressures have both dropped significantly and cardiovascular disease mortality has declined more than 50% and life expectancy has increased by about 5 years⁽³⁴⁾. Other countries have likewise reduced saturated fat intake, but not had this kind of national success in disease reduction. Though iodine and selenium haven't been given official credit for this success, it is likely that they are the unsung heroes of Finland. Iodine has an indirect effect via thyroid hormones, but it is likely to have a direct effect as well.

So, iodine stabilizes the heart rhythm., lowers serum cholesterol, lowers blood pressure, and is known to make the blood thinner as well, judging by longer clotting times seen by clinicians. Iodine is not only good for the cardiovascular system, it is vital.

Insulin Receptors

Iodine also has an impact on glucose metabolism. There have been no studies on this to date, only observations of clinicians who have patients taking high amounts of iodine. It appears that iodine increases the sensitivity of the insulin receptor, which improves glucose control. Lower amounts of insulin are needed to keep blood glucose levels in the normal range. Dr. Flechas has found that iodine can reduce the need for insulin in diabetic patients, using 50 to 100 mg of iodine per day. Of 12 patients, 6 were able to completely come off their medications with random glucose readings below 100 mg/dl and a HbA_{1c} less than 5.8 (normal), and the other 6 were able to reduce the amount and/or number of medications needed to control their diabetes⁽³⁶⁾. More research should be done in this area to confirm and expand these results. In the same way that iodine modifies insulin receptors it is possible for iodine to modify other receptors as well. This is as yet an unexplored area of research.

Bones

Iodine and fluoride are both halides, so they share some chemistry, but they have very opposing effects in the body. For example, iodine and fluoride are both taken up by bone tissue. Radioactive iodine scans show the full outline of the skeletal system. Fluoride also goes to the bones, but it makes bones brittle and susceptible to fractures⁽³⁷⁾. It is likely that natural iodine is what is supposed to be in our bones, not fluoride, for which

there is no known need in our body. Fluoride is toxic to bones as well as to the central nervous system, while iodine nourishes both. Very little research has been done in the area of iodine sufficiency and bone strength, but these ideas need to be evaluated clinically and in research studies.

Lungs

Iodine goes to sites of inflammation or infections, including pulmonary or bronchial infections. Dr. Jonathan Wright recommends using iodine for chronic obstructive pulmonary disease (COPD)⁽³¹⁾, as it helps loosen up secretions and makes them easier to expel, and also helps prevent bacteria from growing in the mucus secretions.

Immune System

Iodine also plays a role in the immune system. Many years ago it was noted that bacterial infections cause an increase in the metabolism of thyroxine^(38, 39). In particular, leukocytes use halogens such as chloride and iodide to help destroy bacteria that they engulf via phagocytosis. Chloride is used because it is available in abundance, but experiments have shown that leukocytes will use iodide just as well as thyroxine as a source of halogens for destroying the engulfed bacteria⁽⁴⁰⁾. The mechanism requires three players—a peroxidase enzyme, hydrogen peroxide, and iodide for destroying the bacteria with by-products of the oxidation of iodide and not just free iodine playing an important role. Leukocytes also use other means of destroying bacteria, but the halogens (chloride and iodide) are an important part of this process.

One application of this is that iodine needs will increase while a person is fighting a bacterial or viral infection. Elevated levels of diiodotyrosine, created from thyroxine by leukocytes as they phagocytose bacteria, were found in critically ill patients fighting sepsis and severe non-systemic infections⁽⁴¹⁾. Having sufficient iodine present in the body to fight infections will improve a person's overall health and disease resistance.

What if that iodine is not supplied? Since chronic infections use up thyroxine faster than normal, is it possible that chronic bacterial or viral infections lead to a hypothyroid condition? Could a shortage of iodine be the connection between Epstein-Barr infections and other infections and chronic fatigue or fibromyalgia?

Central Nervous System

Though sufficiency of iodine nutrition is taken for granted here in the USA, in many parts of the world iodine deficiency is still a top nutrition issue. In 2003 36.5 percent of the world's population had insufficient iodine intake, ranging from 10 percent in the Americas to 60 percent in Europe⁽⁴²⁾.

Infants in particular are vulnerable, especially in the womb, to iodine deficiency. The infant's brain requires iodine for proper development. There is a whole continuum of effects from mild mental retardation to gross neurological impairment⁽⁴³⁾. Even if the mother just has a hypothyroid condition the child can be adversely affected mentally. One study found that seven years later, mothers who had an untreated hypothyroid condition while pregnant gave birth to children that scored an average of 7 points lower

on intelligence tests compared to a age-matched control group of children; 19 percent of the children had a score of 85 or less, compared to just 5 percent of the control group ⁽⁴⁴⁾. Another review of 18 studies comparing iodine-deficient children to iodine-sufficient children found an average drop in intelligence quotient of 13.5 points ⁽⁴⁵⁾. In a small Italian study ADHD disorder was found to more common in a moderately iodine-deficient area (11/16 children) compared with a iodine-sufficient area (0/11 children) ⁽⁴⁶⁾.

A big effect of iodine deficiency is infant mortality. A study in an iodine-deficient area in China showed that adding iodine to the irrigation water (the people wanted to continue using their coarse salt and wouldn't use iodized salt) used for crops resulted in a 65% drop in risk of neonatal mortality over a 3-year period, compared to a control city in the same area ⁽⁴⁷⁾. In an Indonesia study of 617 infants, survival was improved 72% by giving 6-10 week old infants iodized oil ⁽⁴⁸⁾. There was also a delay in the average time to death in this study (48 vs. 17.5 days). Survival improvements were also seen in infant studies in the Congo and in Papua, New Guinea.

So, the result of lack of iodine in children is much more than goiter—intelligence and neonatal survival are the really important issues. This is very uncommon in the USA, but it is possible that the intelligence of children can be enhanced by having sufficient iodine in women before they become pregnant, followed by the iodine-sufficient mother nursing her infant with her breast milk, which would abundantly supply iodine.

Organs with Heavy Metal Accumulations

Heavy metals accumulate in various organs of the body. Now it appears that there is another weapon in our gallery. When Dr. Abraham was checking the bioavailability of Iodoral, a tableted iodine supplement, he found that some individuals had several-fold increased levels of mercury, lead, and cadmium after taking Iodoral (12.5 mg iodide/iodine) for one day ⁽⁴⁹⁾. Arsenic and aluminum were also reported to be detoxified with Iodoral ⁽⁵⁰⁾, along with the halides bromide and fluoride. Iodine can replace the other halides and cause them to be removed from the body. In fact, many of the symptoms that are reported when high doses of iodine are taken are actually from the detoxification of bromide. The use of a natural sea salt (1/4 teaspoon of salt taken 3 times, about 6 hours apart) will increase the renal clearance of bromide and reduce detoxification symptoms due to bromide.

Bromide is used as a pesticide, and now fluoride is also being used as a pesticide on crops. Bromide also makes into our diets as brominated vegetable oil in citrus flavored sodas like Mountain Dew. Bromide resides in the fatty tissue of the body, making it difficult to lose weight as well. Iodine has a very noticeable effect at removing bromide from the body. Iodine will replace bromide and allow the fat to be burned away normally.

In a pilot study of 8 patients Dr. Brownstein found that bromide excretion increased by an average of more than 50% when the patients took 50 mg/day of iodine as Iodoral ⁽⁸⁾. Dr. William Shevin, a medical and homeopathic doctor, has also seen benefits of iodine in getting rid of the bromide burden of the body, assisted with the natural sea salt to enhance the removal of bromide by the kidneys ⁽⁵¹⁾.

Most Effective Forms of Iodine

There are basically three forms of iodine used for supplements—elemental or molecular iodine (I_2), ionic iodine, usually potassium iodide or ammonium iodide, and protein-bound iodide, such as Standard Process's Prolamine. These forms are all utilized by the body, although there is evidence that they are not exactly equivalent. Research by Drs. Eskin and Ghent found that the I_2 was the most beneficial form of iodine for fibrocystic breast disease ^(29, 30), and that it had less affinity for the thyroid. They did research with protein-bound iodine as well and found that it did not work as well for fibrocystic breast disease as the molecular iodine.

It is generally taught that molecular iodine is reduced to ionic iodide before it is absorbed from the gastrointestinal tract. However, a series of studies with rats compared the uptake and distribution in the body of iodide (as NaI) and elemental iodine (I_2). The researchers found that the thyroid much preferred the iodide form compared to I_2 ⁽⁵²⁾, that the iodine was distributed differently in the body, depending on the form used ⁽⁵³⁾, and that I_2 could alter T4 levels ⁽⁵⁴⁾, presumably by reacting with metabolites of T4 in the GI tract, thus reforming T4 ⁽⁵⁵⁾. Eskin and coworkers ⁽⁵⁶⁾ found that this was true in laboratory rats as well. Thyroid gland hyperplasia was reduced with I_2 , but eliminated with I^- , while mammary gland hyperplasia was decreased with I_2 but increased with I^- , and fibrosis of the breast was reduced with I_2 but remained the same with I^- . Rats with chemically-induced breast cancer had 30 percent incidence of breast cancer when they were fed I_2 , compared to a 72% incidence of breast cancer in the control group, along with fewer tumors and longer time until cancer developed. The rats fed T4 or I^- did not differ in incidence of breast cancer from the control group ⁽⁵⁷⁾. So, different tissues of the body take up the I_2 and I^- differently and they are not exactly equivalent.

Elemental iodine is quite reactive and can disassociate in the GI tract and iodinate various proteins and lipids, unlike iodide that is taken up as a free ion into the bloodstream. For about 2 hours elemental iodine is detected in the serum, but only iodide is detected thereafter ⁽⁴⁹⁾.

So, for supplementing iodine it appears that a mix of elemental iodine and iodide (as in Iodoral or Iosol) is called for to supply the thyroid and the rest of the body.

Optimal Amounts of Iodine

The RDA for iodine is 150 $\mu\text{g}/\text{day}$ for non-pregnant adults, 220 $\mu\text{g}/\text{day}$ during pregnancy, and 290 $\mu\text{g}/\text{day}$ during lactation. The RDA for adults is based on the amount of iodine that the thyroid normally accumulates from day to day, and on the prevention of goiter in children. The tolerable upper intake level (an upper limit of intake that is very unlikely to harm anyone) is 1,100 $\mu\text{g}/\text{day}$. The tolerable upper intake level in Japan is provisionally set at 3,000 $\mu\text{g}/\text{day}$, since they do not have sufficient data to determine the optimal iodine intake for the Japanese population ⁽⁵⁸⁾. There have never been any studies done on the optimal amounts of iodine needed for the whole body.

Drs. Ghent and Eskin, and others treated fibrocystic breast disease with 6 to 10 mg/day of iodine in order to reverse this condition. Other female disorders disappeared along with

the breast disease, too. From the research presented here it is clear that the role of iodine in the body goes far and beyond simply making thyroid hormones.

Japanese Experience

As a nation, Japan consumes more iodine than any other nation. The Japanese women have very low rates of breast cancer and fibrocystic breast disease and are one of the healthiest nations in the world. There are many factors that contribute to this record, but it is quite possible that their tradition of using seaweed is one of them.

Also, national surveys of food intake in Japan, show that seaweed intake has been around 4.5 gram dry weight from 1950 to 1963, with a intake of 14 grams in 2001 ⁽⁵⁹⁾. Exact intake of iodine from this source isn't known. But, with a reported average concentration of 0.3% iodine, these seaweed intakes imply that Japanese iodine intakes are between 6 and 20 mg, and higher for some people. Balance surveys such as these are not known for giving accurate measurements of individual intakes of nutrients. Direct measurements of iodine excretion are more reliable. Various studies have shown average urinary iodine excretion to range from 740 µg – 3,290 µg/day, with a very wide range of total excretion, from 90 µg/day to 19 mg/day ⁽⁶⁰⁾. A recent study of thyroid volume and iodine excretion in Japanese children aged 6-12 years showed they had the smallest thyroid volumes in the world compared to other iodine-sufficient areas ⁽⁵⁸⁾. In this study the mean urinary excretion was 282 µg/l, with 16% of the children excreting more than 1,000 µg/l. This “high” level of intake did not have a negative effect on thyroid volume.

These iodine excretion studies show that while some Japanese are consuming lots of seaweed many others are not, with a very wide range of variation. Usual intake of the population is in the milligram range, but the average is not likely to be above 10 mg/day, or perhaps not even above 5 mg/day. Some seaweeds, like Nori and Wakame, contain very little iodine, while others like kelp and Kombu, have very high levels of iodine. So, iodine intake depends on the exact mix of seaweeds consumed from day to day.

Gerson's Protocol

Dr. Max Gerson's therapy for cancer included the use of Lugol's solution, initially for the purpose of stimulating the metabolism and then because “iodine seemed to counteract the neoplastic effect of hormones” ⁽⁶¹⁾. Large amounts were given for the first 3-4 weeks of the therapy (56 mg/day), with smaller maintenance doses (9 mg/day) thereafter ⁽⁶²⁾. In the conditions of the therapy Dr. Gerson did not experience negative complications from these “high” doses, possibly because the detoxification pathways are very strongly supported with the Gerson Therapy.

Too Much Iodine?

There have been reports of too much iodine being harmful, most of which could be undone by using less iodine. These reports include intakes above 500 µg/day in 6-12 year-old children in coastal Hokkaido ⁽⁶³⁾, between 50 and 90 mg/day in Peace Corps workers using iodine-resin water filters ⁽⁶⁴⁾, 32 mg/day from tetraglycine hydroperiodide water purification tablets ⁽⁶⁵⁾, 27 mg/day for 4 weeks in 10 normal male volunteers ⁽⁶⁶⁾, and elevated intakes of iodine in three counties of Jiangsu Province, China (median urine

iodine level 1,053 µg/L) due to high levels of iodine in both shallow and deep water wells⁽⁶⁷⁾. Thirty-three Japanese men and women with hypothyroidism stopped taking any iodine-containing food or medications for a few months. The median TSH level went from 21.9 mU/l (range 5.4-285 mU/l) to 5.3 mU/l (range, 0.9-52.3 mU/l) in the group. Twenty-one patients showed a more than 50% reduction in TSH just from eliminating iodine. Eleven of them became euthyroid⁽⁶⁸⁾. These studies indicate that there are cases where high intakes of iodine have caused harm, usually reversed by reducing the iodine intake. It is possible that proper nutritional support (high antioxidant intake, especially selenium) was not given to accompany this high iodine intake in these cases. Another possibility is that high levels of bromine caused thyroid complications. Some safety testing and clinical observations have been done with high levels of iodine^(36, 69, 70), but not enough to satisfy all of the critics.

Selenium-Iodine Connection

Another factor in how much iodine can be safely used depends on other possible mineral deficiencies. Selenium is very important for thyroid function. Selenium is part of the antioxidant enzyme glutathione peroxidase. Glutathione peroxidase in the thyroid helps quench free-radicals produced by the enzyme thyroid peroxidase (which functions to organify iodide as it enters the thyroid). If high levels of iodide are present in the thyroid without sufficient amounts of glutathione peroxidase it causes free-radical damage to the thyroid, leading to autoimmune thyroid disease. Several of the enzymes that convert T4 into T3 also require selenium. Studies in Zaire have found that supplementing selenium and iodine deficient children with just selenium had adverse effects on thyroid function^(71, 72). Likewise, supplementing iodine when there is a concurrent selenium supplementation could lead to elevated levels of hydrogen peroxide within the thyroid, perhaps causing autoimmune disorders of the thyroid as well. It is not clear that the international studies of high intakes of iodine such as those conducted in China and Japan were done in populations with sufficient selenium status. Indeed, high levels of iodide intake in the USA or in central Hokkaido did not have the same negative impact that these same levels of intake did in coastal Hokkaido⁽⁶³⁾. So, it is important that other mineral interactions also be taken into account when looking at iodine supplementation. A person with superior nutrient intake will be much more likely to respond well to higher intakes of iodine.

The Optimal Amount

So, what is the optimal amount of iodine? There really isn't a simple one-size-fits-all sort of recommendation for iodine. While milligram amounts of iodine are healthy, a few people cannot tolerate those levels. For a generally healthy person following the Hallelujah Diet or similar diet an intake of 1-3 mg of iodine per day is quite likely to be safe and effective without complications. Children would take less, based on body size. The provisional tolerable upper limit in Japan for iodine is 3 mg per day, though many people in Japan consume more than that. If a person is allergic to iodized salt, then they should avoid taking iodine supplements as well, until they get their allergy cleared.

More than 3 mg/day can be taken safely by many people, but it is wise to work up slowly to higher doses, unless a person is under the direct supervision of a knowledgeable health

practitioner who can monitor thyroid function. The optimal amount of iodine may well vary from person to person, and it may well be more than 3 mg/day. However, it is wise to begin slowly and monitor your progress if you increase your iodine intake.

What about people with health conditions associated with the action of iodine? People with cancer, (especially of the esophagus, stomach, breast, ovaries, endometrium, or prostate), women with fibrocystic breast disease or ovarian cysts, people with diabetes, cardiovascular disease, or chronic obstructive pulmonary disease, and people with thyroid disorders (hypothyroid, hyperthyroid, and autoimmune disorders) all would achieve better health with more iodine. Someone with any of these conditions may want to consider undergoing the iodine loading test with FFP Laboratories (877-900-5556) before beginning high dose iodine. Having thyroid function tests checked by a health care professional is also recommended while taking more than 10 mg of iodine per day.

Iodine Loading Test

The iodine loading test was designed to measure the body's saturation with iodine. Initially the loading test was used to measure the bioavailability of Iodoral, a tableted form of Lugol's solution. However, when people showed such high retention of iodine (unlike what is seen at microgram intakes) the usefulness of the test quickly became apparent. In the iodine loading test a person takes 50 mg of iodine as Iodoral. A 24-hour urinary sample is taken to see how much is retained by the body. If less than 90% is excreted (more than 10% retained) Dr. Abraham says this is indicative of an iodine deficient state. The 90% level was chosen because it correlated with feelings of well-being in volunteers who reached that level of saturation. If a very low amount (<15%) is excreted then Dr. Flechas says that the presence of cancer is suspect. After a period of about 3 months using 12 – 50 mg of iodine/iodide a repeat iodine load usually shows a much improved state of iodine balance with much more excreted rather than retained ⁽⁴⁹⁾.

Thyroid TSH Test

When going to get thyroid tests, beware that the thyroid stimulating hormone, or TSH, test is not really the “gold-standard” that doctors have declared it to be. Just because TSH is normal doesn't mean that your body has optimal amounts of thyroid hormone in all organs and tissues. Dr. David Derry states that the TSH test has little clinical value for determining whether a person has a abnormal thyroid hormone condition or not. He says, in an interview with Mary Shomon ⁽¹⁷⁾, “the pituitary cells, which have TSH in them, are the most sensitive cells in the body circulating thyroid hormone. Therefore when one treats hypothyroidism by following the TSH and trying to make it normal the pituitary cells are happy but the rest of the body is short-changed by a considerable amount.” In other words, when the TSH is normal, this only means that the pituitary gland has the right amount of hormone for its needs. The rest of the body may not have enough, and clinical experience indicates that this is so. A recent review pointed out that during iodine deficiency, there can be normal, elevated, or low levels of T3, the active form of thyroid hormone, in different tissues of the body ⁽⁷³⁾. So, a hypothyroid condition can exist in some organs while having normal TSH measurement.

Sources of Iodine

We have examined most available forms of iodine supplements since the fall of 2005. There are two main sources that we can recommend to you. Both of these are a mix of iodine and iodide to supply all parts of the body with the form of iodine best suited for each part.

Lugol's Solution has been clinically used since Dr. Lugol made it in 1829. It is a solution of potassium iodide (KI) and molecular iodine (I₂). Lugol's solution is also useful as a stain for microscopy work, and is sold for this purpose, but not as dietary supplement.

Iodoral is a tableted version of Lugol's solution. Lugol's solution is absorbed onto a colloidal silica excipient and tableted, then coated with a thin layer of pharmaceutical glaze. Each tablet contains 12.5 mg of total iodine, 5 mg of I₂ and 7.5 mg iodide as KI. Each tablet is scored so that it can be easily broken in half if desired. A 50-mg tablet is now available as well for those doing high levels of iodine supplementation. Some people will find the tablet form of iodine more convenient than a liquid supplement.

Iosol is a 4% solution of ammonium iodide and iodine in glycerin. Each drop contains 1.83 mg of iodine, about 0.8 mg as iodide in ammonium iodide and 1.0 mg as iodine (I₂). The drops can be diluted in water, of which a portion can be taken for even lower doses. The doctors who developed Iosol in the 1940s were looking for a form of iodine that had fewer allergic reactions compared to potassium iodide. Their claim is that ammonium iodide is more "available" as free iodide ion compared to potassium iodide, in which they claim the potassium and iodide ion bind more tightly together. Some people have been able to tolerate Iosol more easily than Lugol's solution or Iodoral. However, it has been difficult to determine which of these supplements really works better.

Sea vegetation concentrates iodine from the ocean water. As mentioned above, some species contain relatively high levels (kelp, Kombu) while others have very little (Nori, Wakame). The iodine in sea vegetation is all iodide, so it may not work as well as molecular iodine for some organs in the body. Nevertheless, it is a natural, whole-foods source of iodide, so it comes with many other minerals and nutrients present in whole foods. Contamination with heavy metals can be a serious problem with sea vegetation. Recently, 8 of 9 herbal kelp supplements from a health food store were found to have excessive levels of arsenic in them ⁽⁷⁴⁾. For this reason, and because only iodide is present, this is not a preferred source of this mineral.

These are the three main sources of iodine available, though there are others. Personal preference and convenience may be the determining factor for which one you want to use for yourself. The bottom line is that we need more iodine than the microgram amounts occurring in our foods now and we need to find safe ways to incorporate more iodine into our diets.

References

1. Hetzel BS, Clugston GA. Iodine. In: Shils ME, Olson JA, Shike M, Ross AC, editors. *Modern Nutrition in Health and Disease*. Ninth ed. Baltimore, MD: Lippincott Williams & Wilkins; 1999. p. 253-267.
2. Abraham GE. The concept of orthoiodosupplementation and its clinical implications. *The Original Internist* 2006;11(2):29-38.
3. Spitzweg C, Joba W, Eisenmenger W, Heufelder AE. Analysis of human sodium iodide symporter gene expression in extrathyroidal tissues and cloning of its complementary deoxyribonucleic acids from salivary gland, mammary gland, and gastric mucosa. *J Clin Endocrinol Metab* 1998;83(5):1746-51.
4. Wapnir IL, van de Rijn M, Nowels K, Amenta PS, Walton K, Montgomery K, et al. Immunohistochemical profile of the sodium/iodide symporter in thyroid, breast, and other carcinomas using high density tissue microarrays and conventional sections. *J Clin Endocrinol Metab* 2003;88(4):1880-8.
5. Smanik PA, Ryu KY, Theil KS, Mazzaferri EL, Jhiang SM. Expression, exon-intron organization, and chromosome mapping of the human sodium iodide symporter. *Endocrinology* 1997;138(8):3555-8.
6. Bakheet SM, Hammami MM, Hemidan A, Powe JE, Bajaafar F. Radioiodine secretion in tears. *J Nucl Med* 1998;39(8):1452-4.
7. Flechas JD. Iodine loading and spot test. In: *Recent advances in the use of iodine in medical practice*. Scottsdale, AZ.
8. Brownstein D. *Iodine: Why you need it, why you can't live without it*. West Bloomfield, Michigan: Medical Alternatives Press; 2004.
9. Eskin BA. Iodine and mammary cancer. *Adv Exp Med Biol* 1977;91:293-304.
10. Moon S, Kim J. Iodine content of human milk and dietary iodine intake of Korean lactating mothers. *Int J Food Sci Nutr* 1999;50(3):165-71.
11. Chen AY, Levy L, Goepfert H, Brown BW, Spitz MR, Vassilopoulou-Sellin R. The development of breast carcinoma in women with thyroid carcinoma. *Cancer* 2001;92(2):225-31.
12. Smyth PP, Smith DF, McDermott EW, Murray MJ, Geraghty JG, O'Higgins NJ. A direct relationship between thyroid enlargement and breast cancer. *J Clin Endocrinol Metab* 1996;81(3):937-41.
13. Smyth PP. Thyroid disease and breast cancer. *J Endocrinol Invest* 1993;16(5):396-401.
14. Giani C, Fierabracci P, Bonacci R, Gigliotti A, Campani D, De Negri F, et al. Relationship between breast cancer and thyroid disease: relevance of autoimmune thyroid disorders in breast malignancy. *J Clin Endocrinol Metab* 1996;81(3):990-4.
15. Rasmusson B, Feldt-Rasmussen U, Hegedus L, Perrild H, Bech K, Hoier-Madsen M. Thyroid function in patients with breast cancer. *Eur J Cancer Clin Oncol* 1987;23(5):553-6.
16. Turken O, NarIn Y, DemIrbas S, Onde ME, Sayan O, KandemIr EG, et al. Breast cancer in association with thyroid disorders. *Breast Cancer Res* 2003;5(5):R110-3.
17. Shomon M. Rethinking the TSH test: An interview with David Derry, M.D., Ph.D. [cited Sept 19, 2005]; Available from: <http://www.thyroid-info.com/articles/david-derry.htm>

18. Kilbane MT, Ajjan RA, Weetman AP, Dwyer R, McDermott EW, O'Higgins NJ, et al. Tissue iodine content and serum-mediated ¹²⁵I uptake-blocking activity in breast cancer. *J Clin Endocrinol Metab* 2000;85(3):1245-50.
19. Funahashi H, Imai T, Tanaka Y, Tobinaga J, Wada M, Morita T, et al. Suppressive effect of iodine on DMBA-induced breast tumor growth in the rat. *J Surg Oncol* 1996;61(3):209-13.
20. Funahashi H, Imai T, Tanaka Y, Tsukamura K, Hayakawa Y, Kikumori T, et al. Wakame seaweed suppresses the proliferation of 7,12-dimethylbenz(a)-anthracene-induced mammary tumors in rats. *Jpn J Cancer Res* 1999;90(9):922-7.
21. Funahashi H, Imai T, Mase T, Sekiya M, Yokoi K, Hayashi H, et al. Seaweed prevents breast cancer? *Jpn J Cancer Res* 2001;92(5):483-7.
22. Sekiya M, Funahashi H, Tsukamura K, Imai T, Hayakawa A, Kiuchi T, et al. Intracellular signaling in the induction of apoptosis in a human breast cancer cell line by water extract of Mekabu. *Int J Clin Oncol* 2005;10(2):122-6.
23. Stoddard FR, HShah K, Johannes G, Eskin BA, Brooks A. Iodine alters gene expression profile in the MCF-7 breast cancer cell line. *Thyroid* 2006;16(9):894.
24. Ader DN, Browne MW. Prevalence and impact of cyclic mastalgia in a United States clinic-based sample. *Am J Obstet Gynecol* 1997;177(1):126-32.
25. Ader DN, Shriver CD. Cyclical mastalgia: prevalence and impact in an outpatient breast clinic sample. *J Am Coll Surg* 1997;185(5):466-70.
26. Ader DN, South-Paul J, Adera T, Deuster PA. Cyclical mastalgia: prevalence and associated health and behavioral factors. *J Psychosom Obstet Gynaecol* 2001;22(2):71-6.
27. Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, et al. Benign breast disease and the risk of breast cancer. *N Engl J Med* 2005;353(3):229-37.
28. Kessler JH. The effect of supraphysiologic levels of iodine on patients with cyclic mastalgia. *Breast J* 2004;10(4):328-36.
29. Ghent WR, Eskin BA, Low DA, Hill LP. Iodine replacement in fibrocystic disease of the breast. *Can J Surg* 1993;36(5):453-60.
30. Ghent WR, Ghent RA, Eskin BA, Ghent WR, Ghent RA, Eskin BA; Ghent WR, Ghent RA, Eskin BA; Treatment of iodine deficiency diseases. USA patent 6,019,970. 2000 Feb. 1, 2000.
31. Wright J. One mineral can help a myriad of conditions from atherosclerosis to "COPD" to zits. [cited April 3, 2007]; Available from: <http://www.tahoma-clinic.com/iodide.shtml>
32. Abraham GE. Serum inorganic iodide levels following ingestion of a tablet form of Lugol solution: Evidence for an enterohepatic circulation of iodine. *The Original Internist* 2005;11(3):112-118.
33. West B. Atrial fibrillation, arrhythmias and iodine. *Health Alert* 2006;23(6).
34. Cann SAH. Hypothesis: dietary iodine intake in the etiology of cardiovascular disease. *J Am Coll Nutr* 2006;25(1):1-11.
35. International Council for the Control of Iodine Deficiency Disorders. Finland IDD prevalence and control program data. [cited April 5, 2007]; Available from: http://indorgs.virginia.edu/iccidd/mi/idd_057.htm

36. Flechas JD. Orthoiodosupplementation in a primary care practice. *The Original Internist* 2005;12(2):89-96.
37. Health Effects: Fluoride & Bone: Density Vs. Strength. [cited April 5, 2006]; Available from: <http://www.fluoridealert.org/health/bone/density/strength.html>
38. Woeber KA, Ingbar SH. Metabolism of L-thyroxine by phagocytosing human leukocytes. *J Clin Invest* 1973;52(8):1796-803.
39. Klebanoff SJ, Green WL. Degradation of thyroid hormones by phagocytosing human leukocytes. *J Clin Invest* 1973;52(1):60-72.
40. Klebanoff SJ. Iodination of bacteria: a bactericidal mechanism. *J Exp Med* 1967;126(6):1063-78.
41. Meinhold H, Gramm HJ, Meissner W, Zimmermann J, Schwander J, Dennhardt R, et al. Elevated serum diiodotyrosine (DIT) in severe infections and sepsis: DIT, a possible new marker of leukocyte activity. *J Clin Endocrinol Metab* 1991;72(4):945-53.
42. World Health Organization. Iodine status worldwide. WHO global database on iodine deficiency. 2004 [cited April 12, 2007]; Available from: <http://whqlibdoc.who.int/publications/2004/9241592001.pdf>
43. Dunn JT, Delange F. Damaged reproduction: the most important consequence of iodine deficiency. *J Clin Endocrinol Metab* 2001;86(6):2360-3.
44. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N Engl J Med* 1999;341(8):549-55.
45. Bleichrodt N, Born MP. A metaanalysis of research on iodine and its relationship to cognitive development. In: Stanbury JB, editor. *The damaged brain of iodine deficiency*. New York: Cognizant Communication; 1994. p. 195-200.
46. Vermiglio F, Lo Presti VP, Moleti M, Sidoti M, Tortorella G, Scaffidi G, et al. Attention deficit and hyperactivity disorders in the offspring of mothers exposed to mild-moderate iodine deficiency: a possible novel iodine deficiency disorder in developed countries. *J Clin Endocrinol Metab* 2004;89(12):6054-60.
47. DeLong GR, Leslie PW, Wang SH, Jiang XM, Zhang ML, Rakeman M, et al. Effect on infant mortality of iodination of irrigation water in a severely iodine-deficient area of China. *Lancet* 1997;350(9080):771-3.
48. Cobra C, Muhilal, Rusmil K, Rustama D, Djatnika, Suwardi SS, et al. Infant survival is improved by oral iodine supplementation. *J Nutr* 1997;127(4):574-8.
49. Abraham GE. The historical background of the iodine project. *The Original Internist* 2005;12(2):57-66.
50. Abraham GE. The safe and effective implementation of orthoiodosupplementation in medical practice. *The Original Internist* 2004;11:17-36.
51. Shevin W. Clinical experience with orthoiodosupplementation. In: *Recent advances in the use of iodine in medical practice*. Scottsdale, AZ.
52. Thrall KD, Bull RJ. Differences in the distribution of iodine and iodide in the Sprague-Dawley rat. *Fundam Appl Toxicol* 1990;15(1):75-81.
53. Thrall KD, Bull RJ, Sauer RL. Distribution of iodine into blood components of the Sprague-Dawley rat differs with the chemical form administered. *J Toxicol Environ Health* 1992;37(3):443-9.

54. Sherer TT, Thrall KD, Bull RJ. Comparison of toxicity induced by iodine and iodide in male and female rats. *J Toxicol Environ Health* 1991;32(1):89-101.
55. Thrall KD, Sauer RL, Bull RJ. Evidence of thyroxine formation following iodine administration in Sprague-Dawley rats. *J Toxicol Environ Health* 1992;37(4):535-48.
56. Eskin BA, Grotkowski CE, Connolly CP, Ghent WR. Different tissue responses for iodine and iodide in rat thyroid and mammary glands. *Biol Trace Elem Res* 1995;49(1):9-19.
57. Garcia-Solis P, Alfaro Y, Anguiano B, Delgado G, Guzman RC, Nandi S, et al. Inhibition of N-methyl-N-nitrosourea-induced mammary carcinogenesis by molecular iodine (I₂) but not by iodide (I⁻) treatment Evidence that I₂ prevents cancer promotion. *Mol Cell Endocrinol* 2005;236(1-2):49-57.
58. Fuse Y, Saito N, Tsuchiya T, Shishiba Y, Irie M. Smaller Thyroid Gland Volume with High Urinary Iodine Excretion in Japanese Schoolchildren: Normative Reference Values in an Iodine-Sufficient Area and Comparison with the WHO/ICCIDD Reference. *Thyroid* 2007;17(2):145-55.
59. Abraham GE, Brownstein D. A rebuttal of Dr. Gaby's editorial on iodine. *Townsend Letter for Docotrs & Patients* 2005;Oct 2005.
60. Nagataki S. Japan: status of iodine nutrition. *Iodine Defic Disorders Newsltr* 1993;9(1):11.
61. Ward PS. History of the Gerson therapy. Contract report prepared for the U.S. Office of Technology Assessment. 1988 [cited April 12, 2007]; Available from: <http://gerson-research.org/docs/WardPS-1988-1/index.html>
62. Gerson C, Straus H. The Gerson primer. 4th ed: The Gerson Institute; 1996.
63. 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(4):840-4.
64. Pearce EN, Gerber AR, Gootnick DB, Khan LK, Li R, Pino S, et al. Effects of chronic iodine excess in a cohort of long-term American workers in West Africa. *J Clin Endocrinol Metab* 2002;87(12):5499-502.
65. LeMar HJ, Georgitis WJ, McDermott MT. Thyroid adaptation to chronic tetraglycine hydroperiodide water purification tablet use. *J Clin Endocrinol Metab* 1995;80(1):220-3.
66. Namba H, Yamashita S, Kimura H, Yokoyama N, Usa T, Otsuru A, et al. Evidence of thyroid volume increase in normal subjects receiving excess iodide. *J Clin Endocrinol Metab* 1993;76(3):605-8.
67. Zhao J, Wang P, Shang L, Sullivan KM, van der Haar F, Maberly G. Endemic goiter associated with high iodine intake. *Am J Public Health* 2000;90(10):1633-5.
68. Kasagi K, Iwata M, Misaki T, Konishi J. Effect of iodine restriction on thyroid function in patients with primary hypothyroidism. *Thyroid* 2003;13(6):561-7.
69. Abraham GE, Flechas JD, Hakala JC. Optimum levels of iodine for greatest mental and physical health. *The Original Internist* 2002;9:5-20.
70. Brownstein D. Clinical experience with inorganic non-radioactive iodine/iodide. [cited Oct 26, 2005]; Available from: http://www.optimox.com/pics/Iodine/IOD-09/IOD_09.htm

71. Vanderpas JB, Contempre B, Duale NL, Deckx H, Bebe N, Longombe AO, et al. Selenium deficiency mitigates hypothyroxinemia in iodine-deficient subjects. *Am J Clin Nutr* 1993;57(2 Suppl):271S-275S.
72. Contempre B, Dumont JE, Ngo B, Thilly CH, Diplock AT, Vanderpas J. Effect of selenium supplementation in hypothyroid subjects of an iodine and selenium deficient area: the possible danger of indiscriminate supplementation of iodine-deficient subjects with selenium. *J Clin Endocrinol Metab* 1991;73(1):213-5.
73. Obregon MJ, Escobar del Rey F, Morreale de Escobar G. The effects of iodine deficiency on thyroid hormone deiodination. *Thyroid* 2005;15(8):917-29.
74. Amster E, Tiwary A, Schenker MB. Case report: Potential arsenic toxicosis secondary to herbal kelp supplement. *Environ Health Perspect* 2007;115(4):606-608.