Lab Tests to Prevent Breast Cancer, Fibrocystic Disease, etc. with Urinalysis for Iodine Levels

Copyright 2006 by Dr. Harvey Kaltsas, A.P., D.I.M., Dipl.Ac. (NCCAOM)

Take the Test
Urinalysis has long been used by the Chinese to detect and monitor health problems, dating back at least to the 12th century. Physicians at that time would have patients urinate on rocks and then watch to see if ants gathered any sugar crystals which might have accumulated – an early diagnostic test for diabetes.

Our lab techniques have gotten quite a bit more sophisticated since, and one emerging test of profound importance is the 24 hour urine loading test for iodine.

America today is suffering from several epidemics, among them heart disease, obesity, hypothyroidism, and cancer – especially breast cancer, from which 40,200 women died in 2005. All of these conditions are significantly related to low levels of iodine, yet the Western medical community has failed to appreciate the proper role and function of this mineral in human health.

[There has been vigorous debate between two respected professionals, Dr. Alan Gaby M.D. and Dr Guy Abraham, M.D., regarding the need for iodine supplementation, and this debate is "Reprinted, with permission, from the Townsend Letter for Doctors and Patients" for your consideration. My own personal view that more iodine is needed in the American diet has been tempered by the observations of Dr. Gaby, but I still feel that more iodine is needed. However, you should make your own judgments on the matter and come to your own conclusions.]

Irregular heartbeat is already commonly treated with iodine supplementation, but with a prescription pharmaceutical variety. Non-prescription potassium iodide works better to treat this condition, without the harmful side effects associated with its pharmaceutical alternative.

Obesity in the US afflicts more than 20% of our population and is often directly related to hypothyroidism, which historically had been treated successfully and inexpensively with iodine. Research has shown that the vast majority of patients loses fat and gain muscle mass while taking adequate amounts of iodine (12.5 mg/day).

However, based upon one inconclusive study of rats performed in 1948, the pharmaceutical industry was somehow able to promote widely the notion that moderate amounts of iodine taken in the diet would promote hyper and hypothyroidism. As a result, iodine was removed as an additive to bakery products, from whence it is easily absorbed, and only added in very small amounts – just enough to prevent goiter – to common table salt.

Perhaps not surprisingly, levels of hypothyroidism surged in the 1950s and 1960s, so much so that thyroid hormone replacement medication became and continues to be the most widely prescribed pharmaceutical in the USA. In actuality, to quote a leading expert on iodine, Guy E. Abraham, MD, “the most common cause of hypothyroidism and simple goiter worldwide is iodine deficiency.” Moderate amounts of iodine in the diet allow the thyroid to function properly. On average the Japanese consume 13.5 mg. per day, primarily from seaweed, compared to Americans recommended daily intake of 150 mcg. per day, nearly 1/1000 that of the Japanese.

Dr. Gaby presents well reasoned arguments to support his viewpoints against the need for more iodine, but did the others before him who set America’s policies restricting iodine intake? Was it overt racism on the part of America’s medical community in the 40’s, 50s, and 60s to consider 13.5 mg of iodine daily a toxic dose, when this is the amount taken everyday by 60 million Japanese? Or was it simply the arrogance of
Western medical hegemony, to which we as acupuncturists have so long grown accustomed?

Hai Zao (*sargassum fusiforme*) seaweed has been safely used for many centuries in traditional Chinese medicine. Its taste and property are bitter, salty, and cold. It enters the lung, spleen, and kidney meridians and works as an expectorant, to soften lumps and hardening (as in fibrocystic disease and breast cancer), and as a diuretic. It has long been indicated for goiter, scrofula, tuberculosis of the lymph nodes, chronic bronchitis, hypotension, hypertension, and edema.

Western research has also shown iodine to be a boon to the immune system, and its commonly understood to be an effective first aid disinfectant because of its strong anti-viral, anti-bacterial properties.

This scientific ignorance/cultural arrogance on the part of the Western medical community would not be quite so galling if iodine deficiency were not so very well documented to be a principal cause of fibrocystic breast disease and breast cancer. Some mistakes are forgivable. Repeated fatal mistakes are not.

In Japan, very few women get fibrocystic breast disease and only 3% develop breast cancer. In the US over half our women develop fibrocystic disease and 13% develop breast cancer. Significantly and tragically, after women with fibrocystic breast disease start taking Synthroid, their chances of developing breast cancer double to 25%.

As practitioners of preventive and holistic health care, we can make a dramatic difference in the lives of our patients by recommending appropriate nutrients, and the testing to determine the appropriateness of iodine is both simple and inexpensive. In my clinic, we observe the following protocol.

a. A patient is given four 13.5 mg. tablets of Iodoral® to take home.
b. He/she is instructed to write the lot number of the Iodoral® on a Side Effects Reporting Form which the lab uses to compile a study on side effects [FFP Laboratory, 576 Upward Rd., Suite B, Flat Rock, N.C. 28731].
c. He/she is also given a red plastic solo cup and an orange urine collection container.
d. He/she is instructed to urinate upon waking as normal into the toilet.
e. Then he/she takes the 4 Iodoral® tablets.
f. Thereafter the patient collects all urine for the next 24 hours (including the first urine of the following morning) and places it into the orange urine collection container, which is to be kept refrigerated.
g. Once these 24 hours of urine have been collected, the patient shakes up the orange container and pours 2 ounces of urine into the small plastic bottle provided by the lab.
h. Next, the patient seals the bottle with its cap, wraps it up in a paper towel, and places it into the accompanying cardboard box.
i. The patient fills out a Results Requisition Form and also places it into the cardboard box.
j. The cardboard box is then placed into a prepaid, pre-addressed Fedex shipping envelope and delivered either back to our clinic or directly to a Kinko’s/Fedex shipping office.
k. Within two weeks FFP Labs sends results to our clinic and we report the findings and make recommendations to the patient. The CPT billing code for this lab test is 82941.

The accompanying research papers, provided with enthusiastic permission by their authors, will serve to educate you on the following topics:

**The Safe and Effective Implementation of Orthoiodosupplementation in Medical Practice,** by Guy E. Abraham, M.D., title self-explanatory.

**The Concept of Orthoiodosupplementation and Its Clinical Implications,** by Guy E. Abraham, M.D., discusses the various natural forms of iodine, sources of iodine in nature, iodine metabolism in humans, thyroidal metabolism of iodide, extrathyroidal metabolism of iodide, the concept of orthoiodinosupplementation, clinical implications, and misinformation to be found in medical textbooks.

**Serum Inorganic iodide Levels Following Ingestion of a Tablet Form of Lugol Solution: Evidence of an Enterohepatic Circulation of Iodine,** by Guy E. Abraham, M.D., title self-explanatory.

**The historical background of the Iodine Project,** by Guy E. Abraham, M.D., provides a historical overview of the clinical use of iodine in therapy.

**The Wolff-Chaikoff Effect: Crying Wolf?** by Guy E. Abraham, M.D., explains how one erroneous study from 1948 became the basis for a medical aversion to iodine. This iodinophobia has persisted for nearly the past sixty years and serves to underpin America’s reliance on synthetic thyroid hormone replacement medication.

**Orthoiodosupplementation in a Primary care Practice,** by Jorge Flechas, M.D., is a review of the pathologies caused by iodine deficiency and a recounting of the remarkable responses patients have demonstrated to iodine supplementation.

**Clinical Experience with Inorganic Non-radioactive Iodine/Iodide,** by David Brownstein, M.D., focuses on one doctor’s extraordinary results using Inorganic Non-radioactive Iodine/Iodide particularly in treatment of thyroid problems, fibrocystic breast disease, and polycystic ovarian syndrome.

**Debate between Drs. Alan Gaby and Guy Abraham on Iodine** - "Reprinted, with permission, from the Townsend Letter for Doctors and Patients."

After reading these documents and the enclosed laboratory submission protocols, please take this knowledge into your practice and make an even greater difference in the quality of your patients’ lives.
Orthoiodosupplementation in a Primary Care Practice

Jorge D. Flechas, M.D.

This article will focus on my experience with the use of inorganic non-radioactive iodine/iodide, thereafter referred to as iodine in a primary care practice. My medical practice is situated in the Appalachian Mountains close to Asheville, North Carolina. This area is considered to be a goiter belt. One of the major problems that we encounter in this location is a problem with hypothyroidism. Back in 1997 hypothyroidism involved 11.7% of the U.S. population (1). By 1994 severe iodine deficiency also involved 11.7% of the population (2). Both of these studies were done at separate times by separate groups showing the exact number of 11.7%. This reinforces what we were taught, that iodine deficiency goes hand in hand with the manifestation of hypothyroidism. I have on a weekly basis at least one phone call from a healthcare practitioner questioning whether the intake of iodine causes hypothyroidism and goiter. I often have to go back over the basics of thyroid physiology with these healthcare practitioners, and explain to them that iodine is essential for normal thyroid functions and that it is the manmade organic forms of iodine that are toxic (3).

My practice is family medicine with an integrative medicine twist. I have been using iodine supplementation in my practice over the last four years in amounts needed for whole body sufficiency (orthoiodosupplementation). Orthoiodosupplementation is the daily amount of iodine required for whole body sufficiency (3-5). Whole body sufficiency for iodine is assessed by an iodine/iodide loading test (3). Prior to implementing orthoiodosupplementation, I perform a complete history and physical examination. During a physical examination, I always check the patient’s thyroid. If a mass is picked up on physical then another test that I order is an ultrasound of the thyroid. While undergoing ultrasound to evaluate the mass I will have my technician measure the thyroid volume. Each lobe will have its length measured in centimeters, width measured in centimeters and height measured in centimeters. All three measurements are multiplied times each other and this gives the volume in cubic centimeters. Due to the non-spherical shape of each lobe a correctional factor of 0.52 is used. The two lobe volumes are added together for the total thyroid size. A total volume of 18 cc or more is considered a goiter (6). A volume size of 5 cc or less is suggestive of thyroid atrophy, another manifestation of iodine deficiency.

Any solid mass that is picked up on ultrasound and shows itself to be greater in size than one centimeter by one centimeter will require a radioactive I123 uptake and scan. This test should be done previous to starting any patient on iodine if a nodule is suspected. A nodule that does not pick up radioactive iodide is considered to be a cold nodule and would suggest the presence of thyroid cancer. A needle biopsy of the cold nodule should be done by an E.N.T. doctor, general surgeon or endocrinologist. If cancer is present the thyroid gland should be surgically removed. Thyroid carcinoma is the most common malignancy of the endocrine system. Malignant tumors derived from the follicular epithelium are classified according to histological features.

The incidence of thyroid cancer is approximately nine per 100,000 in the population per year and this usually increases with age plateau after about age 50. Age is also an important prognostic factor. Thyroid cancer at a young age (less than 20) or in older people (greater than 65) is usually associated with a worse prognosis. Thyroid cancer is twice as common in women as men but the prognosis is worse in men. Additional important risk factors include a history of childhood head or neck irradiation, large nodule size greater than four centimeters, evidence for local tumor fixation or invasion into lymph nodes, and the presence of metastasis (7). In my small practice of around 5,000 patients, I have found five thyroid cancers in one year. If multiple nodules of the thyroid gland are found at the time of ultrasound then the diagnosis of multinodular thyroid goiter is considered even if the gland is normal in size.
I request serum T₄ (the main hormone produced by the thyroid), free T₃ (the biologically active thyroid hormone at the cellular level) and a thyroid stimulating hormone (TSH) level. The T₄ level inside the cell correlates very well with the free T₃ that is in the serum (7). Following orthoiodosupplementation, serum T₄ and TSH levels usually go down and free T₃ stays steady (6). I have seen TSH sometimes go up rather than down while T₄ and free T₃ did not change or may have gone up some. This does not mean that the patient was developing hypothyroidism but that the brain was stimulating the body to make more sodium iodide symporters (NIS). The NIS are channels in the cell membrane that transport atoms into a cell as compared to a calcium channel or a sodium channel or a chloride channel where the channel only admits one atom to go through. The NIS transports sodium iodide into cells and has been found in all cell lines tested so far. Thyroid stimulating hormone, prolactin and oxytocin have been found to stimulate the making of NIS (8). While taking iodide, one may see an elevated TSH but we have to recognize that this is not a bad thing. TSH has many actions outside the thyroid that have been discovered (7). While taking iodine, the vast majority of patients lose fat and gain muscle weight (4,5). Very rarely has weight gain occur. Often a check of the patient’s T₄, free T₃ and TSH shows the T₄ to go down, free T₃ going down and TSH going up. Iodide is an essential nutrient that is absorbed by all cell lines. Its highest concentration is seen in the thyroid.

The nutritional status of the patient will determine its response to orthoiodosupplementation (3). It is crucial that the thyroid gland has plenty of antioxidants in its cells and many other nutrients. We have found that giving a multivitamin for women with PMS (Optivite®) improves the response to orthoiodosupplementation. One of my patient’s is a classic example of the above scenario. She is a CNA who is 5’1”. At the time she started taking iodine, she experienced an increase in appetite. Within a short period of time, six to eight weeks she gained about 15 pounds. She then was started on this supplementation. Within six weeks the patient lost 15 pounds with a decrease in her appetite.

Breast tissue has an affinity for iodine (4,9-14). Iodine deficiency causes fibrocystic breast disease (FBD) with nodules, cyst enlargement, pain and scar tissue (13,14). FBD can be characterized by a lumpy painful breast, generally in reproductive aged women. Initially, this syndrome occurs in the premenstrual phase of at least one cycle or involves the whole cycle. These symptoms can also occur in menopausal women on estrogen therapy. In 1928 an autopsy series reported a three percent incidence of FBD, whereas in 1973 an autopsy report quoted an 89% incidence (7). A review by the American Academy of Pathology gives a minimum incidence for FBD of 50% but suggests that 80% of North American women are afflicted with the syndrome during their reproductive lifetime (15).

Ghent et al in 1993, presented data showing that iodine works great to reduce (FBD)(14). He was able to develop a protocol and a scoring system that helps doctors assess how severe a woman’s FBD is. I would recommend that this scoring system be utilized by physicians in their own medical practice. A precise method of recording the patient’s data will help both physicians and patients see the improvement that occurs following orthoiodosupplementation. This simple method numbers the quadrants of each breast one to four. The pathological changes that can occur in FBD are noted as micronodularity, tenderness, fibrous tissue plaques, macrocysts and turgidity. The presence or the absence of changes is recorded. For example if the micro nodularity of macrocysts disease was present in the upper half of the breast the numerical score would be one for micro nodularity and two for the two breast quadrants scoring a total of three. If all five changes occurred in all quadrants in one breast the score would be 4 (all four breast quadrants) x5 (all five changes) equals 20 and for both breasts would be 40. Patients are also encouraged to evaluate their own symptomology as expressed by a number of zero equals symptoms worse, one equals symptoms unchanged, two equals less pain only premenstrual discomfort, three equals no pain unable to predict menstruation. The subjective scoring system was employed and graded as follows. Zero equals no palpable abnormalities normal, one equals score of less than 7.2 and a score greater than 7 but less than the pretreatment score and three equals a score greater than the pretreatment score (See Table I).
Table I

<table>
<thead>
<tr>
<th>Right Breast Quadrants</th>
<th>Score</th>
<th>Left Breast Quadrants</th>
<th>Score</th>
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<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Micronodularity</td>
<td>Micronodularity</td>
<td></td>
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<tr>
<td>Tenderness</td>
<td>Tenderness</td>
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<tr>
<td>Fibrous Tissue (Plaques)</td>
<td>Fibrous Tissue (Plaques)</td>
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<tr>
<td>Macrocysts</td>
<td>Macrocysts</td>
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<tr>
<td>Turgidity</td>
<td>Turgidity</td>
<td></td>
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<tr>
<td><strong>Total Score</strong></td>
<td><strong>Total Score</strong></td>
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Sum of both Total Scores = __________

In my practice, I have over the last four years worked with some 200 women who have FBD. On average, patients come to my office practice with a mean Ghent score of 15.7 and an average age of 41.4 years. On 12.5 mg of iodine, the score after six months will drop from a mean of score 15 down to about 12.8. On 25 mg, the score will drop down to a mean of score is 10.2. On 37.5 mg the score was 8.6. When we prescribe 50 mg of Iodoral® (4 tablets) for 3 to 6 months, the average patient will have a score of 7.6 with a p-value less than 0.001 compared to baseline scores. After a full year at 50 mg iodine per day (4 tablets of Iodoral®), the patients mean score dropped to 3.8. We saw many patients with a score of zero, meaning no evidence of FBD. We often see patients’ breast pain disappear in a 1 to 30 days at a dose of 50 mg. At lower doses, the pain persisted for a much longer time. The other findings of micronodularity, tenderness, fibrous tissue plaques, macrocysts and turgidity will take almost a full year to fully go away. Ghent felt that a score of seven or below was normal. We did not see any of the patients reach the score of zero, meaning the absence of all of the pathological symptoms and physical findings of fibrocystic breast disease while taking between 12.5 to 37.5 mg per day. Once FBD is gone, a patient may opt to drop iodine intake to 12.5 to 25 mg per day. There is a chance that the cysts will return. Optimum amount for most patients for FBD is 50 mg (4 tablets) per day continued indefinitely. Monitoring the patient’s serum TSH, T₄ and free T₃ is done every three to six months. We did not see any major changes in serum T₄, TSH and free T₃ in these patients.

It was while treating a large 320-pound woman with insulin dependent diabetes that we learned a valuable lesson regarding the role of iodine in hormone receptor function. This woman had come in via the emergency room with a very high random blood sugar of 1,380 mg/dl. She was then started on insulin during her hospitalization and was instructed on the use of a home glucometer. She was to use her glucometer two times per day. Two weeks later on her return office visit for a checkup of her insulin dependent diabetes she was informed that during her hospital physical examination she was noted to have FBD. She was recommended to start on 50 mg of iodine (4 tablets) at that time. One week later she called us requesting to lower the level of insulin due to having problems with hypoglycemia. She was told to continue to drop her insulin levels as long as she was experiencing hypoglycemia and to monitor her blood sugars carefully with her glucometer. Four weeks later during an office visit her glucometer was downloaded to my office computer, which showed her to have an average random blood sugar of 98. I praised the patient for her diligent efforts to control her diet and her good work at keeping her sugars under control with the insulin. She then informed me that she had come off her insulin three weeks earlier and had not been taking any medications to lower her blood sugar. When asked what she felt the big change was, she felt that her diabetes was under better control due to the use of iodine. Two years later and 70 pounds lighter this patient continues to have excellent glucose control on iodine 50 mg per day. We since have done a study of twelve diabetics and in six cases we were able to wean all of these patients off of medications for their diabetes and were able to maintain a hemoglobin A1C of less than 5.8 with the average random blood sugar of less than 100. To this date these patients continue to have excellent control of their Type II diabetes. The range of daily iodine intake was from 50 mg to 100 mg per day. All diabetic patients were able to lower the total amount of medications necessary to control their diabetes. Two of the twelve patients were controlled with the use of iodine plus one medication. Two patients have control of diabetes...
with iodine plus two medications. One patient had control of her diabetes with three medications plus iodine 50 mg. The one insulin dependent diabetic was able to reduce the intake of Lantus insulin from 98 units to 44 units per day within a period of a few weeks.

In the Type 1 diabetics that we have been following we have noted that if C-peptide is measurable, this would suggest that the individual is making their own insulin. I have been able to help this group of patients to get off insulin or to greatly reduce the amount they need for good glucose control with Iodoral® at 4 tablets/day (50 mg). If C-peptide is absent then we feel there is no insulin being produced and we have not been able to help this particular group of patients to get off their insulin. We have been able to help these patients lower the total amount of insulin needed to control their glucose.

When patients take between 12.5 to 50 mg of iodine per day, it seems that the body becomes increasingly more responsive to thyroid hormones (3-5). T3 and steroid hormones show the same family of receptors as hydrophobic small molecules (16). Clur (17) has postulated that iodination of tyrosine residues in the hydrophobic portion of these receptors normalize their response to the corresponding hormone. Optimal intake of iodine in amounts two orders of magnitude greater than iodine levels needed for goiter control may be required for iodination of these receptors (4). Insulin resistance is on the increase. The insulin receptor tyrosine kinase plays a major role in signal transduction distal to the receptor as the primary event leads to subsequent phosphorylation of cytoplasmic proteins, called insulin receptors substrate proteins (IRS). The IRS proteins are cytoplasmic proteins, with multiple tyrosine phosphorylation sites, and phosphorylation of IRS proteins has been implicated as the first post receptor step in insulin signal transmission. The IRS proteins have been referred to as the metabolic switch of the cell (18).

Another organ that can concentrate iodine is the liver. An enterohepatic circulation of iodine has been reported recently (19). I have one patient with liver fatty infiltration who had varicosities of the esophagus with bleeding. Once she started on iodine for FDB we noticed that her GI bleeding stopped and the varicose veins of her stomach and esophagus disappeared.

Iodine deficiency may cause the ovaries to develop cysts (20), nodules and scar tissue. At its worse this ovarian pathology is very similar to that of polycystic ovarian syndrome (PCOS). As of the writing of this article I have five PCOS patients. The patients have successfully been brought under control with the use of 50 mg of iodine per day. Control with these patients meaning cysts are gone, periods every 28 days and type 2 diabetes mellitus under control.

Ideally, all patients should have an iodine loading test prior to orthoiodosupplementation. This test is one in which 50 mg of iodine is given after discard of the first morning void. All urine is collected for the next 24 hours including the first morning urine void the next day. The urine sample is then sent to my laboratory, FFP Laboratory for testing (21). The lab is a CLIA approved high complexity testing laboratory in the state of North Carolina. The testing that is done is using the method as described in previous articles (19). To date we have done over 3,000 loading tests. Iodine therapy is then instituted using 50 mg/day. The body becomes iodine sufficient in about three months. Please be aware of the difference between micrograms (mcg) and milligrams (mg). One milligram is equal to 1,000 micrograms. The majority of the loading tests that are performed at FFP Lab are on women ages 31 – 70 years old. In 667 patients analyzed, the mean level of excretion was about 18 mg for all age groups. No patient achieved whole body sufficiency prior to orthoiodosupplementation. The mean excretion drops, as the population gets older (See Fig. 1-6). This suggests that of a total 50 mg of iodine given, the patients on the average retained a mean of 32 mg into their body on the first go around.

We have received many comments over the last two years. Following orthoiodosupplementation, patients have described vivid dreams, dissipated depression, no more cold extremities, more energy and less fatigue.
Patients have noticed an overall feeling of well-being. Patients have noticed a loss of weight. One patient after taking four pills of iodine lost eight pounds of fluid weight in 24 hours. We have had patients note better bowel function. Patients who have been constipated for over ten years have now noted daily bowel movements. We have also had patients noted relief from leg cramps at night. In less than 1% of all the patients treated with I, have we seen an allergic reaction. More often than not, the allergic reaction is hives. After treating over 1,000 patients with iodine, I have at no time seen the Wolff-Chaikoff Effect.

Iodine induces apoptosis and inhibits cells from forming cancer. The absence of iodine in the thyroid causes goiter (3,4). Goiter is associated with breast cancer, stomach cancer, esophageal cancer, ovarian cancer and endometrial cancer (22-24). It is felt by many researchers that the absence of iodine is a promoter of cancer. I feel that those patients with the lowest excretion rates and the highest absorption of iodine on the iodine loading test are the ones with the highest risk for development of cancer. From literally hundreds of phone interviews with patients over the last two years, the levels of iodine excretion that seem to raise the highest alarm are those in which the excretion is somewhere around 10 mg or less per 24 hours in patients age 35 and up. My observations at this point show that there is a definite increase in the incidence of breast cancer, stomach cancer, ovarian cancer or thyroid cancer. If a patient has the iodine loading test and has an iodine excretion of 10 mg or less in a 24-hour period, I initiate a cancer workup. In 1976, a JAMA article showed that 6% of the female population was at risk for breast cancer (25). Women who received thyroid supplementation doubled their risk of breast cancer to 12%. The age groups we used to separate the patients in Figures 1-6 were based on this article. As women get older, the risk of breast cancer increases. In Figures 2-6 the iodine/iodide loading test shows that the older the women are, the lower the rate of iodine excretion.

Reference List


Clinical Experience with Inorganic Non-radioactive Iodine/Iodide

David Brownstein, M.D.

I have been interested in iodine supplementation for years. I have a holistic family practice in West Bloomfield, Michigan. Michigan resides in the Goiter Belt of the United States where the soil is deficient in iodine. Although I long suspected iodine deficiency in many of my patients, my initial uses of potassium iodide gave suboptimal results. Some patients did improve, but many did not notice any appreciable improvement. This article was written to assist the reader in implementing orthiodosupplementation in their practice. This article will be divided into 2 parts: Part I will describe a doctor's (your author) introduction and education about the clinical uses of iodine while Part 2 of this article will give the reader 'clinical pearls' about how to integrate and use iodine in their practice.

Part I: A Doctor's Introduction and Education about the Clinical Uses of Iodine.

Approximately one and a half years ago, I read a letter to the editor in the Townsend Letter for Doctors and Patients titled “Iodine Supplementation Markedly Increases Urinary Excretion of Fluoride and Bromide”. In this letter, Dr. Guy Abraham described the iodine/iodide loading test and its value at assessing whole body sufficiency for iodine. In addition, the article describes the detoxification effects of the toxic halogens, bromide and fluoride when iodine is in the orthiodosupplementation range. I was intrigued at the idea of not only measuring body iodine levels but using a combination of iodine and iodide rather than using iodide alone. This started me on a long journey of researching and learning all that I could about iodine deficiency and iodine supplementation. Dr. Abraham was instrumental in teaching me about iodine.

One and a half years ago, I began testing my patients for the loading test. Although I expected lowered body iodine levels, I was not ready for the magnitude of the results. After testing over 500 patients, I found that 94.7% of my patients are deficient in inorganic iodine. Many of these patients were already being treated by me for thyroid and other endocrine imbalances, including SSKI. When physiologic doses of iodine/iodide were added to their regimen, many of these patients showed dramatic improvement in their condition, especially patients who were non-responders, even though some were taking SSKI.

The illnesses that iodine/iodide has helped are many. These conditions include Fibromyalgia, thyroid disorders, chronic fatigue immune deficiency syndrome, autoimmune disorders as well as cancer. Most patients who are deficient in iodine will respond positively to iodine supplementation. In fact, I have come to the conclusion that iodine deficiency sets up the immune system to malfunction which can lead to many of the above disorders developing. Every patient could benefit from a thorough evaluation of their iodine levels.

Iodine deficiency is often thought of as synonymous with thyroid malfunction, particularly with the development of goiter. The research is clear that iodine deficiency can lead to cysts and nodules of the thyroid gland. David Marine reported the benefits of treating school-aged children with iodine/iodide (Lugol’s solution) nearly 70 years ago. Marine looked at two groups: a control group and a treatment group, which received 9mg/day of iodine/iodide. The iodine/iodide treatment group had a 0.2% incidence of goiter while the control group had a 22% goiter—a 110x difference. This was the first U.S. iodine study showing the decline of goiter formation with the use of iodine. Shortly after this study, iodized salt was initiated which was a great success in eliminating goiter in the U.S.

In medical school, little was taught about iodine. Specifically, we were taught that the iodization of salt was implemented to prevent goiter and therefore no further iodine was necessary in the diet. After studying the
literature on iodine, I realized what I was taught in medical school was incorrect. The iodization of salt was adequate to lessen the prevalence of goiter, but it did not address the rest of the body’s need for iodine.

When I began testing my patients for iodine levels, I was amazed at the prevalence of iodine deficiency. As previously stated, 94.7% of my patients have tested low for iodine. I have noticed those patients with chronic illnesses, from autoimmune disorders to cancer, often have lower iodine levels as compared to relatively healthy patients.

I was initially hesitant to use higher (>1mg) doses of iodine due to my concern about causing adverse effects. In reviewing much of the literature there was concern about larger doses of iodine causing hyperthyroid symptoms. However, a further, more exhaustive review of the literature failed to prove that iodine, in milligram doses ever was shown to cause hyperthyroid symptoms. In fact, as iodine levels have fallen over 50% in the last 30 years in the United States, autoimmune disorders and hyperthyroid symptoms have been increasing at near epidemic proportions.3

After testing individuals and finding low iodine levels, I began to use smaller milligram amounts of iodine/iodide (6.25mg/day). Upon retesting these individuals 1-2 months later, little progress was made. I therefore began using higher milligram doses (6.25-50mg) to increase the serum levels of iodine. It was only with these higher doses that I began to see clinical improvement as well as positive changes in the laboratory tests.

Why would people need the larger doses of iodine? Why have iodine levels fallen 50% in the last 30 years? As I pondered these questions, I came to the conclusion that the toxicity of modern life must be impacting iodine levels. It is well known that the toxic halides, fluoride and bromide, having a similar structure as iodine, can competitively inhibit iodine absorption and binding in the body.

A study was performed in my office to look at the iodine levels as well as the toxic halogen levels bromide and fluoride in 8 random patients. None of the patients had been treated with iodine before the study. The patients were studied at baseline to look not only at their iodine levels but also their bromide and fluoride levels. Next, after taking a loading dose of iodine (50mg of iodide/iodine--Iodoral®) they were rechecked for their levels of iodine, bromide and fluoride. The patients then took a loading dose of iodine (50mg of iodide/iodine--Iodoral®) for 30 days and they repeated a 24-hour urine collection. The results are summarized in Table 1 below.4

<table>
<thead>
<tr>
<th>Table 1: Average Measurement of Urinary Excretion of Halides with Iodine Supplementation in 8 Patients (From Ref. 4)</th>
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<tbody>
<tr>
<td>Mg Excreted/24 Hours</td>
</tr>
<tr>
<td>Bromide</td>
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<td>Fluoride</td>
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<td>Iodide</td>
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</table>

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As can be seen from Table 1, little iodine was secreted at baseline. The data indicates that all of these patients were iodine deficient at baseline. After ingesting 50mg/day of an iodide/iodine supplement (Iodoral®), repeat testing was done on day 1 and after 30 days of supplementation. As iodine was supplemented, as expected, the excretion of iodine increased—from 40.2% to 66.15%. Increasing the iodine load also increased the excretion of the toxic halides bromide and fluoride.

This study showed that the body was adapting to the iodine load and becoming saturated with iodine while at the same time detoxifying from the toxic halides bromide and fluoride. This study provided me with the answer to the two questions previously posed. Because of the elevated levels of toxic halides in the environment and in the food supply, iodine levels have not only fallen but larger amounts of iodine are necessary to correct iodine deficiency as well as to promote a detoxifying effect of heavy metals.

As I started to use larger doses of iodine (12.5-50mg/day), I began to see positive results in my patients. Goiters and nodules of the thyroid shrunk. Cysts on the ovaries became smaller and began to disappear. Patients reported increased energy. Metabolism was increased as evidenced by my patients having new success in losing weight. Libido improved in men and women. People suffering with brain fog reported a clearing of their foggy feelings. Patients reported having vivid dreams and better sleep. Most importantly, those with chronic illnesses that were having a difficult time improving began to notice many of their symptoms resolving.

Betty, a 65 year-old female, saw me for fatigue and a swelling of her neck. Betty was taking Synthroid for a hypothyroid condition and was euthyroid via lab tests at the initial visit. Betty’s main complaint was fatigued. “I always feel tired. I wake up tired and I go to bed tired,” she complained. Upon physical exam, the thyroid was estimated to be 2x normal size and multiple nodules were palpated bilaterally. The left lobe had a nodule estimated on palpation to be 1.5cm in size. Betty was sent for a thyroid ultrasound which reported “multiple thyroid nodules bilaterally and a cystic nodule in the isthmus with overall dimensions of 1.9x0.7x1.3cm containing a heterogeneous area in its inferior aspect measuring 6mm. Betty was sent for a biopsy of the large nodule. While awaiting a biopsy, an iodine loading test was performed which showed a 50% excretion (normal >90%). She was promptly started on 50mg iodine/iodide (Iodoral®). After taking the iodine/iodide pills for 6 weeks, Betty went for the ultrasound-guided biopsy. The radiologist reported that “the borders of the nodular area were difficult to delineate with certainty. Due to this difficulty in clearly delineating the margins, I felt that it would be difficult to biopsy and that follow up of this lesion was recommended.” Six weeks of iodine/iodide therapy had significantly improved her condition to the point of not needing a biopsy! Betty’s story has been repeated over and over in my practice over the last two years.

The breasts are the second main glandular storage site for iodine next to the thyroid gland. The relationship between breast illness and iodine deficiency has been reported for over 100 years. Iodine concentrates in the breast and is secreted from the breast. Normal breast architecture will not develop when there is iodine deficiency present. Diseased breast tissue has been shown to take up more iodine compared to healthy breast tissue. The higher uptake in the abnormal breasts indicates a greater deficiency of iodine is present compared to normal breasts.

Maryann is a 45 year-old R.N. who has been a patient of mine for five years. I diagnosed Maryann with hypothyroidism five years ago and she was being treated with Armour Thyroid. Her hypothyroid conditions (fatigue, hair falling out, etc.) improved significantly with thyroid replacement and she was presently euthyroid. Maryann was also suffering from fibrocystic breast disease. “I was thinking about a mastectomy. I can’t wear a bra because my breasts are so tender,” she said. Maryann was told to avoid caffeine and go on birth control pills to treat the cystic breasts. She could not tolerate the birth control pills and received minimal improvement from dietary changes. When I checked an iodine loading test, Maryann was found to...
be very low on iodine (27% excretion—normal >90%). Within three weeks of taking 50mg of iodide/iodine (Iodoral®), all her breast symptoms were improved. She said, “My pain level declined immediately and after three weeks, it was 70% better. I can now wear a bra without pain.” Two months later, a physical exam revealed no signs of fibrocystic breasts and she was now completely pain free. “I am ecstatic. I can now exercise and I feel just wonderful,” Maryann said.

Iodine/iodide supplementation has markedly improved the course of illness in fibrocystic breasts in almost all of my patients with fibrocystic breast disease. In addition those with breast cancer also improve. Nodules and fibrous changes of the breasts significantly improve in a short time period. I believe that the epidemic of breast disease we are seeing in this country is due, in no small part, to iodine deficiency.

There are many other illnesses also improved with iodine therapy. Table 2 gives examples of some of these illnesses.

<table>
<thead>
<tr>
<th>Table 2: Conditions Treated With Iodine</th>
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<tbody>
<tr>
<td>Breast Disease</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Dupuytren’s Contracture</td>
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<tr>
<td>Excess Mucous Production</td>
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<tr>
<td>Fatigue</td>
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<tr>
<td>Fibrocystic Breasts</td>
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<tr>
<td>Hemorrhoids</td>
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<tr>
<td>Headaches and Migraine Headaches</td>
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<tr>
<td>Infections</td>
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<tr>
<td>Keloids</td>
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<tr>
<td>Ovarian Cysts</td>
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<tr>
<td>Parotid Duct Stones</td>
</tr>
<tr>
<td>Peyronie’s</td>
</tr>
<tr>
<td>Sebaceous Cysts</td>
</tr>
<tr>
<td>Thyroid Disorders</td>
</tr>
<tr>
<td>Vaginal Infections</td>
</tr>
</tbody>
</table>

Iodine has many positive therapeutic actions. It is a potent anti-infective agent. No virus, bacteria or parasite has been shown to be resistant to iodine therapy. I have found that providing adequate iodine to provide the body with iodine sufficiency markedly decreases the number and severity of infections in these patients. Table 3 lists some of the other therapeutic actions of iodine.

<table>
<thead>
<tr>
<th>Table 3: Therapeutic Actions of Iodine and Conditions Iodine Can Treat</th>
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<tbody>
<tr>
<td>Therapeutic Actions</td>
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<tr>
<td>Antibacterial</td>
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<tr>
<td>Anticancer</td>
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<td>Antiparasitic</td>
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<tr>
<td>Antiviral</td>
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<tr>
<td>Mucolytic Agent</td>
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</tbody>
</table>
My clinical experience with using physiologic doses of iodine/iodide (6.25-50mg/day) has been very positive. To date, in my practice, my partners and I have treated over 3,000 patients. The side effects with using these doses have been minimal. Rarely, have I observed iodism (metallic taste in mouth, frontal sinus pressure/pain, and increased salivation). Iodism is easily rectified by adjusting the dose of iodine down or simply telling the patient to await the resolution of these symptoms which takes approximately 1-3 weeks. True iodine allergy to inorganic, non-radioactive iodine is very rare. In treating over 3,000 patients, I have found three patients with "allergy" to non-radioactive inorganic iodine/iodide. An acupressure technique, NAET (NAET.com) has proven very effective to reverse this allergy. Allergy to fish, shellfish or radioactive iodine does not mean there is an allergy to inorganic non-radioactive iodine. In fact, true inorganic iodine allergy is very rare.

Part II: Clinical Pearls

Who should be checked for iodine deficiency?
A: Iodine deficiency is wide-spread. The National Health and Nutrition Survey undertaken by the CDC showed iodine levels falling over 50% in the last 30 years. All patients with chronic illness need to be assessed for iodine status.

How Do You Check Iodine Levels?
A: Urine iodide levels are the accepted method.

Can you do spot urine iodide levels?
A: Yes. This provides information on the iodine status of the body, especially if the patient is not taking any iodine as a supplement. I have found this test very useful.

Should you do an iodine/iodide-loading test?
A: Yes. An iodine/iodide loading test provides useful information on the iodine status of the body. If there is severe iodine deficiency, the body would be expected to hold on to more of the ingested iodine. When there is iodine sufficiency present, 90% of the ingested iodine (50mg) will be excreted.

Should you use iodide only products?
A: No. My experience has clearly shown that iodide only products (SSKI) are inferior to iodine/iodide products. Different tissues of the body will preferentially bind different forms of iodine.

How much iodine do you start with?
A: If there is severe deficiency, spot urine iodine levels at or near zero or low iodine loading tests results (<50% excretion), higher iodine levels are generally needed. To maximize absorption and retention of iodine, doses of 25-50mg may be needed in patients. The sodium-iodine symporter, which pumps iodine into the cells against a gradient will achieve a maximal response when serum iodine levels approach 10^-3 - 10^-6 M concentration.

What are the side effects of iodine?
A: The most common side effects encountered are; acne, metallic taste in mouth, sneezing, excess saliva and frontal sinus pressure. These reactions are relatively rare, occurring in less than 5% of patients.

What about iodine allergy?
A: My experience has shown true allergy to inorganic, non-radioactive iodine is very rare. Out of over 3,000 patients treated with iodine I have found 3 with a true allergy exhibiting symptoms of a skin rash. These patients were treated with NAET (www.naet.com), an acupressure treatment and two were able to overcome their allergy and take the iodine. One of the three above patients has not been able to take iodine due to an allergy.

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Does an allergy to shellfish or radioactive iodine imply an allergy to inorganic non-radioactive iodine?  
A: No. An allergy to organic iodine does not imply an allergy to inorganic non-radioactive iodine.

If someone is on thyroid medication, can they still take iodine?  
A: Yes. The body needs adequate amounts of iodine to properly utilize thyroid hormone. Those individuals already on thyroid medication may need to lower their dose of thyroid medication upon starting iodine therapy. My experience has shown that 1/3 of patients currently taking thyroid medications will need to lower their dose of thyroid hormone after starting iodine supplementation.

How do you know when to lower their dose of thyroid medication?  
A: If the patient exhibits signs of too much thyroid hormone (palpations, nervousness, etc.), it is time to lower the dose. Generally, I have found in those patients on thyroid medication where the addition of iodine causes hyperthyroid symptoms, a 50% reduction in the dose of thyroid hormone will rectify the problem. If the patient is on a low thyroid dose (i.e., <1 grain of desiccated thyroid or <.088mg Levothyroxine), the addition of therapeutic doses of iodine can result in the patient not needing to take any thyroid medication.

Finally, the use of inorganic, non-radioactive iodine has been a wonderful addition to my practice. The use of iodine doses in the ranges described in this article have been used by our medical predecessors and by different cultures safely and effectively. I encourage physicians to check their patients for their iodine status and to correct iodine deficiency when it is present.


2 JAMA. 1937, 108:860-864

3 CDC. NHANES study 1971-2000


5 Eskin. OB-GYN. 1974;44:398-402
The Concept of Orthoiodosupplementation and Its Clinical Implications

by Gay E. Abraham, MD

Introduction

Recommended daily allowance (RDA) of elemental iodine by the Food and Nutrition Board of the National Academy of Sciences was not established in 1980, and it was not confirmed until 1989.1

That year, 1989, the Executive Director of the International Council for Control of Iodine Deficiency Disorders, published a book entitled The Story of Iodine Deficiency.2 In that book, goiter and cretinism were the only aspects of iodine deficiency discussed. One would imagine that the experts on human requirements for iodine already figured out the amounts of iodine needed for the prevention and control of cretinism endemic goiter). However, the 1930 statement of Simpson, et al,3 is still valid today: “The normal daily requirement of the body for iodine has never been determined.” In the ninth edition of the classic textbook of nutrition, Modern Nutrition in Health and Disease, edited by Haskell, et al, and published in 1999, the section on iodine written by no less than Basil S. Hetzel and coauthored by Graeme A. Clugston.4 They reported the latest recommended intakes of iodine established in 1996 by the World Health Organization (WHO), based on age and physiological conditions. The highest recommended daily intakes are for pregnant and lactating women — 200 mcg per day. In a subsection entitled “Iodine toxicity,” the authors stated: “Wolff5 has suggested that human intakes of 2,000 mcg I/day should be regarded as excessive or potentially harmful.” Please note, the unit mcg is used instead of mg in order to make the amount appear really excessive.” For example, if they used the unit mg, that would be 2,000,000 mg, a number that would scare everybody. Reference 39 in this citation was authored in 1969 by the world famous thyroidologist, I. Wolff,6 coauthor of the world famous Wolff-Chaikoff effect published in 1948.6 There was a fly in the Wolff-Chaikoff ointment, however.

Ghent's study did not confirm Wolff's prediction that daily iodine intake of 2,000 mcg (2 mg) was "excessive and potentially harmful" as quoted by Hetzel and Clugston.4 Based on academic credentials and reputation, the opinion of thyroidologist Wolff, from the National Institute of Health, would prevail over the findings of Canadian gynecologist Ghent. However, being interested in facts only, not in preconceived opinions of famous thyroidologists, this author initiated an extensive search of the literature on iodine in medicine.

The concept of orthoiodosupplementation is the outcome of this intensive literature search, which started seven years ago, combined with some original clinical research performed by the author. The clinical aspects of this research were performed under contract at the Flechas Family Practice Clinic in Hendersonville, North Carolina under the supervision of Jorge D. Flechas, MD, and funded with grants from Optimox Corporation. The author designed the protocols and monitored the progress and completion of each project. Informed consent was obtained from all the subjects participating in these projects. Pilot studies were performed with tablets containing Lugol solution in amounts per tablet ranging from 1 to 12.5 mg and compounded by John C. Hakala, RPh, from Hakala Apothecary in Lakewood, Colorado. The results of some of these projects have been published,8-12 with Flechas and Hakala as coauthors in two publications.10,11

From a review of the published data, it soon became evident that medical textbooks contain several vital pieces of misinformation about the essential element iodine, which may have caused more human misery and death than both world wars combined.8,9 The purpose of this manuscript is to present some useful information about iodine and to discuss the concept of orthoiodosupplementation in more detail than in previous publications.9,11 This manuscript was written in response to a request from the eclectic and altruistic physician, a recent collaborator on the iodine project, David Brownstein, MD, to expand further on the concept of orthoiodosupplementation with more details than in the previous publication9 in order to help the practicing physician fully appreciate the impact of this concept on their practice. Dr. Brownstein recently wrote a book about his experience with the implementation of orthoiodosupplementation in his practice.11

The Various Natural Forms of Iodine

The element iodine exists in nature under several forms: (Continued on next page)
a value computed by dividing 70 mcg/day by 43.5 liters/day = 1.6 mcg/L. This is evidence that the iodine present in the food and drink of these subjects is highly bioavailable. Pittman, et al. measured serum inorganic iodide levels in two groups of subjects: one group after iodization of salt, with an estimated daily intake of 750 mcg iodide, and the other group after iodization of bread, with a similar average daily intake of iodates. The expected mean serum level at equilibrium would be 17.2 mcg/L (750 mcg/43.5 L). The mean values observed by Pittman, et al. were 1.7 mcg/L for subjects after iodization of salt, and 18.7 mcg/L for subjects after iodization of bread. These data suggest that iodate in bread is very bioavailable, whereas only 10% of iodide in iodized salt were absorbed. On a molar basis, there is 30,000 times more chloride than iodide in iodized salt. Chloride competes with iodide for absorption in the intestinal tract. To our author’s knowledge, the low bioavailability of iodide in iodized salt has never been reported.

Using ion-selective electrode measurement, following chromatography on anion-exchange resins, serum inorganic iodide levels were measured by the author serially or 24 hours in five normal subjects and one obese man, allowing a single ingestion of 37.5 mg of iodine/iodide from a tablet form of Lugol solution (three tablets of Iodoral®). Baseline serum iodide levels were below the sensitivity of the assay (0.006 mg/L) in all the subjects tested. There was no significant difference in the levels and pattern of serum levels obtained in three normal women (subjects A, B, C) and two normal men (subjects D and E) (Figure 2). The serum inorganic iodide levels increased rapidly to reach peak levels between 1.4 and 1.8 mg/L at 2-3 hours post ingestion, and decreased afterward. The serum levels were still elevated at 24 hours post ingestion, ranging from 0.3-0.5 mg/L. The serum levels observed in an obese man (subject F) (Figure 2) were much lower and approached baseline by 8 hours post ingestion.

Sequestration of iodine by fats may be the explanation for this observation. With selective uptake of iodine, but not iodide by fats, obesity would create a selective iodine deficiency for tissues like the mammary glands possessing a preference for iodine. Following ingestion of 50 mg (four tablets) of the same preparation in six normal premenopausal subjects, the serum inorganic iodide levels followed the same profile as the one observed in the five normal subjects following ingestion of 37.5 mg elemental iodine but with higher serum levels. The baseline inorganic iodide levels were below the sensitivity of the assay in all six subjects.

The expected serum inorganic iodide levels at equilibrium for subjects ingesting 50 mg iodine/iodide would be 1.15 mg/L (50 mg/43.5 L). In eight normal subjects (three males and five females) ingesting four tablets of Iodoral® (50 mg) daily for three months, the serum inorganic iodide levels at equilibrium ranged from 0.85-1.34 mg/L with a mean ± SD of 1.1±0.18 mg/L. This finding confirms the high bioavailability of the Lugol tablet (Iodoral®) routinely used in the iodine/iodide loading test and for orthiodosupplementation.

### Thyroidal Metabolism of Iodide

Serum inorganic iodide is in dynamic equilibrium with the exchangeable pool of inorganic iodide in the thyroid gland. This pool was estimated at 6-7 mg iodide by Koutras, et al. Uptake of inorganic iodide by the thyroidal Na/I symporter system increases with increased peripheral levels, but only up to a point. The maximum daily thyroidal uptake was estimated at 0.6 mg/day when 50 mg of iodide are ingested daily. Based on studies in farm animals by Marine, saturation of the thyroid occurs with 5 mg iodine per gm (dry wt) of thyroid. That would compute to 50 mg iodine per thyroid gland in an adult man, 8 times the exchangeable pool of iodide. Hyperplastic changes in the

<table>
<thead>
<tr>
<th>Table 2</th>
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<tbody>
<tr>
<td>Serum Inorganic Iodide Levels at Equilibrium, Following Increasing Iodine Intake</td>
</tr>
<tr>
<td><strong>Average Total I Intake (Diet &amp; Supplement) (mcg/day)</strong></td>
</tr>
<tr>
<td>75</td>
</tr>
<tr>
<td>150</td>
</tr>
<tr>
<td>350</td>
</tr>
<tr>
<td>690</td>
</tr>
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<tr>
<td>600</td>
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<td>1250</td>
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inorganic sodium and potassium salts of iodates (IO3-) and iodides (I-), inorganic diatomic iodine (I2), and organic monatomic iodine (C-I). The first reported, naturally occurring, halogenated organic compound was 3,5-diodothyroseine, isolated in 1896 by Drexel from the coral, Gorgonia cavolinii.14 Surprisingly, invertebrates and algae have the ability to synthesize the “thyroid hormone” thyroxine (T4).15 Evidence will be presented later for the synthesis of T4 by human leukocytes.

In the US, various forms of iodine have been used in food products: iodides in table salt since the 1920s; iodates in bread from 1960-1980; and diatomic iodine in municipal waters (on an experimental basis only).9 Since the 1940s, radionuclides of iodide became available for diagnostic and therapeutic purposes. The most common forms of iodine used in clinical medicine are listed in Table 1. The organic iodine-containing compounds, whether occurring naturally or manmade, have properties distinctly different from inorganic iodine/iodates/iodides.

**Sources of Iodine in Nature**

The greatest reservoir of iodides is in the oceans of our planet, although present in very diluted concentrations (0.05 mcg/ml of sea water), therefore, this is not a good starting material for industrial production of iodine. However, sea algae can concentrate iodides by several orders of magnitude. For example, iodide concentrations as high as 0.5% wet weight have been reported in red algae,16 a concentration 100,000 times higher than that present in seawater. From the discovery of iodine in 1811 until 1840, France was the sole producer of iodine. Japan did not become a major iodine producer until 1888.17 Currently, the major iodine producers are the US, Japan, and Chile; caliches, oil wells, and deep well water are the major sources.

The iodine cycle starts and ends in the oceans. Under the influence of sunlight, the iodides in seawater are oxidized to diatomic iodine I2. Due to sublimation at ambient temperature and atmospheric pressure, the I2 gas evaporates in the air in an estimated amount of 400,000 tons per year.2 This form of diatomic iodine can be absorbed through the lungs by breathing air, which usually contains approximately 1 mcg/m3, a very insignificant source of iodine. The high voltage currents flowing through clouds reduce the diatomic iodine to iodides dissolved in water droplets which fall on the soil in the form of rain. Rivers return the iodide to the oceans to complete the cycle.

**Iodine Metabolism in Man**

Diatomic iodine (I2) can be absorbed through the lungs and through the skin.18,19 However, ingested food, drinks and iodine/iodide supplementation, are the most common means of supplying iodine to the human body. Without interfering substances present in the gastrointestinal tract, inorganic iodine, iodates, and iodides are quantitatively absorbed. The elimination of peripheral inorganic iodide occurs almost exclusively through renal clearance.20 Organic and inorganic iodine are not cleared by the kidneys. When inorganic iodide is ingested in amounts ranging from 0.001 mg up to 2,000 mg, Childs, et al.20 estimated an average renal clearance of serum inorganic iodide of 50L/day over the whole range of intakes. Fisher, et al.21 and Koutras, et al.22 have measured serum inorganic iodide levels at equilibrium in subjects ingesting increasing amounts of iodide from 75-1,250 mcg/day. Their results are displayed in Table 2. When these data are plotted on an X-Y axis (Figure 1), a high degree of correlation (0.999) was obtained with a slope of 0.023. The slope is an index of renal clearance: 1/0.023 = 43.5 L/day.

To compute the serum inorganic iodide levels at equilibrium in a subject ingesting a narrow range of iodine/iodide, divide the average daily intake expressed as milligrams elemental iodine by 43.5 liters to obtain the serum concentration of inorganic iodide expressed as mg/L of serum. Besides giving accurate information about the peripheral concentrations of iodide available for uptake by the cells and organs of the human body, measurement of serum inorganic iodide levels is very useful for assessing bioavailability of the iodine/iodide ingested. Alexander, et al.23 measured the serum inorganic iodide levels in normal subjects consuming an average of 70 mcg iodide per day, but no iodized salt. He observed a mean value of 1.8 mcg/L. This measured value is very close to

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**Table 1**

**Various Forms of Iodine/Iodide Used in Clinical Medicine**

<table>
<thead>
<tr>
<th><strong>A) Inorganic</strong></th>
<th></th>
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<tbody>
<tr>
<td>1) Non-Radioactive</td>
<td></td>
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<tr>
<td>a) Iodides (I.e., SSKI)</td>
<td></td>
</tr>
<tr>
<td>b) Tincture of Iodine</td>
<td></td>
</tr>
<tr>
<td>c) Lugol Solution</td>
<td></td>
</tr>
<tr>
<td>2) Radioactive Iodides for Diagnostic and Therapeutic Purposes</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>B) Organic</strong></th>
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<tbody>
<tr>
<td>1) Naturally Occurring</td>
<td></td>
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<tr>
<td>a) Thyroid hormones</td>
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</tr>
<tr>
<td>b) Thyroidal Iodolipids</td>
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<tr>
<td>2) Man-made</td>
<td></td>
</tr>
<tr>
<td>a) Radiographic Iodolipids</td>
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</tr>
<tr>
<td>b) Iodine-Containing Drugs (I.e., Amiodarone)</td>
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</tbody>
</table>
Figure 2

Serum Inorganic Iodide Levels Following Ingestion of Three Tablets of Iodoral®, Containing 37.5 mg Elemental Iodine, in Three Normal Women, Two Normal Men and One Obese Man.

(A) 28 yr. old female subject
Ht = 61”
Wt = 121 lbs.
BMI = 22.8

(B) 24 yr. old female subject
Ht = 65”
Wt = 151 lbs.
BMI = 25.1

(C) 43 yr. old female subject
Ht = 67”
Wt = 170 lbs.
BMI = 26.7

(D) 24 yr. old male subject
Ht = 74”
Wt = 167 lbs.
BMI = 21.4

(E) 19 yr. old male subject
Ht = 72”
Wt = 178 lbs.
BMI = 24.1

(F) 35 yr. old male subject
Ht = 71.5”
Wt = 286 lbs.
BMI = 39.2
thyroid gland are observed when iodine concentrations drop below 0.1% dry weight (dry wt).\textsuperscript{31} Thyroidal concentration of 0.1% iodine corresponds to 1 mg iodine/gm thyroid (dry wt). With an estimated weight of the thyroid gland around 10 gm dry wt in the normal adult, the minimum amount of iodine/iodide in the thyroid before hyperplastic changes occur would be 10 mg (1 mg I/gm x 10 gm). F.M. Delange\textsuperscript{32} estimated, from an extensive review of the literature, that daily intake of 0.05 mg iodine and 10-20 mg iodine/thyroid were required to prevent simple goiter. Goiter development correlates better with low thyroidal iodine than with elevated TSH levels, suggesting an autoregulatory role of iodine in the thyroid gland.\textsuperscript{33}

Elevated TSH induces hypertrophy, whereas intrathyroidal iodine deficiency induced thyroid hyperplasia. In iodine-deficient goiter, iodine supplementation abolishes not only hypertrophy, but also hyperplasia of the thyroid gland. On the other hand, suppression of TSH with T4 abolishes hypertrophy, not hyperplasia if there is intrathyroidal iodine deficiency.\textsuperscript{33} Therefore, administration of T4 to iodine-deficient patients does not decrease their risk for thyroid cancer, an effect expected with iodine supplementation.\textsuperscript{34} Stubner, et al,\textsuperscript{33} concluded: “These data indicate that iodine supplementation is the causal therapy for iodine-deficient goiter because it abolishes not only hypertrophy, but also hyperplasia of the glands and restores normal function and regulation.”

Based on the above findings, orthoiodosupplementation is highly recommended in patients receiving thyroid hormone therapy.

There is an inverse relationship between the iodine concentration of the thyroid gland and total DNA content, indicating an autoregulatory effect of iodine on cell proliferation (anticarcinogenic effect). Recent investigations on this autoregulatory effect of iodine on cell proliferation suggest that it is due to iodinated lipids.\textsuperscript{9} Iodination of lipids in thyrocytes requires an amount of iodine/iodide two orders of magnitude greater than the RDA, that is two orders of magnitude greater than required for iodination of thyrosine. Apparently, the thyroid gland requires higher concentrations of iodide in the thyrocyte for the iodination of lipids than for the iodination of thyrosine. For further details on the intrathyroidal metabolism of iodide and synthesis of thyroid hormones, the reader is referred to textbooks of endocrinology and thyroidology where this aspect of iodine metabolism is well described.

Extrathyroidal Metabolism of Iodide
The mammary glands can effectively compete with the thyroid gland for peripheral iodide. Eskin, et al,\textsuperscript{28} measured the 24-hour radioiodide uptake in 57 clinically normal breasts, and in eight clinically abnormal breasts. The mean ± SD percentage uptake was 6.9±0.46% in the normal breasts and 12.5±1% in abnormal breasts. These means were statistically significant at p < 0.005. Considering that these measurements are representative of a single breast, and a woman has two breasts, the percentage uptake per patient is twice these amounts. This brings the 24-hour radioiodide uptake by the mammary glands of a woman in the same range as the 24-hour radioiodide uptake by the thyroid gland. The higher percentage uptake in the abnormal breasts suggests that the abnormal breasts were more deficient in elemental iodine than normal breasts.

Since the radioiodide uptake study of breast tissue by Eskin, et al,\textsuperscript{28} was performed with iodide, not iodine, it is likely that the percent uptake by the breast would even be higher if radioiodine were used. There is some evidence that the udder of a lactating cow has a greater need for iodine than the thyroid gland. When the radioisotope 131I was administered to lactating cows under four different chemical forms — diatomic iodine, methyliodine, iodide, and iodate — the average maximum uptake by the thyroid gland was 3.8% of the administered dose, whereas milk from the same cows contained an average of 14% of the administered dose. A slightly higher concentration of radioactivity was observed in the milk of cows fed radiiodine than those fed radioiodide. Of interest are the findings of Eskin, et al,\textsuperscript{29} that the thyroid gland prefers...
male) were evaluated with 24-hour urinary iodide levels after ingesting one, two, and three tablets of the same preparation. The mean percentage excretions (± SD) were: 22±1.2% for one tablet, 23±2.8% for two tablets, and 25±12.3% for three tablets. In a third group of six subjects, urine iodide levels were evaluated following four tablets of the same preparation. The mean excretion rate was 39±17.2% (Figure 3). For the loading test, a single ingestion of four tablets was chosen because this dose resulted in the highest mean percent iodide excreted and in the widest interindividual variations.

Because of the improved overall well-being reported by the subjects who achieved 90% or more iodide excreted, sufficiency was arbitrarily defined as 90%. Implementation of orthoiodosupplementation, based on the loading test, revealed that sufficiency was not achieved in some subjects even after two years of iodine supplementation at 1-2 tablets/day. To achieve sufficiency within three months, most subjects required 3-4 tablets/day (37.5-50 mg). US physicians over the past century recommended daily intakes between 0.1 ml and 0.3 ml of Lugol solution containing 12.5-37.5 mg elemental iodine.9 Our medical predecessors were already using orthoiodosupplementation based on their keen observation of their patient’s overall well-being. Whole body sufficiency for iodine correlated well with overall well-being, and some subjects could tell when they achieved sufficiency even before knowing the results of the test. Iodine sufficiency was associated with a sense of overall well-being, lifting of a brain fog, feeling warmer in cold environments, increased energy, needing less sleep, achieving more in less time, experiencing regular bowel movements, and improved skin complexion. In some overweight or obese subjects, orthoiodosupplementation resulted in weight loss, decreased percent body fat, and increased muscle mass.

Clinical Implications
The goal of orthoiodosupplementation is not the treatment of disease, but the supply of optimal amounts of an essential nutrient for whole body sufficiency and for optimal mental and physical performance. Whole body iodine deficiency, based on the concept of orthoiodosupplementation, may play an important role in several clinical conditions.

Summary of Findings
Based on the above review of the literature and this author’s clinical research studies,8-12 the concept of orthoiodosupplementation can be summarized as follows:

1) The nutrient iodine is essential for every cell of the human body requiring peripheral concentrations of inorganic iodide ranging from $10^{-6}$M to $10^{-3}$M.

(Continued on next page)
tially concentrates iodide whereas the mammary gland favors iodine. In iodine-deficient female rats, histological abnormalities of the mammary gland were corrected more completely, and in a larger number of rats treated with iodine, than iodide given orally at equivalent doses. Ghent, et al, reported a better response from patients with fibrocystic disease of the breast when inorganic iodine was used, compared with organic iodine and inorganic iodide.

In the rats studied by Thrall and Bull, 20% of the iodide, but not iodine, administered orally was recovered in the skin. This suggests that the skin, like the thyroid gland, has a preference for iodide. Extrathyroidal synthesis of T4 has been demonstrated in thyroidectomized rats by Evans, et al, following administration of iodide in amount of 25 mg/kg BW. For a 70-kg human subject, the corresponding amount would be 1.75 g, well within the range of iodides prescribed for pulmonary patients. Iodotherapy in these thyroidectomized rats reversed the effect of hypothyroidism on growth, on the adrenal glands, the ovaries, testicles, and thymus.

Human leukocytes during phagocytosis synthesized T4 when the incubation media contained 10⁻⁶ M iodide. Extrathyroidal hyperthyroidism with exophthalmia has been reported in patients with leukemia. The administration of Lugol solution was effective in these cases. Iodine deficiency may play an important role in leukemia. Salivary glands and stomach cells oxidized and organized iodide with the synthesis of iodolipids, mono- and diiodothyrosine, when the incubation media contained 10⁻⁶ M iodide. The essential element iodine modulates the adrenal response to stress and improves immune functions.

Certain roles of iodine in well-being and protection against infections, degenerative diseases, and cancer may not involve its action on specific organs and tissues. Instead, such properties, affecting every cell in the human body, may depend on iodine/iodide concentrations in biological fluids. Because of its large size, iodine has the ability to markedly enhance the excited singlet to triplet radiationless transition. Szent-Gyorgy was able, 50 years ago, to demonstrate this effect of iodine on the singlet → triplet radiationless transition, at a concentration of 10⁻⁴ M. To achieve the 10⁻⁴ M concentration of serum inorganic iodide, a daily ingestion of 50 mg elemental iodine would be required. Reactive oxygen species, causing damage to DNA and other macromolecules, are usually excited singlets with a high energy content released rapidly, and characterized by fluorescence; whereas the corresponding triplet state contains lower energy levels, which are released slowly, expressed as phosphorescence. Singlet-oxygen-induced lesions in DNA are processed by an error-prone repair in mammalian cells. The DNA repair mechanisms are efficient in preserving biological activity but highly mutagenic in mammalian cells. Intake of iodine/iodide at 50 mg/day would decrease the oxidative burden and DNA damage. Such an effect would be anticarcinogenic in every organ of the human body. A daily intake of 50 mg is also the amount of elemental iodine that saturates the iodide thyroidal symport system and could serve as a preventive measure against unexpected exposure to radioactive iodine/iodide.

An overview of the available data suggests that, for optimal function of the human body, peripheral inorganic iodide levels between 10⁻⁶ M to 10⁻⁵ M are required — levels two to three orders of magnitude greater than the level of 10⁻⁸ M observed in the US population.

The Concept of Orthoiodosupplementation
Orthoiodosupplementation is the daily amount of the essential element iodine required for whole body sufficiency. Whole body sufficiency for iodine is assessed by an iodine/iodide loading test. The iodine/iodide loading test evolved by serendipity from a project to assess the bioavailability of a tablet form of Lugol solution (Iodoral). From the medical literature, it is stated that urinary iodide levels are the best index of iodine/iodide intake. Studies were performed in five normal subjects (two male, three female), with the assumption that urine concentrations of iodide were a reliable index of bioavailability of the product tested.

Following oral intake of 12.5 mg Lugol in tablet form, iodide levels in the 24-hour urine collection were measured. The subjects excreted in their 24-hour urine samples only 10-30% of the amount ingested, with a mean of 20%. This low recovery of iodide in the urine samples could be due to either low bioavailability of the product tested or high retention in the body. In order to elucidate the cause of this low iodide excretion, we continued the administration of the supplement in those subjects for one month. Then, we repeated the 24-hour urine collection and iodide was measured again in the 24-hour urine samples. In four of the five subjects, the percentage oral dose excreted in the 24-hour urine sample increased significantly, with a mean group value of 50%. Contrary to medical textbooks, 80% of the iodine/iodide ingested was retained. After one month of supplementation, the body still retained 50% of the ingested amount. The iodine/iodide loading test evolved from these observations. However, instead of a one-month loading test, further studies were performed to shorten this test to a single ingestion of the preparation.

Another group of six subjects, (three male and three female).
According to Delange, a daily intake of only 0.05 mg elemental iodine will prevent goiter and cretinism, which are the manifestation of the most severe forms of iodine deficiency. To achieve whole body sufficiency for iodine, 250 to 1,000 times that amount is required.

4) The healthy human adult body contains 15-20 mg of iodine.

Based on calculations derived from the loading test, the retention of iodine by subjects on 50 mg/day for three months ranged from 1,450 to 1,600 mg elemental iodine. This amount was derived by subtracting the amount of iodide excreted from 50 mg prior to and monthly following supplementation. The mean daily amount retained was calculated by averaging. For example, a subject excreted 20 mg iodide/24-hour prior to supplementation and 45 mg after 90 days of supplementation. The amount retained would be:

Day 1 = 50-20 = 30 mg
Day 90 = 50-45 = 5 mg
Daily average = 30 + 5 / 2 = 17.5 mg/day
For 90 days = 17.5 mg/day x 90 days = 1575 mg

The levels of 15-20 mg iodine mentioned in medical textbooks represent severe iodine deficiency based on the concept of orthoiodosupplementation.

5) The thyroid gland contains 70-80% of the total body iodine.

Marine reported that the thyroid gland of farm animals given increasing amounts of iodine contained a maximum of 5 mg iodine per gm thyroid (dry weight). For an adult man, that would compute to 50 mg (5 mg/gm x 10 gm). In an iodine sufficient individual, the percentage of total body iodine present in the thyroid gland would be 3.3% (50 mg/1,500 mg x 100).

6) The normal daily requirement of iodide for an adult is 150-200 mcg (0.15-2 mcg).

If the goal of the International Council for Control of Iodine Deficiency Disorders is to have a world full of sick zombies surviving on antibiotics and toxic drugs, that amount of iodine is more than enough; and the council should not allow more than that amount to be the recommended daily allowance. However, for whole body sufficiency, and for optimal physical and mental health, 100 to 400 times the RDA would be required.

7) The toxic side effects of organic iodine containing drugs are caused by inorganic iodide.

There is a lot of misinformation in the medical literature concerning the safety of the different forms of the element iodine. The inorganic forms are blamed for the severe side effects of the organic iodine-containing drugs. From a publication by Phillippou, et al, published in 1992, it is obvious that the cytotoxicity of the organic iodine-containing drugs is due to the molecule itself, not to the iodine released or present in the molecule. “We can, therefore, conclude that the effect of amiodarone, benzoiodarone, Na iopanate, and other iodine-containing substances with similar effects is due to the entire molecule and not to the iodine liberated. It should be noted that the cytotoxic effect of amiodarone in all cultures is also due to the entire molecule and not to the iodine present in it.”

About the Author

Guy E. Abraham, MD, is a former Professor of Obstetrics, Gynecology and Endocrinology at the UCLA School of Medicine. Some 35 years ago, he pioneered the development of assays to measure minute quantities of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974; the “Medaille d’Honneur” from the University of Liege, Belgium, 1976; the Senior Investigator Award of Pharmacia, Sweden, 1980. The applications of Dr. Abraham’s techniques to a variety of female disorders have brought a notable improvement to the understanding and management of these disorders. Twenty-five years ago, Dr. Abraham developed nutritional programs for women with premenstrual tension syndrome and postmenopausal osteoporosis. They are now the most commonly used dietary programs by American obstetricians and gynecologists. Dr. Abraham’s current research interests include the development of assays for the measurement of iodide and the other halides in biological fluids and their applications to the implementation of orthoiodosupplementation in medical practice.

REFERENCES

1) Food and Nutrition Board, National Academy of Sciences, National (Continued on next page)
2) In non-obese subjects, these concentrations can be achieved with daily intake of 12.5-50 mg elemental iodine.

3) The thyroid gland is the most efficient organ of the human body, capable of concentrating iodide by two orders of magnitude to reach $10^{-6}$M iodide required for the synthesis of thyroid hormones when peripheral levels of inorganic iodide are in the $10^{-8}$M range.

4) Goiter and cretinism are evidence of extremely severe iodine deficiency because the smallest intake of iodine that would prevent these conditions, (i.e., 0.05 mg/day) is 1,000 times less than the optimal intake of 50 mg elemental iodine.

5) The thyroid gland has a protective mechanism, limiting the uptake of peripheral iodide to a maximum of 0.6 mg/day when 50 mg or more elemental iodine are ingested. This amount, therefore, would serve as a preventative measure against radioactive fallout.

6) An intake of 50 mg elemental iodine/day would achieve peripheral concentration of iodide at $10^{-5}$M, which is the concentration of iodide markedly enhancing the singlet $\rightarrow$ triplet radiationless transition. This effect would decrease DNA damage with an anticarcinogenic effect.

7) Orthoiodosupplementation results in detoxification of the body from the toxic metals, aluminum, cadmium, lead, and mercury.

8) Orthoiodosupplementation increases urinary excretion of fluoride and bromide, decreasing the goitrogenic effects of these halides.

9) Most patients on a daily intake ranging from 12.5-50 mg elemental iodine reported higher energy levels and greater mental clarity with 50 mg (four tablets Iodoral®) daily. The amount of iodine used in patients with fibrocystic disease of the breast by Ghent, et al,7 that is 0.1 mg/kg BW/day, is 10 times below the optimal daily intake of 50 mg. In our experience, patients with this clinical condition responded faster and more completely when ingesting 50 mg iodine/iodide/day.

10) Orthoiodosupplementation may be the safest, simplest, most effective, and least expensive way to solve the health-care crisis crippling our nation.

11) For best results, orthoiodosupplementation should be part of a complete nutritional program, emphasizing magnesium instead of calcium.

12) The iodine/iodide loading test and serum inorganic iodide levels are reliable means of assessing whole body sufficiency for elemental iodine and also for quantifying the bioavailability of the forms of iodine ingested.

**Misinformation in Medical Textbooks**

The concept of orthoiodosupplementation requires a major revision of commonly held beliefs expounded in medical textbooks regarding iodine metabolism and requirements.

1) Ingested iodine is reduced to iodide in the intestinal tract prior to absorption.

Ghent, *et al.*,7 and Eskin, *et al.*,29 reported that in women and in female rats, fibrocystic disease of the breast responded better to iodine than iodide. Thrall and Bull36 observed that in both fasted and fed rats, the thyroid gland and the skin contained significantly more iodine when rats were fed with iodide than with iodine; whereas the stomach walls and stomach contents had a significantly greater level of iodine in iodine-fed rats than iodide-fed animals. Peripheral levels of inorganic iodine were different with different patterns, when rats were fed with these two forms of iodine. The authors concluded: “These data lead us to question the view that iodide and iodine are essentially interchangeable.”

2) Urine iodide levels are a reliable index of elemental iodine intake.

Contrary to the opinions of nutritionists and thyroidologists, urinary excretion of iodide is not a good index of iodine/iodide intake. Besides the low bioavailability of some forms of iodine and iodide, such as sodium iodide in table salt, there is also a significant retention of iodine/iodide by the human body until sufficiency is achieved. Based on our experience with the iodine/iodide loading test, only 10-30% of a highly bioavailable preparation of iodine are recovered in the 24-hour urine collection, when subjects ingested from 12.5-37.5 mg/day. Urinary iodide levels approximate intake only in individuals who achieved iodine sufficiency of the whole body (90% or more of the ingested amount is excreted in the 24-hour urine collection). It is then obvious that urinary iodide excretion is not a reliable index of intake, unless the form of iodine ingested is highly bioavailable and whole body sufficiency is achieved.

3) Absence of goiter and cretinism are evidence of iodine sufficiency.

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The Historical Background of the Iodine Project

by Guy E. Abraham, MD

The goal of this article is to provide the background on the Iodine Project which started five years ago and reacquant the reader with the concept of orthiodosulplement— the amount of iodine required for whole body sufficiency based on an iodine/iodide loading test recently developed by the author.1

During the first half of the 20th century, almost every US physician used Lugol solution for iodine suplementation in his/her practice for both hypo- and hyperthyroidism,1 and for many other medical conditions.2 In the old pharmacopoeias, Lugol solution was called Liquor Iodi Compositus. The minimum dose, called minim, was one drop containing 6.25 mg of elemental iodine, with 40% iodine and 60% iodide as the potassium salt. The recommended daily intake for iodine supplementation was 2-6 minims (drops) containing 12.5-37.5 mg elemental iodine. During the second half of the 20th century, iodophobic misinformation, disseminated progressively and deceitfully among the medical profession, resulted in a decreased use of Lugol, with iodized salt becoming the standard for iodine supplementation.1 The bioavailable iodide from iodized salt is only 10%, and the daily amount of iodide absorbed from iodized salt is 200-500 times less than the amount of iodine/iodide previously recommended by US physicians. After World War II, US physicians were educated early in their medical career to believe that inorganic, non-radioactive forms of iodine were toxic. Adverse reactions to radiographic contrast media and other iodine-containing drugs were blamed on iodine. If a patient told his/her physician that he/she could not tolerate seafood, the physician told him/her that he/she was allergic to iodine.

Several forms of iodine prescribed by US physicians are listed in Table 1. The manmade organic forms of iodine are extremely toxic, whereas the inorganic non-radioactive forms are extremely safe.1 However, the safe, inorganic, non-radioactive forms were blamed for the severe side effects of the organic iodine-containing drugs. A new syndrome, medical iodophobia, was recently reported1 with symptoms of split personality, durable standards, amnesia, confusion and altered state of consciousness. Medical iodophobia has reached pandemic proportion, and it is highly contagious (iatrogenic iodophobia). A century ago, non-radioactive forms of inorganic iodine were considered a panacea for all humanills,2 but today, they are avoided by physicians like leprosy. Who or what killed iodine?

The first nail in the iodine coffin was the publication by Wolff and Chaikoff from UC Berkley in 1948,3 describing their finding in rats administered iodide in increasing amounts by intraperitoneal injection. When serum inorganic iodide levels reached 0.2 mg/L, that is 10^−6M, radioiodide uptake by the thyroid gland became undetectable. The correct interpretation would be: that iodide sufficiency of the thyroid gland was achieved when serum inorganic iodide levels reach 10^−6M, as we previously discussed.4 But Wolff and Chaikoff concluded that serum inorganic iodide levels at a concentration of 10^−6M blocks the synthesis of thyroid hormones, resulting in hypothyroidism and goiter. These authors did not measure thyroid hormones in the rats studied. Hypothyroidism and goiter were not observed in those rats. This fictitious phenomenon became known as the Wolff-Chaikoff effect.5 Because these law-abiding rats refused to become hypothyroid and instead followed their normal physiological response to the iodide load, they were unjustly accused of escaping from the law of the Wolff-Chaikoff effect. Labeling these innocent rats as fugitives was a great injustice against these rodents.

The second and final nail in the iodine coffin was hammered in by Dr. Wolff in 1969.5 By 1969, Wolff had moved to the National Institute of Health from UC Berkley. Wolff arbitrarily defined four levels of “iodine excess.” The first level of excess started with intake above 0.2 mg/day, and iodide intake of 2 mg or more was considered “excessive and potentially harmful.” In the next issue of this journal, this author discusses the Wolff-Chaikoff effect and presents evidence that the data reported in the rats by Wolff and Chaikoff6 did not justify the interpretation of these data as applied to rats. Even worse, extrapolation of these findings to human subjects by Wolff6 was inappropriate, and unscientific. By the 1970s, physicians concluded that one must avoid inorganic, non-radioactive iodine like leprosy, unless it was incorporated into the toxic, organic iodine-containing drugs. Then iodine could be tolerated because iodine could be blamed for the toxicity of these drugs.

Against this background, a 1993 publication by Ghent, et al,6 reported the beneficial effects of 5 mg iodine ingested daily for approximately one year in 1,368 patients (Continued on next page)
syrups of different flavors. The syrup would contain 1% hydrogen iodide. This would compute to 10 mg iodide per ml. So, the recommended daily amount of elemental iodine was 20-40 mg.

After overcoming the delusion that inorganic, non-radioactive forms of iodine are toxic and becoming aware that the inorganic, non-radioactive forms of iodine were extremely safe and used extensively by US physicians for many medical conditions, the author initiated the Iodine Project. Clinical studies were performed five years ago to confirm Ghent’s findings, combined with some original research. The clinical aspects of this research were performed under contract at the Flechas Family Practice Clinic in Hendersonville, North Carolina under the supervision of Jorge D. Flechas, MD, and funded with grants from Optimox Corporation. The author designed the protocols and monitored the progress and completion of each project. Informed consent was obtained from all subjects participating in these projects.

Because administration of iodine in liquid solution is not very accurate, may stain clothing, has an unpleasant taste, and causes gastric irritation, we decided to use a precisely quantified tablet form of Lugol. To prevent gastric irritation, the iodine/iodide preparation was absorbed unto a colloidal silica excipient; to eliminate the unpleasant taste of iodine, the tablets were coated with a thin film of pharmaceutical glaze. John C. Hakala from Hakala Apothecaries, in Lakewood, Colorado, compounded the tablets.10

To confirm the safety of the Lugol tablets, pilot studies were performed with tablets of Lugol containing 1.0-12.5 mg of elemental iodine. Following the pilot studies, 10 female subjects, seven with breast symptomatology, were studied for three months at 12.5 mg/day. Pre- and post-supplementation evaluation of blood chemistry, hematology, thyroid function tests, and ultrasonometry of the thyroid gland were performed. The results obtained in these female subjects using a tablet form of Lugol solution (Iodoral®, Optimox Corporation, Torrance, CA) at 12.5 mg/day for three months confirmed Ghent’s observations, and the safety of the Lugol tablets. This was reported in The Original Internist in 2002.10

In order to build a database that could be used to develop a protocol for the implementation of iodine supplementation in FDB and other clinical conditions, a long-term study of Lugol tablets in female patients with FDB, using Ghent’s scoring of FDB, was initiated four years ago at Dr. Flechas’ clinic, supported by grants from Optimox Corporation. Dr. Flechas will present a preliminary report of his results on the use of Lugol tablets in FDB, using daily amounts of 12.5-50.0 mg of elemental iodine (See page 89). In 2003, Dr. David Brownstein joined the Iodine Project and became a very efficient spokesman for the orthoiodosupplementation program. He wrote a booklet published in 2004, describing his experiences with this approach in his practice. Dr. Brownstein was invited to outline some key recommendations for the benefit of other health care practitioners based on his and his partners’ experience so far in 3,000 patients. His article will be in next month’s issue.

Five years ago, urine samples were sent to local laboratories for the measurement of iodine levels before and after orthoiodosupplementation. The iodophobic mentality became evident immediately. The reports came back with statements like “Greater than 500 µg iodide/24 hr., check for contamination.” The author then switched to a large commercial laboratory catering to some 30,000 health care practitioners. The normal range of urine iodide levels for that laboratory was 0.02-0.50 mg/24 hr. Together with urine iodide levels, this laboratory also performed urine levels of minerals, trace elements, and toxic metals.

The bioavailability of a Lugol tablet (Iodoral®) containing 12.5 mg elemental iodine was evaluated by measuring 24-hour urine levels of iodide together with the minerals, trace elements, and toxic metals before and after administration of this preparation. The results obtained following iodine supplementation revealed that in some subjects, the urine levels of mercury, lead, and cadmium increased by several times after just one day of supplementation. For aluminum, this increased excretion was not observed usually until after one month or more on the iodine supplementation.

Based on data available in the medical literature, urinary iodide levels are considered the best index of iodine intake.12 The initial results of the bioavailability study suggested that the Lugol tablets were not well absorbed since only 20-30% of the administered amount was recovered in the 24-hour urine collection of five subjects tested.12 Just in case medical textbooks were wrong, and the explanation for the low recovery of iodide is body retention of iodine/iodide, the supplementation was continued for one month and then urine iodide levels were measured again in the 24-hour urine collection. Medical textbooks were wrong. The subjects excreted a mean of 50% of the amount ingested, with one subject excreting 96% of the ingested amount.12

The implication of such observation was that an iodine/iodide-loading test could be developed to assess not just thyroid sufficiency for iodine but requirement of the (Continued on next page)
fects was rare and this topic will be discussed by Drs. Flechas and Brownstein in other articles. The Wolff-Chaikoff effect was not observed in some 4,000 patients on orthoiodosupplementation for as long as three years with daily intake ranging from 12.5-50.0 mg. This is the combined experience of Drs. Flechas and Brownstein.

The serum level of inorganic iodide supposedly causing hypothyroidism and simple goiter by the Wolff-Chaikoff effect is 0.2 mg/L. The author previously calculated that in an adult, this level would be achieved with a daily ingestion of 12.5 mg elemental iodine. Since this amount of Lugol solution was used safely by three generations of US physicians for iodine supplementation, and since we have observed that patients reported optimal mental and physical performances on 3-4 times that amount, we would like to propose a redefinition of the Wolff-Chaikoff effect as optimal mental and physical performances. This seems to be the most congenial solution to the Wolff-Chaikoff forgery. In this way, the names of Wolff and Chaikoff would continue to be mentioned in the medical literature, but associated with the real and pleasant outcome of orthoiodosupplementation, that is optimal mental and physical performances, not the gloomy, fictitious outcome proposed by Wolff.

Three years ago, the author decided to set up the iodide assay in situ, using the ion-selective electrode procedure. To improve specificity, chromatography separation of the halides was performed on anion-exchange resins. Halides and other substances interfered in the assay of iodide (Table 2). One full year was required to optimize the assay for iodide. In January 2003, Dr. Flechas and John C. Hakala were invited as guests of Optimox Corporation to attend a two-day workshop in order to learn this technology. Dr. Flechas quickly learned this procedure and set it up in his own clinical laboratory. At first, the loading test was performed on his patients only, but eventually, he made this service available to other clinicians. Packets containing four tablets of Iodoral® were made available for the loading test. In another article in this issue, Dr. Flechas will present the results of the loading tests he gathered during the previous two years and his experience with the implementation of orthoiodosupplementation in his practice.

In order to test the reliability of commercial laboratories in the performance of urine iodide assay at the levels observed following the loading test, Optimox Corporation financed a pilot study on five subjects who underwent the loading test. Samples were sent to two commercial laboratories for iodide measurement. These laboratories used the ICP-MS method. The same samples were also measured by the author in situ (Table 3). Lab #1 consistently underestimated and Lab #2 consistently overestimated the levels measured in the potentiometric laboratory of the author. Physicians using the iodine/iodide loading test to follow their patients on orthoiodosupplementation will depend on the results of these tests for evaluation of whole body iodine sufficiency and clinical response. Therefore, the measurement of urine iodide levels must be accurate at concentrations two orders of magnitude greater than the normal range of these laboratories, that is 0.02-0.50 mg/24 hr.

The supervisor of Lab #1 was contacted. He was very helpful and explained that his equipment was calibrated to measure the range of urine iodide levels expected in the US population, that is 0.02-0.50 mg/24 hr, and therefore, it would not be reliable at levels 100 times higher. He performed recovery experiments and confirmed that his equipment underestimated the true value by 50%.

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<table>
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<tr>
<th>Halides</th>
<th>Interferences*</th>
<th>Procedures for preventing interference</th>
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| Chloride | OH⁻ = 80 Br⁻ = 3 x 10⁻³ I⁻ = 5 x 10⁻⁻⁷ | 1) Acidification  
2) Chromatographic separation from other halides |
| Fluoride | OH⁻ | Acidification with Orion special ISA: TISAB, added to urine samples at equal volumes |
| Bromide | OH⁻ = 3 x 10⁰ Cl⁻ = 400 I⁻ = 2 x 10⁻⁴ | Chromatographic separation from other halides |
| Iodide | Cl⁻ = 10⁻⁶ Br⁻ = 5 x 10⁻³ | Chromatographic separation from other halides |

* The maximum allowable concentrations of interfering substances express as the molar ratio of the interfering ion concentration to the sample halide concentration. If the ratio is exceeded, the data generated by electrode will become unreliable. Information supplied by Thermo Orion Corporation.
Figure 1
Effect of Increasing Intake of Iodine/Iodide on Percentage Urinary Excretion of Ingested Amounts

![Graph showing the effect of increasing intake of Iodine/Iodide on percentage urinary excretion of ingested amounts.](Image)

Because of the improved overall well-being reported by the subjects who achieved 90% or more iodide excreted, sufficiency was arbitrarily set as 90%. Implementation of orthiodosupplementation based on the loading test revealed that sufficiency was not achieved in some subjects even after two years of iodine supplementation at 50 mg/day. In three patients with polycystic ovary syndrome with oligomenorrhea, orthiodosupplementation resulted in regularization of the menstrual cycle. In patients on thyroid hormones, orthiodosupplementation resulted in a decreased requirement to much lower levels of thyroxine and in some cases, resulted in the complete discontinuation of this hormone. This decreased requirement for thyroid hormones following orthiodosupplementation was observed in a female patient with total thyroidectomy, suggesting that iodine not only improves thyroid function but also has an effect at the target organ level. In diabetic patients on insulin, orthiodosupplementation resulted in better control of this condition, and in some cases alleviated this condition without the need for insulin. In hypertensive patients, whole body iodine sufficiency resulted in normalization of blood pressure without medications. Similar observations were reported by other physicians using this program. Best results were achieved when orthiodosupplementation was combined with a complete nutritional program emphasizing magnesium instead of calcium. The occurrence of side ef-
rum iodide levels were still elevated 24 hours after the loading dose, ranging from 0.3-0.6 mg/L.\(^3\)\(^7\)

In order to assess the presence of iodine and iodate (the oxidized forms) in serum following orthoiodosupplementation, serum iodide levels (the reduced form) were measured by ion-selective electrode before and after reduction with sodium metabisulfate. The three inorganic forms of the element iodine consumed by human subjects are 1) the negatively charged reduced iodide; 2) the negatively charged highly oxidized iodate IO\(^3\); and 3) the neutral oxidized iodine I\(_2\). The iodide selective electrode is influenced only by negatively charged forms of this element, that is, iodide I\(^-\) and iodate IO\(^3\). Experiments performed by the author with sodium iodate revealed that the iodate molecule, because it is larger in size than iodide, did not have any appreciable effect on the electromotive force (EMF) of the electrode, even at concentrations 10,000 times higher than the amount of iodide influencing significantly the EMF of the selective electrode.

Pilot studies were performed in order to quantify the amount of the reductant needed for the reduction of iodine and iodate to iodide. Almost 10 times more reductant was required for the reduction of iodate to iodide than iodine to iodide. The reduction of iodate resulted in the formation of iodine first, then iodide. When this procedure was applied to urine samples, no significant difference was observed between pre- and post-reduction levels, suggesting that only iodide, the reduced form, was present in urine. However, serial serum samples obtained for 24 hours following the loading test, showed a significant difference in the serum iodide levels between pre- and post-reduction samples within the first two hours in a female subject, with post-reduction levels 5-10% higher. This suggests the presence of serum iodine early after ingestion of the Lugol tablets. Iodine obviously is not completely reduced to iodide in the intestinal tract during absorption as mentioned in medical textbooks. In another female subject post-orthoiodosupplementation for one month, a second peak of serum iodine was observed eight hours after the first peak. Apparently, iodine is not reduced to iodide by the liver during enterohepatic circulation. There was no significant difference in the iodide measured following the addition of reductant to serum for the conversion of iodine to iodide or following the addition of 10 times more reductant for the conversion of iodate to iodide. Therefore, there was no evidence of iodate in the serum samples analyzed. The oxidation of iodine to iodate in biological systems has not been reported and this metabolic pathway of iodine probably does not occur in vivo. The only source of peripheral iodates would be from ingested food and drink. The author has not been able to locate a publication dealing with the measurements of serum iodate following ingestion of iodate. It is an easy experiment to carry out.

 Serum inorganic iodide levels are a good index of the bioavailability of ingested iodine/iodide. Serum inorganic iodide is cleared rapidly by the kidneys with a daily clearance rate of 43.5 L.\(^7\) At steady state condition, the serum iodide levels expected for patients receiving 50 mg iodine/day should be approximately: serum iodide (mg/L) = daily intake (mg)/43.5 L = 50 mg/43.5 L = 1.15 mg/L.\(^7\) If patients continue to excrete low levels of iodide after orthoiodosupplementation for three months, serum inorganic iodide levels are indicated to assess whether this is due to decreased absorption or increased demand. Malabsorption of iodine/iodide would result in very low serum inorganic iodide levels (10\(^{-8}\)M) in the presence of low urinary excretion. We have not observed a case of malabsorption of iodine yet, when iodine supplementation was in the range of 12.5-50.0 mg/day. However, the author has previously reported low absorption of sodium iodide from salt.\(^7\) On a molar basis, there is 30,000 times more chloride than iodide in iodized salt. Due to competition for absorption by the halide chloride, only 10% of iodide in iodized salt is absorbed. Obesity increases the requirement for iodine\(^7\) and up to 100 mg elemental iodine/day may be required to achieve and maintain sufficiency. Another factor in-

(Continued on next page)

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**Table 3**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Commercial Lab 1 (mg/24h)</th>
<th>Commercial Lab 2 (mg/24h)</th>
<th>Optimox R&amp;D Lab (mg/24h)</th>
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<td>F</td>
<td>14.0</td>
<td>37.8</td>
<td>23.1</td>
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<td>20.8</td>
<td>19.0</td>
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<td>3</td>
<td>M</td>
<td>7.0</td>
<td>23.8</td>
<td>12.5</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>11.0</td>
<td>99.0</td>
<td>34.7</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>12.0</td>
<td>41.9</td>
<td>19.0</td>
</tr>
</tbody>
</table>

* Urine iodide levels measured by Induction-Coupled Plasma — Mass Spectrometry.
** Urine iodide levels measured by Ion Selective Electrode Assay.

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within the range of iodide levels expected for the loading test. He showed great interest in offering this service to his clients, and the author supplied him with the details of the technique using ion-selective electrode, following chromatography on strong anion exchangers.

The chromatographic system was modified in order to measure accurately the other halides: chloride, fluoride, and bromide, using a positive displacement manifold designed by the author.8 The flowchart for this chromatographic separation is displayed in Figure 2. Comparison of results obtained before and after chromatographic purification of the halides chloride, fluoride, bromide, and iodide revealed the following. In 24 urine samples analyzed, the values obtained for chloride and fluoride by the direct assay, using Thermo Orion reagents and the values obtained after chromatography were not significantly different. However, for bromide and iodide, the direct assay overestimated significantly the values obtained following chromatography. For iodide, the direct assay overestimated by two-fold on the average, the levels obtained following chromatography in urine samples obtained prior to iodine supplementation. Even after iodine supplementation, significant differences were observed in the iodide levels of some samples measured by these two procedures. It was decided to perform chromatography on all samples prior to analysis by the iodide-selective electrode, no matter the expected iodide levels.

Orthiodosupplementation resulted in marked increase in bromide excretion, and to a lesser extent in fluoride also. The results obtained in the first five subjects studied are displayed in Table 4. The results observed for bromide in subject #5 were so surprising that they were published as a letter to the editor of Townsend Letter.13 These findings have since been replicated in a large number of tests. Female patients with breast cancer seem to retain more iodine on the loading test than normal subjects and excrete more bromide than normal subjects. This needs to be confirmed using a well-designed protocol since this observation is anecdotal on a small number of patients.

Recently, the author extended the ion-selective electrode assay to serum samples.8 Evidence for an enterohepatic circulation of inorganic iodine was observed for the first time. Serum iodide levels reached peak values of 1.5-2.2 mg/L between two and four hours post ingestion of Iodoral® in subjects ingesting 3-4 tab/day. A second peak of serum iodide after eight hours following the first peak was observed in some subjects suggesting that serum iodide undergoes an enterohepatic circulation. Se-

(Continued on next page)
vey of US thyroidologists, some 70% used radioiodide to treat hyperthyroidism instead of the Lugol solution used previously to treat this condition safely and effectively with a success rate as high as 90%, compared to a thyroid destruction rate of 90% with radioiodide. The love affair of thyroidologist for radioiodide is not limited to its therapeutic application. Radioiodide is used extensively for diagnostic purposes although safer methods exist to obtain the same information. Fluorescence scanning of the thyroid gland gives more useful information than isotope scanning.19 Okerlund commented, “The types of images obtained from fluorescent thyroid scanning are indistinguishable from those of isotope scanning, since the same electronics and data presentation systems are used. The size, shape, and positional relationships of the thyroid lobes are therefore comparable to isotope scanning, with the right lobe larger in the majority of normal cases, the two lobes of equal size in a smaller number, and the presence of a larger left lobe in a still smaller number.” Fluorescent scanning gives additional information on the amount of stable iodine in the thyroid gland.

Okerlund20 reported that thyroid hormone therapy and irradiation of the thyroid gland cause a depletion of iodine from the thyroid gland. Ingestion of thyroid hormones for three months or more resulted in very low levels of thyroidal stable iodine reaching the detection limit of the equipment. “The finding that previously irradiated thyroid glands are sometimes iodide depleted, coupled with the observation that the iodide depleted gland in experimental animals is physiologically more sensitive to the effects of pituitary thyrotropin (TSH), may lead to changes in the understanding of radiation-induced thyroid disease and to changes in the clinical management of at least some of these patients, who are known to be at high risk for thyroid tumor development.” Okerlund20 is suggesting that patients on thyroid hormones and receiving radioiodide or radiation therapy should be supplemented with iodine as a preventative measure against the carcinogenic effect of these interventions in iodine depleted thyroid glands.

For the US population, Okerlund20 reported a mean value of around 10 mg iodine/thyroid, with a range of 4-19 mg. In 56 patients suffering from autoimmune thyroiditis, but with normal thyroid function, a mean value of 4.8 mg/thyroid was reported. In 13 patients with autoimmune thyroiditis and hypothyroidism, the mean value was 2.3 mg/thyroid. In 12 patients treated with amiodarone, a toxic form of sustained-release iodine, Jonckheer21 reported a mean ± SD of 30.5±9.2 mg/thyroid. In five patients who experienced thyroid dysfunction during amiodarone therapy, (three with hypothyroidism, two with hyperthyroidism), the iodine content of the thyroid gland was very low, being 4-10 times lower. The author previously calculated that the theoretical maximum of thyroidal iodine in the adult is 50 mg.7 In the 12 patients on amiodarone therapy, the mean ± SD was 30.5±9.2 mg, giving a 95% confidence limit ranging from 12.0-48.9 mg/thyroid. The upper limit of measured iodine in the thyroid gland of these patients, 48.9 mg is very close to the theoretical maximum of 50 mg/thyroid.

Why don’t thyroidologists use fluorescent scanning of the thyroid instead of isotope scanning?9 One possible reason is the fact that this procedure exposed the harmful effect of thyroid hormone therapy and radioiodide in depleting the thyroid gland of iodine. Low thyroid iodine is associated with thyroid hyperplasia and cancer.1 Could thyroid hormones cause the same iodine depletion in breast tissue? The prevalence of breast cancer is higher in women on thyroid hormones.4 Thyroidologists use thyroid hormones extensively in their practice without supplementing their patients with iodine. Fluorescence scanning of the thyroid gland should be implemented. Thyroidologists would then have to face the damages they are causing to the thyroid gland and consequently to their patients.

Medical iodophobia resulted in the removal of iodate from bread 20 years ago, replacing it with the goitrogen bromate. This was associated with an increased prevalence of obesity, diabetes, and hypertension, as well as thyroid and breast cancer.1 A recent publication reported an association between low iodine intake in women during pregnancy and attention deficit and hyperactivity disorder (ADHD) in their offspring.22 However, children diagnosed with ADHD do not demonstrate prenatal thyroid dysfunction, reflected in the newborn serum thyroxine levels.23 The most plausible explanation is a decreased sensitivity of the nuclear thyroid hormone receptor to thyroid hormones. We previously reported evidence for improved receptor response to thyroid hormones following orthoiodosupplementation.1,4 Therefore, iodine is not only necessary for the synthesis of thyroid hormones but also for their effect on target cells. This effect is probably due to iodination of the thyroid hormone receptor.1,4 The essential element iodine, which is the inorganic, non-radioactive forms, deserves more attention from researchers and clinicians. It may be the missing link in patients currently resistant to conventional hormonal therapy.

About the Author

Guy E. Abraham, MD, is a former Professor of Obstetrics, Gynecology, and Endocrinology at the UCLA

(Continued on next page)
volved in the increased demand for iodine is the presence of excessive amounts of goitrogens from the diet and lifestyle. For example, smoking increases serum thiocyanate levels, interfering with the sodium/iodide symporter function. Sources of goitrogens are available from medical textbooks, although the halides fluoride and bromide are not listed as goitrogens. Fluoride interferes with the uptake of iodide by the thyroid gland symporter system, but it is itself not transported inside the thyrocyte, suggesting that fluoride causes oxidative damage to the halide-binding site of the symporter. The author previously discussed the goitrogenic effect of bromide even at low concentrations. Patients who used water from wells and municipal plants may be exposed to potassium perchlorate, a very powerful goitrogen that behaves like fluoride, binding to the halide-binding site of the symporter without itself being symported. A recent Internet publication by Kirk, et al., reported the presence of high concentrations of perchlorate in dairy milk sold in grocery stores and in human milk. The mean levels of perchlorate were five times higher in breast milk than dairy milk. Perchlorate has a selectivity factor of at least 30 over iodide. To compete effectively against this goitrogen, the peripheral concentration of inorganic iodide must be at least 100 times higher than the concentration of perchlorate. Kirk, et al., observed that breast and dairy iodide levels were inversely correlated with the levels of perchlorate. Perchlorate and fluoride, due to their high redox potential, may cause oxidative damage to the halide-binding site, decreasing its efficiency for iodide transport.

If the pre-orthiodosupplementation loading test report shows 90% or more of the ingested iodine in the 24-hour urine collection of patients on a Western diet, serum inorganic iodide levels are indicated to rule out an iodide transport defect or damage not just in the thyroid gland but throughout the whole body. In our experience, this is very rare and was observed in only two cases. The intestinal absorption of iodine/iodide involves a different mechanism than the uptake of iodide by target cells via the sodium/iodide symporter. For example, chloride competes with iodide in the intestinal tract but chloride has no detectable effect on the iodide symporter system. This explains why a patient with iodide transport damage is able to absorb iodine/iodide efficiently but unable to transfer peripheral iodine/iodide into the cells. Peripheral iodide is cleared very rapidly by the kidneys, resulting in quantitative recovery of ingested iodine/iodide in the urine in a patient who is very iodine-deficient, if the cellular transport system is defective. In those cases, serum inorganic iodide levels 24 hours after the loading test will be low, even though the loading test suggests whole body sufficiency for iodine. In two obese female patients with poor clinical response to orthiodosupplementation, high urinary iodide excretion was associated with serum inorganic iodide levels below $10^{-6}$M (0.13 mg/L). The expected serum levels associated with high urinary iodide excretion should be between $5 \times 10^{-6}$M to $10^{-5}$M.

Although congenital hypothyroidism due to sodium/iodide symporter defect is extremely rare, milder forms of iodine/iodide transport defect/damage throughout the whole body may be more common and undetected. As of 1997, only 38 cases of congenital hypothyroidism due to sodium/iodide symporter defect were reported. Of interest is that in one of these cases, a male Japanese subject, the diagnosis was not made until he was 30 years old. At the time of evaluation, he was euthyroid with a goiter while on the high iodine Japanese diet, but he got hypothyroidism on a Western diet. Administration of 50 mg iodide restored euthyroidism. An active transport system for iodide by a sodium/iodide symporter has been demonstrated in several organs besides the thyroid gland, capable of concentrating peripheral inorganic iodide 20-40-fold against a gradient. The cellular uptake of iodide in some tissues may involve other mechanisms than the symporter system. Inorganic iodine/iodide has been detected in every organ and tissue examined, with relatively high levels in the thyroid gland, liver, lung, heart, and adrenal glands. The highest quantity of iodine was found in fat tissue and muscle. Exposure to fluoride and perchlorate can cause oxidative damage to the halide-binding site of the sodium/iodide symporter system, due to their high redox potential. In such cases, more than 50 mg iodine/day may be required to overcome the low efficiency of the iodine transport system. If the high iodide excretion prior to orthiodosupplementation is due to significant amount of iodine in the diet of the patient, such as the diet of mainland Japanese, or if due to ingestion of medications containing iodine, fasting serum inorganic iodide levels will be between $5 \times 10^{-6}$ and $10^{-5}$M (0.65-1.30 mg/L). This is the range of serum iodide levels observed by the author when sufficiency is achieved.

As mentioned previously, medical iodophobia has reached pandemic proportion, is highly contagious, and has wreaked havoc in the practice of medicine and on the US population. More misery and death in the US may have resulted from the Wolff-Chaikoff effect than both World Wars combined. Due to thyroid fixation, thyroidologists dictate the need for iodine. However, thyroidologists suffer from selective iodophobia for the inorganic, non-radioactive forms of iodine combined with a paradoxical iodophylia for radioiodide. In a sur-

(Continued on next page)
School of Medicine. Some 35 years ago, he pioneered the development of assays to measure minute quantities of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974; the Medaille d’Honneur from the University of Liege, Belgium, 1976; the Senior Investigator Award of Pharmacia, Sweden, 1980. The applications of Dr. Abraham’s techniques to a variety of female disorders have brought a notable improvement to the understanding and management of these disorders. Twenty-five years ago, Dr. Abraham developed nutritional programs for women with premenstrual tension syndrome and postmenopausal osteoporosis. They are now the most commonly used dietary programs by American obstetricians and gynecologists. Dr. Abraham’s current research interests include the development of assays for the measurement of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974, Am J Med, 1979; 149-160.

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14) Delange FM. “Iodine deficiency.” In Werner & Ingbar’s The Thyroid. Braverman LE and Utiger RD, editors. Lippincott Williams & Wilkins, 2000; 295-316.

Table 4

Fluoride and Bromide Levels Measured in 24-hour Urine Collections of 5 Subjects Following the Iodine/Iodide Loading Test Before and After 1 Month on Iodoral® at 3 Tab/Day

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Control</th>
<th>Before Iodoral®</th>
<th>After 1 Month of Iodoral®</th>
<th>Control</th>
<th>Before Iodoral®</th>
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<td>0.40</td>
<td>0.80</td>
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<td>3</td>
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<td>—</td>
<td>4.8</td>
<td>5.2</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>0.35</td>
<td>0.62</td>
<td>0.44</td>
<td>6.8</td>
<td>34.8</td>
<td>32.0</td>
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<tr>
<td>5</td>
<td>M</td>
<td>0.05</td>
<td>0.93</td>
<td>0.79</td>
<td>18.4</td>
<td>336.0</td>
<td>288.0</td>
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<tr>
<td>6</td>
<td>M</td>
<td>1.20</td>
<td>1.40</td>
<td>1.20</td>
<td>12.2</td>
<td>24.5</td>
<td>24.0</td>
</tr>
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</table>

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when higher amounts of iodide were ingested. Essentially, the thyroid iodide transport system will pick up increasing amounts of iodide as peripheral iodide levels increase, but up to a point. When saturation is reached, however, thyroid hormone levels were maintained within normal limits.

Let us recapitulate by defining the W-C effect. When normal rats are injected with a single intraperitoneal dose of potassium iodide mixed with radioiodide tracer, in amounts five times or more greater than the total amounts of iodide measured in the thyroid gland of those rats, the organic binding of radioiodide by the thyroid becomes undetectable as long as serum levels of inorganic iodide are maintained above 19 g percent \(10^{-6}\)M. As we previously discussed, radioiodide uptake by the thyroid gland should be zero when stable (non-radioactive) iodide sufficiency of the thyroid gland is achieved. Therefore, the so-called blockage of organification of radioiodide by the thyroid gland when serum inorganic iodide reached \(10^{-6}\)M is really the amount of serum inorganic iodide needed for thyroid sufficiency. There is no blockage of organification of stable iodide by the thyroid gland.

The fictitious W-C effect initiated the iodophobic era, which is still alive and well more than 50 years later. This was the beginning of the end of inorganic, non-radioactive iodine in the form of Lugol solution, used extensively by pre-World War II US physicians for both hypothyroidism and hyperthyroidism. What was it about this publication that caused the capitulation of US physicians who exchanged Lugol solution for thyroid hormones in iodine deficiency-induced hypothyroidism and simple goiter and for toxic goitrogens and radioiodide in iodine deficiency-induced hyperthyroidism? The answer is medical iodophobia, the fear of using and recommending inorganic, non-radioactive iodine in amounts previously used safely and effectively in medical practice. What was it in the 1948 Wolff-Chaikoff publication\(^1\) and in Wolff’s review\(^7\) that resulted in medical iodophobia? The answer is that they were iodophobic publications. What is an iodophobic publication? It is a publication that promotes iodophobic misinformation in order to discourage the use of inorganic, non-radioactive iodine in the proper amount.

Medical iodophobia resulted in the thyroid hormone thyroxine replacing iodine in iodine deficiency-induced simple goiter and hypothyroidism. Thyroxine has been the most prescribed drug in the US for several years. So, the manufacturers of thyroxine benefited tremendously from this deception. It also resulted in the destruction of the thyroid gland by means of radioiodide in patients with hyperthyroidism caused by iodine deficiency, although this condition had previously been treated successfully with Lugol solution.\(^3\) The radioablation of the thyroid gland with radioiodide resulted in 90% of these patients becoming hypothyroid within the first year and eventually joining the ever-increasing thyroxine-consuming population.\(^3\)

Supplying thyroid hormones to iodine-deprived individuals masks the iodine deficiency and can result in a zombie-like effect. The patients are capable of performing physical work but are not able to think and reason at maximum capacity. An even greater negative effect is realized if iodine deprivation is combined with goitrogens and perchlorate in the food and water supply.

Iodine is involved in many vital mental and physical functions, and yet whole body sufficiency for iodine has never been determined. Why? Medical textbooks discuss inorganic, non-radioactive iodine only in relation to the most severe deficiencies of this essential element: cretinism, hypothyroidism, and endemic goiter. Based on an iodineiodide loading test developed by the author to assess whole body sufficiency for iodine, the amounts of iodine needed for whole body sufficiency and optimal physical and mental health are 250-1,000 times higher than the amount of iodine needed to control cretinism, hypothyroidism, and endemic goiter.\(^3,4\)

The use of optimal amounts of iodine in the prevention of cancer of the female reproductive organs was proposed by Stadel, from the National Institute of Health in 1976, 29 years ago.\(^12\) So far, no such study has been published. There seems to be a moratorium on iodine research in effective amounts, thanks to the W-C effect. Dr. B. Eskin has attempted to reproduce in human subjects his excellent results on iodine and breast cancer observed in female rats.\(^13-15\) He proposed clinical studies in human subjects using iodine in amounts based on bodyweight equivalent to those observed to be effective in the rats. He was told this could not be done because of the W-C effect.\(^16\)

The W-C effect, combined with medical stupidity, has caused enough damage. It is time US physicians and other health care professionals wake up and realize that they have been deceived. They should stop crying Wolff and shake off the W-C effect.

Since our series of publications exposing the damaging effect of medical iodophobia,\(^2,4,17-20\) there is evidence that the anti-iodine side has called to action its damage (Continued on next page)
Wolff’s review.7 More than 50 years after the Wolff-Chaikoff forgery, it is still quoted in iodophobic publications.

Children as Victims: Shortly after the publication on “excess iodine” in newborns,22 another publication in the American Journal of Clinical Nutrition23 reported that urine iodide concentrations greater than 0.5 mg/L was associated with increased thyroid volume in multietnic groups of children between six and 12 years old. Analysis of the data in Table I of that publication revealed only children from Hokkaido, Japan, showed increased thyroid volumes of significance compared to the other groups: 2.16 to 2.59 ml for all the other groups; and 2.86 and 4.91 ml for the 2 groups from Hokkaido. This area of Japan is known to have a high incidence of euthyroid goiter. Suzuki, et al9 first reported this finding in 1965 but did not think that iodine was the cause of this goiter. He commented: “Considering the paucity of reported cases of iodine goiter with the widespread usage of iodine medication, we cannot exclude factors other than excessive intake of dietary iodine as a cause of the goiter.”

Diverting Attention from the Anticarcinogenic Effect of Iodine in Seaweed

Based on an extensive review of breast cancer epidemiological studies, R.A. Wiseman24 came to the following conclusions: 92-96% of breast cancer cases are sporadic; there is a single cause for the majority of cases; the causative agent is deficiency of a micronutrient that is depleted by a high-fat diet; and if such an agent is detected, intervention studies with supplementation should lead to a decline in the incidence of breast cancer. It is the opinion of several investigators that this protective micronutrient is the essential element iodine.2 Demographic surveys of Japan and Iceland revealed that both countries have a relatively high intake of iodine and low incidences of simple endemic goiter and breast cancer. Whereas in Mexico and Thailand, just the reverse is observed — a high incidence of both endemic goiter and breast cancer.25 Thomas, et al26,27 have demonstrated a significant and inverse correlation between iodine intake and the incidence of breast, endometrial, and ovarian cancer in various geographical areas. Thyroid volume, measured by ultrasonometry and expressed as ml, is significantly larger in Irish women with breast cancer than controls with mean values of 12.9±1.2 in controls and 20.4±1.0 in women with breast cancer.28 Intervention studies in female rats by Eskin13-15 are very suggestive of a facilitating role of iodine deficiency on the carcinogenic effect of estrogens and a protective role of iodine in maintaining normality of breast tissues. The risk for breast cancer is higher in women with fibrocystic disease of the breast (FDB), and iodine supplementation is effective against FDB.2,24

With this background of extensive information on the beneficial roles of iodine in seaweed against breast cancer, one would expect that a publication dealing with the protective role of iodine-rich seaweed against breast cancer would mention iodine as a possible factor in the list of bioactive substances. Here comes toxicologist Skibola, from UC-Berkeley, the birthplace of the Wolff-Chaikoff effect. In the August 2004 issue of BMC Complementary and Alternative Medicine,29 Skibola reported the effect of brown seaweed on menstrual cycle length and hormonal status in three pre-menopausal women with short menstrual cycles and prolonged menstrual flow. The seaweed was administered orally in a powder form compounded in gelatin capsules (seaweed supplements). In all three women, administration of seaweed resulted in a prolongation of the menstrual cycle, a decrease in menstrual flow, a marked drop in serum estradiol 17-B levels, and a marked increase in serum progesterone.29 In the list of potential substances in seaweed capable of eliciting such a beneficial effect on the ovaries, iodine was not mentioned once. In fact, the word “iodine” was completely omitted in the publication. The amount of iodine in the seaweed used in her study was not reported. In a subsequent publication, Skibola, et al30 reproduced in female rats the results obtained with seaweed in women. Again they failed to mention iodine as a possible factor involved in the results obtained. These results reported by Skibola demonstrate a dramatic effect of seaweed on the ovaries of these women, normalizing ovarian function. The element iodine was reported by Russian scientists 40 years ago to elicit a similar effect in normalizing ovarian function in women with cystic ovaries.31

Two Russian scientists31 published in 1966 their results regarding the effect of oral administration of potassium iodide in daily amounts equivalent to 10-20 mg elemental iodine, on 200 patients with “dyshormonal hyperphasia of mammary glands.” They postulated that this form of mastopathy was due to excess estrogens from ovarian follicular cysts which were caused by iodine deficiency. The duration of iodine supplementation of their patients varied from six months to three years. Within three months, there was significant reduction of swelling, pain, diffuse induration, and nodularity of the breast. In five patients with ovarian follicular cysts, there was a regression of the cystic ovaries following five months to one year of iodine supplementation. Ghent, et al32 obtained similar results in FDB treated with iodine. We have observed similar responses to iodine supplementation.

(Continued on next page)
control team. We have previously documented the relatively high intake of iodine by mainland Japanese with a mean daily intake of 13.8 mg. This amount was confirmed by spot urine samples from a large group of mainland Japanese. This author calculated that Japanese fetuses are exposed to maternal serum iodide levels of $10^5$M to $10^6$M, which is the ideal range for optimal function. Mainland Japanese are one of the healthiest populations on earth. More than 95% of the iodine consumed by mainland Japanese is obtained from seaweed. By removing seaweed from the Japanese diet, their daily intake of iodine would drop 100-fold and would reach the low levels of intake observed in the US.

If iodine gains publicity as the active ingredient in seaweed, protecting mainland Japanese from the degenerative diseases of the Western World, this would be a deathblow to medical iodiophobia. In order to maintain the iodophobic mentality, it is necessary to keep emphasizing the toxicity of iodine in seaweed; and then, divert attention from the fact that iodine is the active ingredient in seaweed that is detrimental to cancers of the female reproductive organs and many of the diseases of Western civilization. In your list of possible bioactive anticarcinogenic substances in seaweed, avoid mentioning iodine at all costs.

This is a form of doublespeak. Seaweed is bad for you because it contains the toxic element iodine; seaweed is good for you because of some unknown factors protecting you against breast cancer, but more research is needed. This kind of confusion works effectively in a population that is already iodine-deprived. It would become totally ineffective if the target population becomes iodine-sufficient because the improved cognition induced by iodine sufficiency would render this deception very transparent.

With the above information as background, let us now examine iodophobic propaganda in action. There are two major ways that this is being done:

1) Emphasizing the toxicity of iodine in seaweed, using newborns and children as victims to get the greatest emotional impact.

2) Diverting attention from the fact that iodine is the active ingredient in seaweed against the carcinogenic effect of estrogens on female reproductive organs and against many other diseases of the Western World, while pointing to some other factors in seaweed eliciting these beneficial effects.

And to do all this effectively, they make sure the iodophobic publications get wide coverage on the Internet.

Nishiyama, et al did not fail to mention the fictitious W-C effect as the cause of elevated TSH and reduced thyroxine in these 15 infants even though these infants had normal free thyroxine levels and Wolff and Chaikoff never demonstrated elevated TSH and low thyroxine in their rats, or, for that matter, in any animal species: "Because of antithyroid effects of an iodine excess, the so-called Wolff-Chaikoff effect, which blocks the uptake of iodine by the thyroid gland, leads to reduced T4 and increased TSH."

According to Wolff, iodine intake of 2 mg or more is considered "excessive and potentially harmful." So, Nishiyama, et al divided those 15 infants into two groups: one group with maternal intake of iodine below 2 mg and another group with maternal intake above 2 mg. However, in both groups, the reported intake of iodine by the pregnant women was much lower than the national average intake of iodine.

Nishiyama, et al reported that their so-called control group of pregnant women ingested only 0.25-0.48 mg iodine/day, which is within the range of iodine intake in the US. Women in their control group were asked to abstain from seaweed for a few days. How convenient! In the mothers who supposedly ingested "excessive iodine" from their diet, the amount of iodine ingested was 5-10 times lower than the national average intake by mainland Japanese. Normal thyroid hormones and TSH were observed in these women. All 15 infants from these mothers had normal serum free T4 levels. The physical and psychomotor developments of the 15 infants were normal.

After centuries of consuming safely large amounts of iodine from seaweed, why would iodine in seaweed suddenly become toxic to mainland Japanese? The data presented in Nishiyama’s publication do not justify the alarming implication of the title of that publication. The expression “excessive iodine intake” is taken from (Continued on next page)
to destroy a nation is the removal of iodine from the food supply. Iodophobic bioterrorism is a real threat to our nation, and the enemies within our gates masquerade as guardians of our thyroid gland.

About the Author

Guy E. Abraham, MD, is a former Professor of Obstetrics, Gynecology, and Endocrinology at the UCLA School of Medicine. Some 35 years ago, he pioneered the development of assays to measure minute quantities of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974; the Medaille d’Honneur from the University of Liege, Belgium, 1976; the Senior Investigator Award of Pharmacists, Sweden, 1977; and Guy E. Abraham, MD, is a former Professor of Obstetrics, Gynecology, and Endocrinology at the UCLA School of Medicine. Some 35 years ago, he pioneered the development of assays to measure minute quantities of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974; the Medaille d’Honneur from the University of Liege, Belgium, 1976; the Senior Investigator Award of Pharmacists, Sweden, 1977; and

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16) Eskin B. Personal communication.
tion at daily amounts of 50 mg iodine in the form of Lugol tablets in patients with polycystic ovary syndrome, resulting in the regularization of the menstrual cycle. Why Skibola chose to completely ignore iodine in her publications remains a mystery. Next to the thyroid gland, the ovaries contain the largest concentration of iodine. A sodium iodide symporter is present in the ovaries. This ovarian symporter is blocked by goitrogens. There is overwhelming evidence that iodine is the active ingredient in seaweed, eliciting the effects observed by Skibola on the ovaries of women.

Most Internet users do not go further than the information supplied on the Web. Rarely do they search further in the original studies. So, what is on the Net about Skibola’s studies? In an interview with Amy Norton, Skibola did mention iodine as a potentially toxic substance: “Adding seaweed to the diet is probably going to be beneficial,” Skibola said. However, she offered a word of caution about the kelp supplements sold at health food stores. Kelp contains high amounts of iodine, as well as low levels of heavy metals, and taking the seaweed in supplement form makes it easier to get too much of these potentially toxic substances. According to Skibola, kelp is not recommended for women who are pregnant or nursing, or for people with an overactive thyroid gland.”

Here, we have a perfect example of doublespeak. Skibola, who became an instant expert on iodine, advises against kelp supplements sold in health food stores because of the presence of the toxic substances iodine and heavy metals. Yet, she used in her studies, seaweed supplements made up of seaweed powder obtained from the same company that sells bulk seaweed powder to manufacturers who supply seaweed capsules to health food stores. Skibola is very concerned about toxic substances, such as iodine in seaweed from health food stores. Kelp contains high amounts of iodine, as well as low levels of heavy metals, and taking the seaweed in supplement form makes it easier to get too much of these potentially toxic substances. According to Skibola, kelp is not recommended for women who are pregnant or nursing, or for people with an overactive thyroid gland.”

The worst form of domestic bioterrorism is the dissemination of iodophobic misinformation in order to discourage the use of adequate amount of iodine for whole body sufficiency (orthiodosupplementation). Today, the public relies heavily on the Internet for health information. Rarely do they search for the original publications. Whoever supplies health information on the Internet controls the health of the Internet user. Control of health information on the Internet is a real threat to a population who depends on this source of information to make health-related decisions. Such a population is vulnerable and most likely will end up adopting iodophobic decisions to their detriment. Once caught in the iodophobic Net, it becomes a vicious cycle, difficult to exit.

Iodophobic bioterrorism can be prevented through education of health care professionals and the public at large. Remember that the easiest and most effective way (Continued on next page)
24 hrs, (eight samples) following the ingestion of the preparation.

Group II consisted of six normal women with normal body weight. This group was studied twice: Before and after 1 month of iodine supplementation at 50 mg elemental iodine/day (four tablets Iodoral®). For the loading test, four tablets (50 mg) were ingested and blood samples were obtained at time zero, 10 min, 20 min, 30 min, 1 hr, 2 hrs, 3 hrs, 4 hrs, 8 hrs, and 24 hrs (10 samples). Serum samples obtained, following further processing, were frozen in plastic containers until assayed.

Results
The serum levels of inorganic iodide in Group I subjects receiving three tablets of Iodoral® are compared with the levels obtained pre-supplementation in Group II subjects who ingested four tablets (Figure 2). At time zero, the serum iodide levels were undetectable in both groups. Since 10 ml of serum was used in Group I and 3 ml in Group II, the sensitivity of the assay was 0.006 mg/L for Group I and 0.02 mg/L for Group II.

The serum levels obtained at 10 and 20 minutes in Group II were omitted from this figure for ease of comparisons since these two samples were not available in Group I. Also, Group I subjects did not have a three-hour blood sample, and Group II subjects did not have a six-hour blood sample. By 30 minutes post ingestion of three tablets (Group I) and four tablets (Group II), mean serum iodide levels were 0.4 mg/L and 0.7 mg/L respectively for Group I and Group II. Peak levels were achieved in both groups between two and four hours. Serum inorganic iodide levels were still detectable at 24 hours with 0.4 mg/L and 0.45 mg/L. The mean peak levels for Group I were around 1.5 mg/L; whereas, for Group II, the mean peak levels were between 1.8 mg/L and 2.2 mg/L. After one month of supplementation at 50 mg/day in Group II, four of six subjects reached peak levels at 10 minutes. These levels were maintained for 2-3 hours, forming a plateau, followed by a sharp drop, and a second peak at eight hours post ingestion.

The data on one of the subjects pre- and post-supplementation are displayed in Figure 3. Prior to supplementation, the iodide levels were below 0.02 mg/L at 10 minutes, became measurable at 20 minutes (0.2 mg/L), increased progressively to reach a peak 1.8 mg/L at two hours, and decreased afterward to levels of 0.4 mg/L at eight and 24 hours. Following one month of supplementation with four tablets of Iodoral® (50 mg), the peak levels were three times higher and shifted to the left by two hours. A plateau was maintained between 10 minutes and three hours with levels fluctuating between 4.6 mg/L and 5 mg/L. At four hours, the serum iodide level dropped sharply to 1.4 mg/L. No blood samples were obtained at six hours. A second peak of 3.2 mg/L was achieved.

Figure 1

This flowchart describes the combined measurement of chloride, fluoride, bromide, and iodide in the same urine or serum sample, by prior chromatography on anion-exchange resin cartridges fitted with 10 ml plastic syringes, in a Positive Displacement Manifold (PMD).
observed at eight hours, suggesting an enterohepatic circulation of iodine. Following one month of supplementation, steady state conditions were achieved in this subject, and the serum iodide levels were 1.3 mg/L pre-loading and 1.2 mg/L 24 hours post-loading. As previously discussed, at a daily intake of 50 mg iodine, expected serum levels at steady state would be equal to 50 mg/day divided by 43.5 L/day which computes to 1.15 mg/L. The renal clearance rate of iodide is 43.5 L/day.

The second peak of serum iodide levels eight hours after the first peak, following supplementation with 50 mg iodine for one month, was confirmed in a female subject who collected urine samples individually without pooling for 24 hours following the loading test with 50 mg (four tablets). This subject excreted 42% of the oral amount of 50 mg. A total of eight samples of voided urine were collected over the 24-hour period (Figure 4). The values shown on Figure 4 are expressed as percentage of the total iodide excreted in 24 hours, recovered in the voided sample expressed per hour, therefore representing excretion rate. This value was computed by dividing the amount of iodide measured in the sample by the interval of time in hours between collections. For example, if 20% of the total iodide excreted was recovered in a sample with a time interval of two hours from the previous void sample, the excretion rate would be 10%/hr. The first peak of urine iodide excretion rate occurred in sample #2, collected at five hours post ingestion, representing a three-hour period (time interval 2-5 hours from ingestion of iodine). This peak at 2-5 hours coincides with the serum data with peaks observed between two and four hours post-iodine administration. Serum iodide is efficiently cleared by the kidneys. A second peak was observed in sample #6, obtained at 13 hours post ingestion with a 2-hour interval (11-13 hrs). The interval of time between the two peaks is approximately eight hours, confirming the peak observed at eight hours in serum samples when the first peak was at 10 minutes.

**Discussion**

The effect of orthoiodosupplementation on the profile and levels of serum iodide following a loading test is suggestive of an effect of iodine on the efficiency and rapidity of absorption of iodine. Possibly, this effect of iodine supplementation on iodine absorption may be applicable to the absorption of other nutrients.

The second peak of serum iodide following the loading test was not observed in the subjects prior to iodine supplementation (Figure 2) because such a peak would be expected eight hours after the first peak. Since the first peaks occurred 2-4 hours after ingestion of iodine in Figure 2, the second peak would have occurred at 10-12 hours after the iodine load. No blood sample was obtained between eight and 24 hrs in those subjects.

(Continued on next page)

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**Figure 2**

Serum inorganic iodide levels following ingestion of 37.5 mg (three tablets Iodoral®) in Group I and 50 mg (four tablets Iodoral®) in Group II. Peak level are observed between two and four hours. V is less than 0.006 mg/L for Group I and less than 0.02 mg/L for Group II.
iodine were found in descending order in the thyroid gland, liver, lung, fat tissues, adrenal glands, and the heart.

When a tablet form of Lugol solution (Iodoral®) is ingested at a daily amount of 50 mg elemental iodine, whole body sufficiency is achieved in approximately three months; and the estimated amount of iodine retained in the body is approximately 1.5 g. This is the same amount of iodine retained in patients on amiodarone following 4-7 weeks at 300 mg/day. Clinical response to amiodarone is observed after the same period of time (4-7 weeks) on amiodarone therapy. These data are suggestive of an important role of inorganic iodine released from amiodarone in the therapeutic effect of this drug; and that whole body sufficiency for iodine is a requirement for optimal cardiac function. If amiodarone is a toxic form of sustained release iodine, and inorganic iodine is the active ingredient, why not give inorganic iodine to these unfortunate patients, saving them from the toxicity of the amiodarone molecule? Inorganic non-radioactive iodine/iodide is an essential nutrient, not a drug. Therefore, the body has the metabolic mechanism for using inorganic iodine beneficially, effectively and safely. Iodide is the safest essential nutrient, with a track record of 180 years of use in medicine. Published data confirms its safety even when used in pulmonary patients in amounts four orders of magnitude greater than the US RDA.

About the Author

Guy E. Abraham, MD, is a former Professor of Obstetrics, Gynecology and Endocrinology at the UCLA School of Medicine. Some 35 years ago, he pioneered the development of assays to measure minute quantities of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974; the “Medaille d’Honneur” from the University of Liege, Belgium, 1976; the Senior Investigator Award of Pharmacia, Sweden, 1980.

The applications of Dr. Abraham’s techniques to a variety of female disorders have brought a notable improvement to the understanding and management of these disorders. Twenty-five years ago, Dr. Abraham developed nutritional programs for women with premenstrual tension syndrome and post menopausal osteoporosis. They are now the most commonly used dietary programs by American obstetricians and gynecologists. Dr. Abraham’s current research interests include the development of assays for the measurement of iodide and the other halides in biological fluids and their applications to the implementation of orthoiodosupplementation in medical practice.

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mend radioiodine ablation of the thyroid to allow the reintroduction of amiodarone treatment in patients with a prior history of amiodarone-induced thyrotoxicosis. To quote Hermida, et al., “However, hypothyroidism should be viewed as a goal, rather than a complication, of treatment in these patients.” They have gone berserk!

Implementation of orthiodosupplementation in the above cases would be appropriate, not as a treatment for cardiac arrhythmias, but as a means of supplying these patients with adequate amounts of an essential nutrient for whole body sufficiency. Who knows? Orthiodosupplementation and whole body iodine sufficiency may be the answer to several clinical conditions currently treated with toxic drugs.

An enterohepatic circulation of amiodarone has been reported by Andreasen, et al. Since we have observed an enterohepatic circulation for inorganic iodine, could the iodine present in amiodarone and released from amiodarone play a role in this enterohepatic circulation? Broekhuysen, et al. using balance studies of amiodarone and the iodine released from amiodarone, reported the following. In two subjects treated with 300 mg of amiodarone/day, the total amount of iodine measured in urine and feces was very low during the first three days, with a mean of 19% and 7% of the total iodine ingested suggesting that 80-90% of the iodine ingested was retained in the body. After 25-27 days of therapy with 300 mg/day, the mean percentage excretion of combined urine plus feces in these two subjects increased 48% and 75%. Therefore, after approximately one month, the percentage of iodine retained by the body had decreased to 25% and 50%. No inorganic iodine/iodide was found in feces, only the organic form, amiodarone; whereas, in urine, inorganic iodide was excreted.

In two other subjects treated with 300 mg/day for seven weeks, balance studies revealed at the end of the study that the total excreted iodine in urine and feces averaged 97.4% and 96.9%. The authors commented, “These results suggest that iodine is retained in the body until a mechanism is triggered that adjusts the excretion of iodine to balance completely the intake.” They estimated that the body retained 1.5-2.0 g of iodine before the ingested iodine in amiodarone is completely excreted, and before therapeutic efficacy.

In three patients who died following long-term treatment with amiodarone, the levels of inorganic iodine present in various organs and tissues were measured. The total body iodine content was estimated at approximately 2 g with the greatest amount found in fat tissues (700 mg) and striated muscle (650 mg). Iodine was present in every tissue examined. The highest concentrations of (Continued on next page)

Figure 4

![Figure 4](image-url)

**Figure 4**

<table>
<thead>
<tr>
<th>Percent of total urinary iodide measured over 24 hr excreted per hour</th>
<th>10</th>
<th>8</th>
<th>6</th>
<th>4</th>
<th>2</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample #</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Time interval after ingesting 4 tab Iodoral®</td>
<td>0-2 h</td>
<td>2-5 h</td>
<td>5-8 h</td>
<td>8-9 h</td>
<td>9-11 h</td>
<td>11-13 h</td>
</tr>
</tbody>
</table>

Urinary excretion of iodide per hour in consecutive samples of urine collected over 24 hours after ingestion of four tablets of Iodoral® in a female subject.
The Safe and Effective Implementation of Orthoiodosupplementation In Medical Practice

by Guy E. Abraham, MD

I. Introduction
Of all the elements known so far to be essential for health, iodine is the most misunderstood and the most feared. Yet, it is by far the safest of all the trace elements known to be essential for human health. It is the only trace element that can be ingested safely in amounts up to 100,000 times the RDA. For example, potassium iodide has been prescribed safely to pulmonary patients in daily amounts of up to 6.0 gm/day, in large groups of such patients for several years.\(^1\)\(^-\)\(^3\) It is important, however, to emphasize that this safety record only applies to inorganic, non-radioactive iodine/iodide, not to organic iodine-containing drugs and to radioiodides. Unfortunately, the severe side effects of iodine-containing drugs have been attributed to inorganic iodine/iodide, even though published studies clearly demonstrate that it is the whole organic molecule that is cytotoxic, not the iodine covalently bound to this molecule. To quote Phillipou, et al.:\(^4\) “We can, therefore, conclude that the effect of amiodarone, benziodarone, Na iopanate, and other iodine containing substances with similar effects is due to the entire molecule and not to the iodine liberated. It should be noted that the cytotoxic effect of amiodarone in all cultures is also due to the entire molecule and not to the iodine present in it.” Several forms of iodine are used in clinical medicine (Table 1). Unless otherwise stated, this presentation is concerned only with inorganic, non-radioactive iodine/iodide.

Medical iodophobia is the unwarranted fear of using and recommending inorganic, non-radioactive iodine/iodide within the range known from the collective experience of three generations of clinicians to be the safest and most effective amounts for treating symptoms and signs of iodine/iodide deficiency (12.5-37.5 mg). The range of daily intake of this essential nutrient is hereafter referred to as orthoiodosupplementation because it is the range of iodine/iodide intake required in order to achieve whole body sufficiency for this element based on a recently developed iodine/iodide loading test. (See Section VII for more details on the loading test.)

Medical iodophobes suffer from: A) a split personality which results in iodophobia within the orthoiodosupplementation range previously used safely and successfully in medical practice and iodophylia for megadoses of iodide (up to 12gm/day); B) double standards, which render those physicians intolerant to the minor side effects of the inorganic forms and extremely tolerant to the severe side effects of the radioactive and organic forms; C) amnesia pertaining to the inorganic, non-radioactive forms when making therapeutic decisions; D) confusion, attributing the severe side effects of organic iodine-containing drugs to inorganic iodine/iodide; and E) an altered state of consciousness, allowing doublethink, doublespeak, and contradictory logic to become acceptable. Although the factors involved in medical iodophobia are still unknown, decreased cognition seems involved. Since low iodine intake is associated with intellectual impairment, deficiency of this essential element cannot be ruled out, and if present, would create a self-perpetuating phenomenon. Needless to say, medical iodophobia is contagious and can be transmitted to patients and other physicians (iatrogenic iodophobia). Medical iodophobia will remain a syndrome until the causes are discovered and effective therapy implemented. It is very likely however, that medical iodophobia will eventually be classified as an iodine-deficiency disease.

Discovered in Imperial France\(^5\) a century before the concept of essential trace elements was proposed by Gabriel Bertrand,\(^6\) the first trace element tested in human subjects and recognized as essential to human health,\(^7\)^\(^8\) the most deficient trace element in the world,\(^9\) iodine had the misfortune of attracting the attention of endocrinologists

(Continued on next page)

Table 1
Various Forms of Iodine/Iodide Used in Clinical Medicine

<table>
<thead>
<tr>
<th>A) Inorganic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Non-radioactive</td>
</tr>
<tr>
<td>a) Iodides (i.e., SSKI)</td>
</tr>
<tr>
<td>b) Tincture of iodine</td>
</tr>
<tr>
<td>c) Lugol solution</td>
</tr>
<tr>
<td>2) Radioactive iodides for diagnostic and therapeutic purposes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B) Organic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Naturally occurring</td>
</tr>
<tr>
<td>a) Thyroid hormones</td>
</tr>
<tr>
<td>b) Thyroid iodolipids</td>
</tr>
<tr>
<td>2) Man-made</td>
</tr>
<tr>
<td>a) Radiographic contrast media</td>
</tr>
<tr>
<td>b) Iodine-containing drugs (i.e., amiodarone)</td>
</tr>
<tr>
<td>c) Iodinated lipids for goiter prevention</td>
</tr>
</tbody>
</table>
because it is incorporated into some very important hormones of the thyroid gland. Starting out as a panacea for all human ills, iodine, as an essential element, eventually became associated exclusively with the thyroid gland. This thyroid fixation resulted in endocrinologists dictating the human needs for this nutrient. All human applications of iodine became eventually subserent to the dictates of misinformed endocrinologists.

For example, disinfection of water for human consumption and in swimming pools is far superior, safer, and less expensive with the use of iodine at 1 to 2 ppm, than with the use of chlorine and its derivatives at the same concentrations. However, unfounded concern about the adverse effects of iodine at these levels on the thyroid gland has prevented the widespread use of iodine for these applications, with toxic chlorine and its derivatives used by default. All studies published so far favor iodine over chlorine for treatment of municipal waters and swimming pools, "Because of the increasing difficulty experienced by many communities in achieving satisfactory disinfection of public water supplies with acceptable concentrations of chlorine, a feasibility study on the use of iodine for this purpose was undertaken." The effectiveness, ease of administration and palatability were prime reasons for considering iodine as a disinfectant of community water supplies... effective bacteriological control of the water was maintained by all concentrations of iodine used in this study." At an iodine concentration of 1 mg/liter (1 ppm), the water met all standards for safety and palatability (1962 USPHS Drinking Water Standards). During the five years in which this study was conducted no instances of urticaria or iodism were observed." "No evidence of iodine-induced allergic phenomena was detected during this study." "Comparative data indicate that disinfection of an Olympic-size swimming pool can be accomplished with iodine at half the dose of chlorination... Use of the iodinated swimming pool caused no significant changes in either the RAI uptakes or PBI concentrations.." The advantage of iodine over chlorine as a disinfectant in the treatment of municipal waters is that it could be used as a disinfectant and also as a source of a very important essential element. It is obvious that the benefits of such an approach would outweigh the risks, based on the studies mentioned above.

When different groups of competitive swimmers were asked about their preference between chlorine and iodine as a disinfectant of swimming pools, they overwhelmingly chose iodine. None preferred chlorine. "All members of the swimming teams of five universities who participated in AAWU swimming championships that were held in the Stanford pools were asked to express their opinions of iodine-treated water as compared with chlorine-treated water... Seventeen of the 20 freshmen and varsity swimming team members expressed a preference for the iodine-treated pool in respect to eye irritation. The other three had no preference, but none preferred the chlorine treatment. Of the championship swimming contestants, 48 preferred the iodine-treated pool, five had no preference, but none preferred the chlorine-treated pool... Twenty-eight of the subjects who had been exposed to the iodine-treated water for one month were examined by the three physicians of the research staff, each of whom made his observations independently of the others. Twenty-seven of the swimmers examined received a completely negative rating for eye irritation. In only one student was a mild conjunctivitis found on medical examination. This student wears contact lenses and stated that his eye irritation had improved in a miraculous way since the pool had been treated with iodine."

In the early 1960s, iodine was added to bread as a dough conditioner. One slice of bread contained the full RDA of 150 µg. As would be expected, because of isotope dilution effect, the percent of radioiodide uptake by the thyroid gland decreased from 20-30% to 10-20%. In 1965, London, et al from the National Institute of Health evaluated the amount of iodine present in 32 bakery products from 12 different commercial bakeries. They reported that a typical diet contributed to approximately 1 mg of iodine per day and 726 µg came from bakery products. Concern was expressed over the inhibition of thyroid hormone synthesis in thyrotoxic patients at those levels of iodine. The last sentence of their publication read, "One milligram of iodine will suppress the uptake of radioactive iodine by the normal thyroid gland, probably by simple dilution of the dose, and may considerably reduce organic binding of iodine in the thyroid glands of thyrotoxic persons." Reference 7 of their manuscript is a study published in 1949 by Stanley one year after the Wolff-Chaikoff Effect was reported in rats. The first paragraph of Stanley’s manuscript stated the objective, "The interest of thyrologists was recently aroused by the demonstration by Wolff and Chaikoff (1) that, with levels of serum iodide higher than 20 to 30 micrograms per cent, organic binding of iodine in the rat thyroid was inhibited. Extension of these observations to man was undertaken."

The interest of thyrologists could not have been aroused so quickly by the publication of Wolff and Chaikoff in The Journal of Biological Chemistry, a journal involved in publishing research in the basic sciences, not clinical medicine. The thyrologist with aroused inter-

(Continued on next page)
est was Stanley himself who obviously had insider information in order to publish his manuscript within a year following the Wolff-Chaikoff publication, considering the fact that it takes several months for the review process in peer review journals, and that it would have required several months for him to design and perform his experiments after reading the Wolff-Chaikoff paper. During the year Stanley published his “extension of the Wolff-Chaikoff Effect to man,” he co-authored a paper with Astwood on using goitrogens to manage patients with Graves’ disease as an alternative to using inorganic iodine/iodide. It is a strange coincidence that the investigators who authored the iodophobic publications regarding the so-called inhibition of organic binding of radioactive iodide in the thyroid gland by the administration of inorganic, non-radioactive iodide, were also involved in testing goitrogens in laboratory animals and in normal human subjects and in implementing the use of these goitrogens as an alternative to inorganic iodine/iodide in patients with Graves’ disease (See Section IV).

Stanley concluded, “Thus, the observations of Wolff and Chaikoff in the rat were extended to man.” However, in a review published in 1969, Wolff stated, “The rarity of iodide goiter in the face of the extensive exposure of a great many patients to iodide has not been satisfactorily explained.” Without preconceived ideas, it is easily explained — inorganic, non-radioactive iodine/iodide is safe. “The demonstration of the Wolff-Chaikoff Effect in man remains presumptive.” Several researchers erroneously concluded that the rapid decrease in serum thyroxine (T4) following oral ingestion of inorganic iodine/iodide in thyrotoxic patients was due to the Wolff-Chaikoff Effect, that is sustained inhibition of T4 synthesis. However, Wartofsky, et al. in 1970, evaluated the effect of Lugol solution, administered at five drops (30 mg iodine/iodide) three times a day in five thyrotoxic patients. Following a well-designed protocol, they concluded that “the rapid decrease in T4 secretion induced by iodine is not the result of an acute sustained inhibition of T4 synthesis (The Wolff-Chaikoff Effect), but rather results from an abrupt decrease in the fractional rate of thyroid T4 release.” Therefore, in hyperthyroidism, iodine/iodide in Lugol at a daily dose of 90 mg induced a physiological trend toward normalization of thyroid function, a beneficial effect.

One can appreciate the thyroid fixation of confused endocrinologists who ignore the rest of the human body in favor of misinterpreted laboratory tests assessing thyroid function. The concern about decreased uptake of radioiodide by the thyroid gland following ingestion of increasing amounts of inorganic, non-radioactive iodide shows a lack of understanding of the physiological inter-

pretation of the iodide tracer. Theoretically, as we previously discussed, the uptake of radioactive iodide by the thyroid gland should be zero in order to achieve sufficiency of the thyroid for inorganic, non-radioactive iodide. Decreased thyroid uptake of inorganic radioiodide is an effect to be desired, not avoided. Besides, a low radioiodide uptake by the thyroid resulting from adequate intake of inorganic, non-radioactive iodine/iodide (orthiodosupplementation) serves as a preventive measure against unexpected exposure to radioactive iodide/iodine. Based on a review of the literature, we computed the daily amount of iodine/iodide needed for sufficiency of the thyroid gland and the whole human body. This amount, called orthiodosupplementation, amounted to 100 times the RDA.

In the 1980s, thanks to iodophobia, iodine was replaced with bromine in the bread-making process. Bromide is a goitrogen and interferes with iodide utilization by the thyroid gland, and possibly by the mammary gland. Iodine has an anticarcinogenic effect on the breast. The last national nutritional survey showed a trend of decreasing iodine intake by the US population. Currently 15% of the US adult female population excreted in their urine less than 0.05 mg iodide/L, a level classified by the World Health Organization (WHO) as iodine deficiency. One must keep in mind that the amounts of daily intake of iodine set by the WHO were recommended with the goal of preventing simple goiter and stupidity (cretinism), not sufficiency of the whole human body for iodine, an amount we estimated to be 100-fold higher than the recommended daily intake. Concurrent with the decreased intake of iodine/iodide and increased intake of bromine in the US population, a trend of increasing prevalence of cancers of the mammary and thyroid glands was reported.

Velicky, et al. in a 1997 publication, reported that rats consuming low levels of bromide, similar to levels presently consumed by human subjects, developed goiter, even though those rats received the normal amount of iodide in their diet. Under histological examinations, increased mitotic activity of the follicular epithelium was observed. The values of the mitotic index increased with increasing intake of bromide. The authors discussing their results, commented, “This finding is important in connection with the data showing an increasing exposure of living organisms to environmental bromine which represents an important environmental factor contributing to the development of endemic goiter; this is caused by a decreased utilization of the consumed iodine which produces a relative iodine deficiency even when the iodine intake is sufficient... The transport of iodine

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and its organification can be blocked by Br- ions due to a mutual competition between bromide and iodide anions... This results in a thyroxin and triiodothyronine deficiency, which in turn increases secretion of TSH... Each stimulation of cell proliferation is obviously a key factor in the tumor growth of the thyroid (Williams, 1992) and an increased incidence of thyroid carcinoma in humans is higher in regions with iodine deficiency (Gaitan, et al, 1991).”

Shimomura, et al66 observed that bromine enhances the biological activity of a tumor promoter. Sangster, et al37 reported a decreased ability to concentrate and sleepiness in normal male subjects ingesting 4 mg sodium bromide/kg bw/day. This hypnotic effect could be due to oxidation and organification of bromide in the central nervous system. Torii, et al38 tested an organic bromine compound, isolated from the cerebrospinal fluid of patients with bromism. In cats, this organic bromine induced REM sleep. Therefore, bromine has a zombifying potential. Why iodine was replaced with a goitrogen possessing carcinogenic and zombifying potentials in a population already very iodine deficient, even by the very low RDA standard, remains a mystery! Nevertheless, it is a very effective way to keep a nation sick and zombified.

The purpose of this manuscript is to review studies published during the late 1800s and early 1900s describing the effect of oral ingestion of inorganic, non-radioactive iodine/iodide in patients with simple goiter and in Graves’ disease, both conditions due to iodine/iodide deficiency. This physiological approach will be compared with the current non-physiological trend of pre-supplementation with goitrogens, not excess iodide, is the cause of autoimmune thyroiditis. Last, the concept of orthoiodosupplementation will be presented, including the description of a simple iodine/iodide loading test to assess sufficiency of the whole human body. Orthoiodosupplementation is the safest and most effective method of supplementing patients with this essential trace element in amounts for whole body sufficiency.

II. The Discovery of Iodine

The discovery of the stable halides — chloride, iodide, bromide, and fluoride — seems to have been a French enterprise. All four halides were identified by French scientists, (Table 2) with H. Davy from Great Britain, sharing the discovery of chloride with Gay-Lussac in 1809-1810.39

Bernard Courtois, a French chemist, was a saltpeter (potassium nitrate) manufacturer. Saltpeter was one of the compounds needed for the manufacture of gunpowder. Seaweed ash was used as a valuable source of sodium and potassium salts. Sulfuric acid was added to remove interfering compounds before the salts could be precipitated. One day toward the end of 1811, Courtois added too much acid to the suspension of seaweed ash. The iodides in seaweed were oxidized to iodine, which sublimated and formed a violet vapor above the preparation. The crystals obtained from condensation of the iodine vapor were analyzed by Courtois, and he prepared several iodide salts, but he never published his findings. Some of these crystals ended up in the hands of Gay-Lussac and Ampere, who gave some to H. Davy. An anonymous paper was published in 1813, written by Gay-Lussac, giving full credit to Courtois for the discovery of iodine.5 In the same year, C.B. Desormes and N. (Continued on next page)

Table 2

<table>
<thead>
<tr>
<th>Halide</th>
<th>Discovery</th>
<th>Country</th>
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<tbody>
<tr>
<td>Chloride</td>
<td>1809</td>
<td>Gay-Lussac</td>
</tr>
<tr>
<td>1810</td>
<td>H. Davy</td>
<td></td>
</tr>
<tr>
<td>Iodide</td>
<td>1811</td>
<td>B. Courtois</td>
</tr>
<tr>
<td>Bromide</td>
<td>1826</td>
<td>A.J. Balard</td>
</tr>
<tr>
<td>Fluoride</td>
<td>1886</td>
<td>F. Moissan</td>
</tr>
<tr>
<td>Astatin*</td>
<td>1940</td>
<td>Carson, McKenzie, Segre</td>
</tr>
</tbody>
</table>

*All isotopes are radioactive — exist naturally in minute amounts. First isolated as a byproduct of bombardment of a bismuth target with alpha particles in a 60-inch cyclotron.
century has resulted in the recommended daily amount of 0.1 to 0.3 ml of Lugol, containing from 12.5-37.5 mg elemental iodine, for iodine/iodide supplementation. Interestingly, this is the range of iodine/iodide intake required for whole body sufficiency based on a recently developed iodine/iodide loading test (discussed in Section VII). We have confirmed the observations of our medical predecessors who were keen observers.

In 1831, French chemist and agronomist J.G. Boussingault proposed iodized sodium chloride (table salt) as a means of preventing goiter. Such a proposal was implemented first in Europe and then in the 1920s in the US. That was a very bad idea because it gave a false sense of iodine sufficiency and resulted in the public relying on iodized salt for supplementation instead of the previously used forms of iodine and iodide, such as the Lugol solution. In order to ingest 12.5 mg of elemental iodine from salt, one would have to consume 165 gm of salt; and obviously three times that amount of salt would be required for supplying 37.5 mg elemental iodine. Besides, table salt contains iodide only, not iodine. To be discussed later, iodine is very important for normal function of breast tissue. Therefore, supplementation should contain both forms, iodine and iodide.

In 1926, physician C.L. Hartsock, from Cleveland, Ohio wrote, “Iodized salt is now being very much more extensively used by the public than other forms of iodine, such as sodium iodide, iodoastarine, and compound solution of iodine (Lugol’s solution), probably because of the propaganda to insure its use.” Iodized salt was unfortunately used as a substitute for the previously recommended forms of iodine/iodide. The average daily intake of iodide from iodized salt represents less than 1% of the recommended daily intake of Lugol solution. Implementation of iodization of salt was associated with an increased incidence of autoimmune thyroiditis. In Section VI of this manuscript, we propose a mechanism that could explain how inadequate iodide intake, combined with goitrogens in a previously iodine-deficient individual, caused oxidative damage to thyroid peroxidase and thyroglobulin, resulting in an autoimmune reaction to those proteins. The same mechanism can explain autoimmune thyrotoxicosis (Graves’ disease). Hartsock recommended the use of a tablet of iodine/iodide in known and fixed amounts as the best form of supplementation, just like the most popular form of supplementation used today for vitamins, minerals and trace elements. “Tablets containing definite amounts of iodine seemed to be the method of choice.”

Following Coindet’s original success in treating goiter with tincture of iodine in 1819 and 1820, “In the first flush of enthusiasm for the newcomer, physicians and surgeons tested it and tried it for every conceivable pathological condition.” However, no attempt was made to study the optimal daily requirement of the human body for iodine, because the concept of essential trace elements was not proposed until the end of the 19th century by Gabriel Bertrand. Even after iodine was recognized as an essential element in the 1920s, mainly due to Marine’s studies, no attempt was made to assess the optimal daily requirement of this nutrient for sufficiency of the whole human body. Marine used a daily average of 9 mg iodide in the prevention of goiter in adolescent girls, an amount 60 times the current RDA for iodine. In 1930, Thompson et al stated: “The normal daily requirement of the body for iodine has never been determined.” This statement is still true today, more than 70 years later. We still don’t know the iodine/iodide requirements for whole body sufficiency.

In 1821, Francois Magendie was the first to put iodine into a pharmacopoeia. The number of preparations containing iodine and iodide compounds increased rapidly afterward. To quote Kelly, “In the Great Exhibition at the Crystal Palace in Hyde Park in May 1851, iodine and iodide compounds were publicly shown for the first time by 10 pharmaceutical firms... by 1890, to choose a date at random, the sixth edition of Martindale’s Extra Pharmacopoeia sponsored 30 medicaments derived from iodine; the ‘Iodine Centenary Volume’ compiled by The Prescriber in 1914, mentions 45 iodine preparations; by 1928 Martindale had extended its coverage to 128 iodine items; and, in an international index published in 1956, and devoted exclusively to iodine pharmaceuticals, no less than 1,700 approved pharmacopoeial names, proprietary names, synonyms, and alternative designations are alphabetically listed.”

As late as 1995, the 19th edition of Remington’s Science and Practice of Pharmacy, continued to recommend between 0.1 to 0.3 ml daily of Lugol 5% solution in the treatment of iodine deficiency and simple goiter. The 5% Lugol solution contains 50 mg iodine and 100 mg potassium iodide per ml with a total of 125 mg elemental iodine/ml. The suggested daily amount of 0.1 ml to 0.3 ml is equivalent to 12.5 mg to 37.5 mg, with 40% iodine and 60% iodide as the potassium salt (orthiodosupplementation). This amount was based on the collective experience of clinicians over the last century. We have recently confirmed the keen observation of our medical predecessors. The range of Lugol solution they recommended is exactly the range of iodine/iodide intake for whole body sufficiency based on a recently developed iodine/iodide loading test (discussed (Continued on next page)
Clement presented Courtois’ discovery at a meeting of the Imperial Institute of France. Gay-Lussac named the new element “iode” from the Greek *ioeides* meaning “violet-colored.” H. Davy anglicized the name “iode,” calling it “iodin,” which became “iodine” in the 1930s.

By 1813, Gay-Lussac had synthesized several products from iodine and fully characterized this new element, but he gave full credit to Courtois for the discovery of iodine. According to the *Dictionary of Scientific Discovery,* Davy, in an attempt to eclipse Gay-Lussac in the characterization of iodine, did the unthinkable for a scientist of his rank, “A large part of Davy’s claim for the originality of his study of iodine depends on his complete honesty in claiming certain knowledge before that of Gay-Lussac and in particular in dating as 11 December a paper read to the Institute on 13 December (that is the day following Gay-Lussac’s publication).” Courtois did not benefit from his discovery. “In 1831, the Institute awarded him a prize of 6,000 francs for the discovery. By this time Courtois had given up the saltpeter business and, from the 1820s, attempted to make a living by preparing and selling iodine and iodine compounds. This enterprise also failed, and he died in poverty.”

The history of iodine in medicine and pharmacy was reviewed by F.C. Kelly from its discovery in 1811 up to 1961. The review of the history of iodine by L.E. Braverman, covering the period from 1961 to 1994, was limited to the thyroid gland exclusively, because by then, thyroid fixation had become pandemic, and the only role of iodine as an essential element was assumed to be due to its incorporation in the thyroid hormones. Detailed information about the intrigue and the political climate may be found in the *Dictionary of Scientific Biography* edited by C.C. Gillispie and published in 14 volumes by Simon and Schuster. The scientists are listed alphabetically with their accomplishments.

### III. The Use of Inorganic, non-radioactive Iodine/Iodide in Simple Goiter

Centuries before the discovery of iodine, seaweed was used in the treatment of thyroid enlargement (goiter). In his review, F.C. Kelly mentioned Chinese physician Ke-Hung (281-361 AD), who used seaweed in the treatment of goiter. Five centuries later, Wang Tao listed 36 prescriptions for goiter, 27 of which contained seaweed. The name “thyroid” was assigned to this gland by British physician Thomas Wharton in his book *Adenographia,* written in Latin and published by himself in 1656. The goal of this book was “a description of the glands of the entire body.” The name “thyroid” (shield) was assigned to the gland because the thyroid cartilage behind the gland was in the shape of a shield. Wharton postulated that the role of the gland was purely esthetic. He observed that the thyroid was larger in women than in men, “It (the thyroid gland) contributes much to the beauty of the neck… particularly in females, for this reason, a larger gland has been assigned, which renders their necks … more beautiful.”

After the discovery of iodine from seaweed, a Swiss physician, J.F. Coindet, who previously used successfully burnt sponge and seaweed for goiter, reasoned that iodine could be the active ingredient in seaweed. In 1819, he tested tincture of iodine at 250 mg/day, an excessive amount by today’s standard, in 150 goiter patients with great success. He could reduce significantly the size of goiter within a week. He published his results in 1820. He later reported some side effects to iodine, including iodine-induced thyrotoxicosis. “I have observed goitrous patients who have been greatly affected by the treatment: acceleration of the pulse, palpitations, dry frequent cough, insomnia, rapid emaciation, loss of strength, in others only swelling of the legs or tremor of a painful hardening of the goiter, sometimes a shrinkage of the breast, remarkable and sustained increase in appetite.” He was the first physician to use iodine in medical practice. To be discussed later, the use of combined inorganic iodine/iodide (Lugol solution) in the right amounts resulted in better response with less complications than iodine and iodide alone.

Because iodine is not very soluble in water, (330 mg/L), alcoholic tinctures were first used externally as an antiseptic and internally as a treatment for every conceivable medical and surgical condition. In 1829, Jean Lugol, a French physician researching the medical uses of iodine in infectious diseases, observed that the presence of potassium iodide in water increases markedly the aqueous solubility of iodine, from 0.33 gm/L to 50 gm/L. The Lugol solution contains 5% iodine and 10% potassium iodide in water. He used his preparation for the treatment of “les maladies scrofulueuses.” The antiseptic properties of iodine were widely used from the discovery of iodine until today. In 1873, the French bacteriologist Davaine used tincture of iodine as an agent to treat anthrax in patients suffering from this infection. Orthoiodosupplementation may be the best preventive measure against bioterrorism. It is important to point out that iodides have no antiseptic and antibacterial properties. Only iodine, the oxidized state, is antiseptic. Since iodine is not very soluble in water, the best preparation of an aqueous solution of iodine is Lugol solution because it allows the administration of a relatively large amount of iodine in small volumes of water. The collective experience of a large number of clinicians over the last
in Section VII). In the early 1920s the influence of Plummer increased further the popularity of Lugol solution among clinicians. In 1932, physician B.N. Cohn wrote: "... The widespread use of compound solution of iodine, USP, (for the reader’s information, that is Lugol solution) is the result of a paper by Plummer and Boothby, published in that year (1923). Since then compound solution of iodine has been used by nearly every clinician."

With the availability of thyroid extracts in the early 1900s and thyroid hormones in the 1930s, thyroidologists started using these preparations in patients with iodine deficiency and simple goiter instead of the previously used inorganic iodine/iodide preparations. The situation was aggravated in the 1930s by the fact that during the same period, the public was relying on iodized table salt instead of iodine/iodide preparations from apothecaries for supplementation, due to the propaganda favoring the use of iodized salt. The thyroidologists assumed that, with iodization of table salt, iodine deficiency became a thing of the past because of the positive effect of iodized salt on the incidence of goiter. That was the beginning of thyroid fixation. By the 1950s most physicians neglected the rest of the human body, in terms of sufficiency for iodine, and forgot that their predecessors were using amounts of iodine/iodide two orders of magnitude greater than the amounts present in the average daily consumption of table salt. This was mainly due to iodophoric publications appearing in the mid 1940s (discussed in Section IV) and the erroneous assumption that absence of goiter means iodine sufficiency. A textbook entitled Diagnosis and Treatment of Diseases of the Thyroid, edited by Amy Rowland and published in 1932, contained chapters from 24 thyroidologists of that time. Although the most common cause of hypothyroidism and simple goiter worldwide is iodine deficiency, the recommended treatment of hypothyroidism was summarized in two sentences, “The treatment of hypothyroidism of any type consists merely in the substitution of thyroid extract for the deficient secretion. Any form of prepared gland or the active principle, thyroxin, may be used.” However, not all physicians abandoned iodine/iodide, and many continued up to the present day to use Lugol solution and potassium iodide in the treatment of iodine deficiency and simple goiter. Today, this is called alternative medicine, but 100 years ago it was mainstream medicine. In 1921, S.P. Beebe stated, “We may say that medical treatment of simple goiter is contained in this one word — iodine.”

It is unfortunate that mainstream endocrinologists today do not share Beebe’s enthusiasm for iodine. In the eighth edition of The Thyroid published in 2000, Brent and Larsen wrote the chapter on the treatment of hypothyroidism in the adult. They stated, “The goal of treatment of hypothyroidism is to normalize thyroid status in peripheral tissues, whatever the cause of the hypothyroidism. The usual approach is to give sufficient T4 to ameliorate all symptoms of hypothyroidism and, in patients with primary hypothyroidism, to reduce serum TSH concentrations to within the normal range.” In the battle royal for supremacy, T4 became the uncontested winner in the treatment of simple goiter and hypothyroidism, caused by iodine deficiency and goitrogens, but the female patients became the real losers with increasing prevalence of obesity, diabetes, hypertension, and cancers of the breast and thyroid glands.

IV. The Use of Inorganic, Non-radioactive Iodine/Iodide in Graves’ Disease

Since Graves’ disease represents up to 90% of hyperthyroidism, we will limit our discussion to Graves’ disease, called by different names in different publications: exophthalmic goiter or goitre, hyperthyroidism, and toxic goiter.

Iodine was used in the treatment of toxic goiter as early as 1840 by Von Basedow and in 1854 by Stokes. In 1863, Trousseau inadvertently used tincture of iodine successfully in a patient with exophthalmic goiter. “In the course of October, 1863, I was consulted by a young married lady, who habitually resides in Paris. She was suffering from subacute exophthalmic goiter... I still found her heart beat at the rate of 140 to 150 times in the minute... I wished to administer at the same time tincture of digitalis, but preoccupied with the idea that there would be some danger in giving iodin, I wrote iodin instead of digitalis, so that the patient took from 15 to 20 drops of tincture of iodin a day for a fortnight. (For the reader’s information, “tincture of iodin” is a 10% solution of iodine in 95% ethanol. The daily amount ingested was 75-100 mg). When she then came back to me, her pulse was only 90. I found out my mistake, and I substituted tincture of digitalis for that of iodin, but, after another fortnight, the pulse had again gone up to 150, so that I at once returned to the iodin.” Trousseau had the distinction of performing the first double-blind study of iodine in a cohort of one patient with Graves’ disease. He also achieved remission of Graves’ disease with prolonged administration of potassium iodide.

Thompson, et al, in a 1930 publication, quoted several
authors in the late 1800s and early 1900s who used Lugol solution alone successfully in Graves' disease, with complete remission of the disease, eliminating the need for surgery. Destruction of the thyroid gland with goitrogens and radioiodide was fortunately not then available for the management of Graves' disease. Professor Kocher came on the scene in the early 1900s and had an adverse iodophobic effect on the treatment of Graves' disease. Professor Theodore Kocher carried a lot of weight, being the recipient of the Nobel Prize in Medicine and Physiology in 1909, for his work on "thyroid surgery," the only Nobel Prize assigned to research on the thyroid gland. He was against the use of iodine/iodide in exophthalmic goiter and all forms of hyperthyroidism.58,59

Cowell and Mellanby in their 1925 publication60 give a glimpse of Kocher's influence over the thyroidologists of that time, bordering on intimidation, "Kocher taught that the administration of potassium iodide must never be carried out in exophthalmic goiter, and on the whole, this advice has been taken. As evidence of this fact may be mentioned the discussion on the treatment of exophthalmic goiter at the Royal Society of Medicine in 1923. No speaker mentioned iodine or any preparation of iodine as being of any value in the treatment of the disease, and it can be inferred that therapy involving the use of iodine has been deliberately avoided."

The influence of Kocher divided thyroidologists into two schools: the iodine/iodide school which favored the use of Lugol solution first and then adding surgery later for the patients not responding to this approach alone, while continuing the iodine/iodide supplementation; and the surgical school discouraged the use of iodine/iodide, prior to and post surgery. In 1927, DeCourcy61 stated, "That the administration of iodine prior to operation for exophthalmic goiter controls the symptoms, lowers the basal metabolic rate and lessens the hazards of operation, is no longer questioned. This teaching, however, is directly contrary to that of only a few years ago. Formerly the surgical school led by Kocher opposed the use of iodine in any form of Graves' disease, holding that it increases the severity of the symptoms and may, in fact, be responsible for the development of exophthalmic from simple goiter." In the same publication, DeCourcy's own experience revealed that out of 30 cases of exophthalmic goiter in children, Lugol solution 5-10 drops (30-60 mg) three times a day "made operation unnecessary" in 11 cases. That is a 36% success rate.

Some brave souls defied Kocher's moratorium and continued to use inorganic iodine/iodide successfully in Graves' disease. Retrospectively, Kocher's stand against inorganic iodine/iodide in Graves' disease proved to be the main cause of the high rate of pre- and post-operative mortality, following thyroidectomy. In 1924, Plummer and Boothby from the Mayo Clinic62,63 reported their experience with 600 cases of Graves' disease, who received Lugol solution for several days pre-operatively and post-operatively, resulting in zero medical mortality, "In the Mayo clinic we now give 10 minims of Lugol's solution as a routine three times a day for at least seven days previous to a thyroidectomy. (For the reader's information, one minim is one drop of Lugol, containing 6.25 mg of total elemental iodine. The daily amount was about 180 mg.) The solution is administered for a longer period to patients who have been in a particularly bad condition and are at the end of this period rapidly improving. To patients in a crisis or near-crisis, 50 minims are given during the first two or three hours, by mouth if it can be retained, otherwise by rectum. If the patient is in a crisis, this is followed by 50 minims during the following forenoon. To the patients having so-called post-operative recurrences that can be controlled are given 10 minims of the solution daily over an indefinite period. This period is generally determined by stopping the iodin at intervals of a few weeks, and noting the patient's condition at the end of 10 days. If there is any recurrence of hyperthyroidism, the administration of iodine is again resumed... From January 1 to September 1, 1924, from 600 to 700 new cases of exophthalmic goiter were observed in the Clinic. During this period there were no medical death."

In 1925, Frank H. Lahey64 from the Lahey Clinic in Boston reported his experience with Lugol solution in Graves' disease. “The introduction of Lugol’s solution by Dr. Henry S. Plummer as a method of preparation for operation in exophthalmic goiter marks a step of forward progress in the surgical management of this disease. It has practically eliminated preliminary pole ligation in our Clinic and has made it possible to complete the operation of subtotal thyroidectomy in one stage upon a great majority of our patients. It has saved for us many of those delirious and desperately toxic cases which previously died before any operation could be done upon them, and it has almost completely done away with post-operative thyroid reactions. It has been a real boon to the patient suffering from exophthalmic goiter or primary hyperthyroidism." Thompson, et al57 published the results obtained in 24 patients with exophthalmic goiter treated with Lugol solution alone without surgery, using a daily dose of one drop. As mentioned previously, goitrogens and radioiodide were not available for use in Graves' disease until

(Continued on next page)
the mid 1940s, coincident with the appearance of iodo- 
phobic publications by the same authors who promoted 
the goitrogens as an alternative to Lugol solution in the 
management of Graves’ disease. Thompson, et al stated: 
“Twenty-four patients with exophthalmic goiter (14 mild 
and 10 severe or moderately severe cases) have been 
treated in this clinic with iodine alone, either continu­ 
ously or intermittently for periods ranging from one and 
one-half months to three years. The period of treatment 
was a year or more in 13 instances. With three excep­ 
tions (all unsatisfactory responses to iodine) the patients 
pursued their daily work throughout the period of obser­ 
vation, thus eliminating the effect of rest.” That is an 
88% success rate.

S.P. Beebe from New York reported favorably in 1921, 
on the use of Lugol solution in hyperthyroid forms of 
goiter,49 based on his experience over a period of 10 
years, which did not confirm Kocher’s iodophbic atti­ 
dute, “In going over these statements in the literature, it 
seems probable that the actual basis for the conclusions 
has been theoretical considerations and preconceived 
notions rather than careful clinical observations... In this 
writer’s experience iodine is one of the most valuable 
therapeutic agents we have in the treatment of the hyper­ 
thyroid forms of goiter. As in the case of any potent 
drug, injury can be done with it. So can we do injury 
with digitalis and salvarsan. During the last 10 years the 
writer has treated a large number of cases of hyperthy­ 
roidism, and with most of them the administration of 
iodine has been a part of the treatment. There is no dan­ 
ger in so doing if the dose is properly regulated. The 
 extreme sensitiveness described by some writers is a rare 
event. If the dose is properly regulated there need be no 
fear of iodism or iodine Basedowism.”

Starr, et al65 from the Massachusetts General Hospital 
used 15 drops (90 mg) of Lugol daily for the treatment 
of exophthalmic goiter, with a 92% success rate, elimin­ 
ating the need for surgery. “Of these 25 cases, 20 
(80%) responded to iodin by a more or less extensive 
remission of the disease. Of these 20, 12 (48%) re­ 
sponded with the acute iodine remission resembling the 
effect produced by subtotal thyroidectomy. In the re­ 
main ing eight (32%) the remission occurred, but was 
less extensive. In five unsuccessful cases (20%) two of 
the patients were pregnant, and one had cardiac decomp­ 
sensation. If these are omitted from the calculation, io­ 
dine administration was successful in 20 of 23, or 92% 
of our hospital cases.”

A cursory review of the literature suggests that the use of 
Lugol solution in Graves’ disease, the preferred ap­ 
pro ach by thyroidologists of that time, resulted in a 
higher success rate with fewer complications than the 
use of iodine and iodide alone.45,57,60-66 The daily amount 
of Lugol solution used in Graves’ disease ranged from one 
drop (6.25 mg) to 30 drops (180 mg). A complete nutri­ 
tional program in our experience improved further the 
response to orthoiodosupplementation in Graves’ disease 
and other thyroid disorders.

No serious attempt was made by physicians of the early 
1900s to incorporate a complete nutritional program 
with Lugol supplementation in the management of thy­ 
orid disorders. The reason is that not much was known 
about vitamins, minerals, and essential trace elements at 
that time. Today, the importance of good nutrition in 
overall well-being is commonly accepted, and more and 
more publications are emphasizing the interaction be­ 
tween micronutrients in their overall effects on bio­ 
l ogical systems. We have incorporated a total nutritional 
program with orthoiodosupplementation, emphasizing 
magnesium instead of calcium (discussed further in Sec­ 
 tion VII). The effect of this nutritional program with 
orthoiodosupplementation on thyroid function tests in a 
40-year-old female patient with severe hyperthyroidism 
is displayed in Table 3.

She was a classic case of Graves’ disease with exoph­ 
thalmia. After researching the medical literature, she 
refused treatment with radioiodides, goitrogens and sur­ 
gery. She was placed on the nutritional program, includ­ 
ing 1,200 mg of magnesium/day for one month prior to 
iodine supplementation, followed by the same program 
with the addition of 12.5 mg elemental iodine (1 tablet 
Iodoral®) daily afterward. TSH was undetectable at 
<0.01 µU/ml. Total T4 was 18 µg/dL; Total T3 442 
ng/dL; Free T4 = 5 ng/dL. Following one month on a 
high magnesium program, she stated she felt calmer, 
with less palpitation, could sleep better. The burning, 
irritation, and lacrimation of the eyes improved. TSH 
remained undetectable at 0.03 µU/ml; Total T4 dropped 
to 16 µg/dL and Total T3 from 442 to 299 ng/dL. Free 
T4 did not change appreciably. After the first week on 
iodine/iodide at 12.5 mg/day, she noticed a clearer mind 
with improved cognition. Following one month on this 
program, she slept better and was better organized with 
improved social activities. Her palpitation decreased 
markedly with normal pulse rates. Serum TSH became 
normal at 2.3 µU/ml; Total T4, Total T3 and Free T4 were 
all within the normal range at 8.0 g/dL, 195 ng/dL, and 
1.2 ng/dL. She continued to improve. After three 
months on the same program, TSH was not measured, 
but Total T4, Total T3 and Free T4 remained within the 
normal range (Table 3). She experienced some diarrhea 
following four months on magnesium at 1,200 mg/day,

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and the daily amount was decreased to 600 mg/day. As of this writing, the thyroid function tests remained within the normal range; she has no exophthalmia; she gained 16 pounds; and her social activities have improved to the point of matrimony. She praises God every day for saving her thyroid gland and making her healthy again.

Published studies on the safe and effective use of Lugol solution in Graves’ disease mysteriously disappeared during the 1940s and afterward, concurrent with the appearance of iodophobic publications and the promotion of goitrogens as an alternative to Lugol solution in the management of Graves’ disease. (See Table 4.) Introduced in 1943 by E.B. Astwood69 for the management of Graves’ disease in the forms of thiourea and thiouracil, these goitrogens evolved into more powerful ones,68 and eventually the thionamides: methimazole, carbimazole, and propylthiouracil. These goitrogens rapidly replaced inorganic iodine/iodide in the management of Graves’ disease. The synchronization of iodophobic publications with the introduction of goitrogens to replace inorganic iodine/iodide (Table 4) was a brilliant move, and it worked wonderfully. Obviously, no one was awake to ask questions. In 1953, when Godley and Stanbury69 introduced a new goitrogen, potassium perchlorate, in the treatment of hyperthyroidism, they acknowledged that the thionamides were used widely in Graves’ disease, instead of inorganic iodine/iodide. “At the present time propylthiouracil, methylthiouracil and 1-methyl-2-mercaptoimidazole (methimazole) are widely employed in the preparation of thyrotoxic patients for surgery, and to a lesser extent in the chronic control of the overactive thyroid gland (5).” This new goitrogen, that is potassium perchlorate, was so toxic that it was removed from circulation shortly after its introduction. Reintroduction of this goitrogen is currently being attempted by lowering the recommended dosage.80

Astwood and his associates reported very high remission rates in Graves’ disease with the use of goitrogens, which mislead thyroidologists and encouraged them to use these drugs instead of inorganic iodine/iodide. In two studies published in 1953 and 1966, his teams reported a remission rate of 50-75%.71,72 However, his findings could not be reproduced by others. Wartofsky73 in 1973, and Reynolds and Kotchen74 in 1979, observed much lower remission rates of 11-16%. Increased ingestion of iodine/iodide by the patients was blamed by Wartofsky for the low success rate. Wartofsky’s study was done at a time when one slice of bread contained the full RDA for iodine. In an attempt to improve success rate with goitrogens, patients were told to limit their intake of iodine, which discouraged further its use by the patients. Wartofsky, et al73 failed to realize that iodization of bakery products started several years before the second study by Astwood, et al72 published in 1966, which reported a very high success rate. In 1965, London, et al25 reported an estimated iodine intake of 1 mg/day with 726 g coming from bakery products. In the end, one concludes that Astwood’s optimistic reports on the use of goitrogens in Graves’ disease could not be reproduced by others. Since the word “goitrogens” implies goiter-causing drugs, Astwood called them antithyroid drugs. So, instead of normalizing thyroid function physiologically with sufficient amounts of inorganic, non-radioactive iodine/iodide, thyroidologists became destructive in their approach with goitrogens and radioiodide, resulting in hypothyroidism in the majority of those unfortunate patients who eventually join the ever increasing T4 consuming population.

In the 1980s, thyroidologists in the US decreased their use of goitrogens in Graves’ disease due to low remission rates.

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### Table 3

<table>
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<tr>
<th>Table 3: Effect of Supplementation with a Complete Nutritional Program Combined with Iodine/Iodide at 12.5 mg/day on Thyroid Function Tests in a 40-year-old Female Patient with Graves’ Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I. Before Supplementation</strong></td>
</tr>
<tr>
<td>TSH &lt; 0.01 µU/ml</td>
</tr>
<tr>
<td>Total T₄ = 18 µg/dL</td>
</tr>
<tr>
<td>Total T₃ = 442 ng/dL</td>
</tr>
<tr>
<td>Free T₄ = 5 ng/dL</td>
</tr>
<tr>
<td><strong>II. After One Month on Complete Nutritional Supplementation with 1,200 mg Magnesium/day</strong></td>
</tr>
<tr>
<td>TSH &lt; 0.03 µU/ml</td>
</tr>
<tr>
<td>Total T₄ = 16 µg/dL</td>
</tr>
<tr>
<td>Total T₃ = 299 ng/dL</td>
</tr>
<tr>
<td>Free T₄ = 5.6 ng/dL</td>
</tr>
<tr>
<td><strong>III. After One Month on Iodoral® — 1 Tablet/Day</strong></td>
</tr>
<tr>
<td>TSH = 2.3 µU/ml</td>
</tr>
<tr>
<td>Total T₄ = 8.0 µg/dL</td>
</tr>
<tr>
<td>Total T₃ = 195 ng/dL</td>
</tr>
<tr>
<td>Free T₄ = 1.2 ng/dL</td>
</tr>
<tr>
<td><strong>IV. After Three Months on Iodoral® — 1 Tablet/Day</strong></td>
</tr>
<tr>
<td>TSH not measured</td>
</tr>
<tr>
<td>Total T₄ = 9.0 µg/dL</td>
</tr>
<tr>
<td>Total T₃ = 156 ng/dL</td>
</tr>
<tr>
<td>Free T₄ = 1.6 ng/dL</td>
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</tbody>
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ziodarone, Na iopanate, and other iodine containing substances with similar effects is due to the entire molecule, and not to the iodine liberated. It should be noted that the cytotoxic effect of amiodarone in all cultures is also due to the entire molecule, and not to the iodine present in it.” It is most amazing that no one so far has proposed the use of inorganic, non-radioactive iodine/iodide at 9 mg/day in patients with cardiac arrhythmia. Indeed, we have a zombified medical profession. Case in point, patients are told to protect their thyroid gland from radioactive fallout by ingesting inorganic, non-radioactive iodide. However, the same patients, if diagnosed with Graves’ disease, are told to stop taking inorganic, non-radioactive iodide/iodide in order to allow the largest concentration of radioactive iodide to penetrate their thyroid gland, a destructive dose that is! Does that make any sense?

V. Hypo- and Hyperthyroidism Caused by Organic and Inorganic Forms of Stable Iodine/Iodide

A critical evaluation of some review articles on iodine-induced hypothyroidism and iodine-induced hyperthyroidism reveals that in most cases, organic forms of iodine are involved. However, the titles of those articles suggest that the review is about inorganic iodine/iodide. For example, in the latest published review on “iodine-induced hypothyroidism” by Markou, et al.77 in 2001, the list of iodine-containing products causing hypothyroidism consisted predominantly of organic forms of iodine, such as amiodarone and radiology contrast agents. The title of that review should have been “Drug-induced hypothyroidism.” In 1984, Leger, et al.78 reported 85 cases of “iodine-induced thyrotoxicosis.” Amiodarone alone accounted for 50% of the cases. All the patients received organic forms of iodine-containing drugs. The title of that review should have been “Drug-induced hyperthyroidism.”

In 1983, Fradkin and Wolff79 published a review on “iodide-induced thyrotoxicosis.” Since organic forms contain iodine, not iodide, using “iodide” in the title implies we are dealing with the inorganic forms. However, in the first paragraph of that review, we read, “Three recent events have revived interest in this side reaction to iodide: alarming reports from Germany regarding the dangers to the thyroid gland of radiographic contrast media; the widespread use of the iodine-containing drug, amiodarone; and the proposed use of potassium iodide (KI) (100-200 mg/day) as the most effective protective measure against released radioactive iodine isotopes after loss of coolant accidents in nuclear reactors.” This review was written before the drug amiodarone was approved for use in the US, after causing havoc in Europe. Amiodarone contains organic iodine. The use of inorganic iodine/iodide at 9 mg/day was never tested in similar patients as an alternative to amiodarone, a drug releasing about 9 mg iodine per day. It would not be surprising if 9 mg inorganic iodine/iodide/day resulted in the beneficial effects without the severe side effects. Radiographic contrast media contains organic iodine. Last, the authors mentioned potassium iodide (KI) at a daily dose of 100-200 mg, which is the only inorganic form of iodide included in the list of agents causing “iodide-induced thyrotoxicosis.” However, in the same review, the authors stated, “Although there are scattered case reports of IIT (iodide-induced thyrotoxicosis) after the use of KI, these must be considered in the light of over 10^8 tablets of KI prescribed annually in this country. Reports of experience with KI (1.6-6.4 g/day) in large series of pulmonary patients revealed no hyperthyroidism in 2,404 and 502 patients.” Nevertheless, when iodine is incorporated into drugs, inorganic iodide is blamed for the side effects. “Hyperthyroidism occurring after administration of iodine-containing drugs has been ascribed to iodide.”79 The thyrotoxicosis induced by iodine-containing drugs is blamed on inorganic iodide even though the use of inorganic iodide alone was not associated with thyrotoxicosis in the two studies referred to. Does that make any sense? Iodophobia, induced by whatever motivation, causes an altered state of consciousness, which makes doublespeak and contradictory statements acceptable.

There is a great need to educate physicians about the great difference between organic iodine and inorganic iodine/iodide. One good example to demonstrate this difference is the thyroid hormones T₄ and T₃. They are organic iodine-containing substances that occur naturally. Their effects are well described and distinctly different from the effects of inorganic iodine/iodide. No physician has ever attributed the effects of thyroid hormones to inorganic iodine/iodide. So, why is it so hard for them to extrapolate this observation to organic iodine containing drugs? Here again, the answer may be in two symptoms of medical iodophobia: an altered state of consciousness and split personality, allowing a complete dissociation in their thinking process between the organic iodine-containing thyroid hormones and the organic iodine containing drugs.

VI. Iodization of Salt and Chronic Autoimmune Thyroiditis: A Proposed Pathophysiology

In several communities worldwide, an increased incidence of chronic autoimmune thyroiditis was reported following implementation of iodization of sodium chloride.80 In areas of the US where this relationship has been studied, mainly in the Great Lakes Region, a simi-
Table 4

Synchronization of Iodophobic Publications with the Promotion of Goitrogens as an Alternative to Inorganic Non-radioactive Iodine/Iodide

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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Publications testing and promoting goitrogens in the treatment of Graves’ disease

<table>
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<tr>
<th>Year</th>
<th>Event</th>
<th>Reference</th>
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sion rate and side effects and relied more and more on inorganic iodide, but unfortunately the wrong kind (i.e., the radioactive kind). Thyroidologists en masse joined the nuclear age. In 1990, a survey by the American Thyroid Association revealed that the majority of their members relied predominantly on radioiodide, with the exception of the very young and the pregnant, whom the compassionate thyroidologists protected by giving them goitrogens! Only 2% opted for surgery, 28% used goitrogens, and 70% joined the nuclear age. There was no mention of inorganic, non-radioactive iodine/iodide as an option. In the last edition of Werner and Ingbar’s *The Thyroid* published in 2000, D.S. Cooper wrote the chapter on treatment of thyrotoxicosis. “This chapter considers the three forms of treatment of thyrotoxicosis — antithyroid drugs, radioactive iodine (radioiodine), and thyroidectomy — that are in wide use now.” In a subsection entitled “Other drugs used in the treatment of thyrotoxicosis caused by Graves’ disease,” Cooper stated, “The effects of iodide on thyroid function are complex and are discussed in detail in the section on the effects of excess iodide in Chapter 13.” The reader is pre-conditioned to be in an iodophobic mode when he goes to Chapter 13, an ominous number, with “excess iodide” in the title and where inorganic iodide/iodide is blamed for the severe side effects of organic iodine-containing drugs, such as amiodarone, and is called “a pathogen.”

Obviously, the unsuspecting thyroidologist relying solely on this textbook for information will avoid inorganic iodide/iodide like leprosy. However, if he is inquisitive and searches the literature carefully, he may read the publication by Phillipou, et al, who studied the effect of inorganic iodide on thyroid functions and compared his results with the effects of amiodarone, “We can, therefore, conclude that the effect of amiodarone, ben-

(Continued on next page)
ence of $H_2O_2$ and organic substrate reverts to its peroxy-
dase function which is the primary function of halopa-
oxydases, causing oxidative damage to molecules near-
est to the site of action: TPO and the substrate thy-
roglobulin (Tg). Oxydized TPO and Tg elicit an auto-
immune reaction with production of antibodies against
these altered proteins with subsequent damage to the
apical membrane of the thyroid cells, resulting in the
lymphocytic infiltration and in the clinical manifesta-
tions of Hashimoto’s thyroiditis. In laboratory animals
prone to autoimmune thyroiditis, the genetic defect may
be in the production of $H_2O_2$ in excess of what is
needed.

The iodination of thyrosine residues by TPO requires
the presence of Tg, $H_2O_2$, and iodide. The
supply of $H_2O_2$ comes
from the NADPH
oxydase system.91
This system is inhib-
ited by certain iod­i-
nated lipids92-95 and is
enhanced by cytosolic
free calcium Ca++.89
The equation for organification
of iodide by TPO is
displayed in Figure 1,
Together with the feed-
back system control-
ing the production of
$H_2O_2$. The logical deduction from this equation is that
increased cytosolic free calcium will cause an excess of
$H_2O_2$. Increased levels of iodinated lipids, on the other
hand, would limit the production of $H_2O_2$. How much
iodide is required for the production of iodinated lipids?
In 1976, Rabinovitch, et al96 reported their results re-
garding the effect of three levels of iodide supple-
mentation on the production of iodinated lipids in the thyroid
glands of dogs: low iodide diet, normal iodide diet, and
high iodine diet. The dogs were kept on those diets for
six weeks. Iodinated lipids in the plasma membrane and
in the cell total lipids were observed only in the dogs
receiving the high iodide diet. What about human sub-
jects? In 1994, Dugrillon, et al97 reported for the first
time the presence of 5-hydroxy-6-iodo- 8,11,14-
eicosatrienoic delta lactone (delta iodolactone) in a hu-
man thyroid, following the ingestion of 15 mg io-
dide/day for 10 days in the host. It was the first time
this biologically active iodolipid was isolated from hu-
man thyroid glands. The amount of iodide the host re-
ceived was 100 times the RDA, but it is the amount of
iodine/iodide we recommended for orthiodosupple-
thiodosupplementation results in decreased levels of
delta-iodo-lactone. Combined magnesium and io-
dine/iodide deficiency based on the concept of orthio-
dosupplementation are the basic factors involved in the
oxidative damage caused by excess $H_2O_2$ and reactive
oxygen species. If this proposed mechanism is valid,
orthiodosupplementation, combined with magnesium
intake between 800-1,200 mg/day, a daily amount this
author recommended 21 years ago98 for magnesium suf-
ficiency, should reverse autoimmune thyroiditis. This
nutritional approach is also effective in Graves’ autoim-
une thyroiditis as previously discussed.

VII. Implementation of Orthiodosupplementation
as Part of a Total Nutritional Program
The thyroid gland, like the rest of the body needs ade-
quate amounts of all the macro- and micronutrients to
function optimally. Ideally, besides orthiodosupple-
mentation and magnesium in adequate amounts, a com-
plete nutritional program would be most appropriate
since other essential nutrients are important for thyroid
(Continued on next page)
lar trend was reported. In 1966 and 1968, Weaver, et al. from Ann Arbor, Michigan reported, “The salient histopathological feature of the thyroid glands, removed at operation in a five-year period before iodine prophylaxis (1915-1920), was the paucity of lymphocytes in their parenchyma, and, more importantly, the absence of thyroiditis of any form... It should be emphasized that the thyroid glands prior to the use of iodized salt were devoid of lymphocytes, and nodular colloid goiters with dense lymphocytic infiltrates were found after the introduction of iodized salt in 1924.” It is of interest to note that prior to iodization of salt, autoimmune thyroiditis was almost non-existent in the US, although Lugol solution and potassium iodide were used extensively in medical practice in amounts two orders of magnitude greater than the average daily amount ingested from iodized salt. This suggests that inadequate iodide intake aggravated by goitrogens, not excess iodide, was the cause of this condition. To be discussed later, autoimmune thyroiditis cannot be induced by inorganic iodide in laboratory animals unless combined with goitrogens, therefore inducing iodine deficiency.

Furszyfer, et al. from the Mayo Clinic studied the average annual incidence of Hashimoto’s thyroiditis among women of Olmsted County, Minnesota during three consecutive periods covering 33 years of observation, from 1935 to 1967. They found the incidence to be higher in women 40 years and older versus women 39 years and less. However, in both groups there was a progressive increase in the incidence of Hashimoto’s thyroiditis over time. During the three periods evaluated, that is 1935-1944, 1945-1954, and 1955-1967, the average annual incidence of Hashimoto’s per 100,000 population was 2.1, 17.9, and 54.1 for women 39 years and less. For women 40 years and older, the average annual incidence over the same three periods was 16.4, 27.4, and 94.1. The authors commented, “From this study it appears that there has been an increase in the incidence rate of Hashimoto’s thyroiditis in Olmsted County between 1935 and 1967... One of the more attractive hypotheses with respect to the change in the incidence of Hashimoto’s thyroiditis (and perhaps other thyroid disorders) is that increased ingestion of iodide (For the reader’s information, they are talking about iodization of salt) triggers the disease, but obviously, this is not the only factor to be considered in its pathogenesis.”

Doctor Hashimoto’s name became a household word thanks to four thyroid glands. In 1912, pathologist H. Hashimoto published in a German medical journal and in German, his histological findings in four thyroid glands removed at surgery: numerous lymphoid follicles, extensive connective tissue formation, diffuse round cell infiltration, and significant changes of the acinar epithelium. He called this pathology of the thyroid “struma lymphomatosa.” At the time of this publication, autoimmune thyroiditis was not observed in the US population until the iodization of salt. Hashimoto’s thyroiditis is now classified as goitrous autoimmune thyroiditis because the gland is enlarged, in distinction to atrophic autoimmune thyroiditis where atrophy and fibrosis are predominant. Both conditions are chronic, progressing over time to hypothyroidism in a significant percentage of patients. It is important to point out that the Mayo Clinic study started 10-15 years after implementation of iodization of salt in the area. Therefore, even during the first decade of observation, the prevalence of autoimmune thyroiditis was already significant. Again, it must be emphasized that prior to the implementation of iodized salt as observed by Weaver, et al., this pathology of the thyroid gland was not reported in the US, even though the Lugol solution and potassium iodide were used extensively in medical practice at that time in daily amount two orders of magnitude greater than the average intake of iodide from table salt.

The mechanism by which iodide induces autoimmune thyroiditis is poorly understood. Experimentally induced autoimmune thyroiditis in laboratory animals by acutely administered iodide required the use of antithyroid drugs, essentially goitrogens, to produce these effects. These goitrogens induced thyroid hyperplasia and iodide deficiency. Antioxidants either reduced or prevented the acute iodide-induced thyroiditis in chicks and mice. Bagchi, et al. and Many, et al. proposed that the thyroid injury induced by the combined use of iodide and goitrogens occurs through the generation of reactive oxygen species.

We would like to propose a mechanism for the oxidative damage caused by low levels of iodide combined with antithyroid drugs: inadequate iodide supply to the thyroid gland, aggravated by goitrogens, activates the thyroid peroxidase (TPO) system through elevated TSH, low levels of iodinated lipids, and high cytosolic free calcium, resulting in excess production of H₂O₂. The excess H₂O₂ production is evidenced by the fact that antioxidants used in Bagchi’s experiments did not interfere with the oxidation and organification of iodide and therefore neutralized only the excess oxidant. This H₂O₂ production is above normal due to a deficient feedback system caused by high cytosolic calcium resulting from magnesium deficiency and low levels of iodinated lipids which requires for their synthesis iodide levels two orders of magnitude greater than the RDA for iodine. Once the low iodide supply is depleted, TPO in the pres- (Continued on next page)
function and are involved in overall well-being. Since thyroid disorders occur predominantly in women, it is appropriate to mention the beneficial effects of a magnesium-emphasized nutritional program on the well-being of women suffering from premenstrual tension syndrome, post-menopausal osteoporosis, and fibromyalgia. This nutritional program, combined with orthoiodosupplementation, is the safest of the options available to prevent and treat thyroid diseases in women.

Radioiodide in the treatment of Graves' disease induces hypothyroidism in 90% of patients within the first year, with a continuing rate of 2-3% per year thereafter. The use of radioiodide in the treatment of Graves’ disease has been associated with leukemia and other forms of cancer. Fever and arthralgia are reported in 1-5% of patients on goitrogens (antithyroid drugs). Patients on goitrogens may be more prone to infections due to inadequate supply of iodide to leukocytes during phagocytosis, discussed in the following paragraph. Goitrogens can induce severe hepatotoxicity, requiring liver transplantation and sometimes resulting in death.

A totally neglected area is the effect of goitrogens on other haloperoxydases, such as myeloperoxydases, involved in the defense mechanism against infections. Myeloperoxydase is present in high concentrations in the granules of polymorphonuclear leukocytes and monocytes. It catalyses the oxidation of iodide, bromide, and chloride in the presence of 

\[ \text{H}_2\text{O}_2 \] to yield products that oxidize and halogenate microbial components. Chloride, due to its high concentration in leukocytes is believed to be the main halogen used by myeloperoxydase. However, leukocytes have the ability to concentrate iodide 300-fold during phagocytosis and even deiodinate thyroid hormones to generate inorganic iodide when iodide supply is inadequate. Incubated in the presence of 10 µg iodide/100 ml of incubation media, phagocytosing leukocytes concentrated inorganic iodide 300-fold to achieve intracellular concentration of 0.003% inorganic iodide. Leukocyte proteins contained even higher concentrations of organic iodine, 0.04%, that is a 4,000-fold higher concentration of iodine than present in the incubation media. Thyroxine synthesis was observed during phagocytosis of leukocytes, when the iodide supply was adequate (10 g/100 ml). However, in the absence of non-radioactive iodide, phagocytosing human leukocytes metabolized thyroid hormones added to the incubation media in order to generate free inorganic iodide. Klebanoff and Green commented that iodide, on a molar basis, was much more effective than chloride in the antimicrobial activity of myeloperoxydase of leukocytes and stated, “When the iodide supply is diminished, the concentration of chloride... may be adequate.” These authors observed a significant interference with the antimicrobial activity of myeloperoxydase of leukocytes by antithyroid drugs (goitrogens).

Based on our previous calculations, the concentration of iodide used by Stole (i.e., 10 µg/100ml, roughly 10^-6 Molar) is equivalent to the expected serum levels of inorganic iodide in patients on orthoiodosupplementation and also in mainland Japanese who consume an average daily amount of 13.8 mg of elemental iodine, the only population in the world on orthoiodosupplementation and one of the healthiest based on cancer statistics. From data available in published studies regarding the effect of increasing amounts of iodide on serum inorganic iodide levels at steady state conditions, we have calculated the expected serum levels of inorganic iodide at steady state conditions, when a patient is on orthoiodosupplementation (Figure 2).

It is of interest to note that a daily ingestion of 12.5 mg iodine/iodide resulted in serum inorganic iodide level of 2 x 10^-10 M, which is the serum level reported by Wolff-Chaikoff to cause inhibition of organic binding of iodine and therefore inhibition of synthesis of thyroid hormones. Since this amount of Lugol solution was used safely by three generations of physicians for iodine supplementation, and since we have observed that patients reported optimal mental and physical performances on 3-4 times that amount, we would like to propose a redefinition of the Wolff-Chaikoff Effect as a beneficial effect on mental and physical performances.

The breakdown of thyroid hormones by phagocytosing leukocytes in an iodine-deficient patient could explain the high incidence of hypothyroxiinemia in patients with chronic infections, such as chronic active hepatitis. Accelerated thyroid hormone degradation during bacterial infection has been reported in man and rhesus monkeys. Such findings would not be expected in mainland Japanese and in patients on orthoiodosupplementation because the calculated serum levels of iodide in those subjects would approximate the concentration of iodide in Stole’s incubation media. Wartofsky and Burman in their review article on the “euthyroid sick syndrome” wrote, “This review will address the effects of nonthyroidal illness on thyroid function and attempt to establish guidelines for the determination as to whether such patients are truly euthyroid or not. Indeed, the ultimate question for the clinician often is whether to treat the individual with severe nonthyroidal illness for low serum thyroxine (T4).”

Although the recommended treatment in such cases (Continued on next page)
would obviously be the administration of thyroid hormones; it would be more physiological to implement orthoiodosupplementation in these patients since the thyroid hormones administered to the iodine-deficient patient will be deiodinated to generate free iodide. So why not give them inorganic, non-radioactive iodine/iodide in the form of orthoiodosupplementation? Thyroid hormones are very expensive forms of the element iodine, which is what these patients really need to start with.

The concept of orthoiodosupplementation is based on the self-evident fact that the whole body, not just the thyroid gland, needs iodine. The whole body needs this essential trace element, which plays different roles in different organs and tissues. In order to assess whole body sufficiency for iodine/iodide, a simple loading test was developed, based on the concept that the more deficient a patient is in this nutrient, the greater the percentage of ingested iodine/iodide that will be retained, the smaller the percentage excreted in the urine.

During the late 1800s and early 1900s, orthoiodosupplementation was administered with Lugol solution 0.1-0.3 ml containing 12.5-37.5 mg of iodine/iodide. Because administration of Lugol solution is not very accurate, may stain clothing, has an unpleasant taste, and causes gastric irritation, we decided to use a precisely quantified tablet form (Iodoral®) containing 5 mg iodine and 7.5 mg iodide as the potassium salt. To prevent gastric irritation, the iodine/iodide preparation was absorbed into a colloidal silica excipient. To eliminate the unpleasant taste of iodine, the tablets were coated with a thin film of pharmaceutical glaze. Ten clinically euthyroid Caucasian women were evaluated before and three months after ingesting a tablet daily. The evaluation included thyroid function tests and assessments of thyroid volume by ultrasonometry. The results suggest that this form and amount administered daily for three months to euthyroid women had no detrimental effect on thyroid volume and functions.

When tested in the loading test, one tablet was not sufficient to distinguish between different degrees of iodine deficiency because the interindividual variation was very small. We were interested in a loading test that would result in 40-50% of the ingested dose excreted in the 24-hour urine and also with a wide range of values in different subjects. For six subjects tested, the following percent dose excreted were obtained, expressed as mean ±SD (range): one tablet = 22±1.2 (20-26); two tablets = 23±2.8 (22-25); three tablets = 25±12.3 (14-37). Another group of six normal subjects on a similar Western diet was tested with four tablets and the values were = 39±17.2 (14.2–66.0). (See Figure 3)

We chose four tablets for the loading test. Sufficiency of the whole human body for iodine/iodide was arbitrarily defined as 90% or more of the ingested amount excreted in the 24-hour urine collection, using 50 mg of the

(Continued on next page)
iodine/iodide preparation (four tablets). Orthoiodosupplementation with one tablet a day required up to 18 months to achieve sufficiency in some patients, and in others, sufficiency was not achieved even after two years of supplementation with one tablet/day. With 3-4 tablets/day, however, sufficiency was achieved within three months in most cases. These data support the keen observations of clinicians over the past century, regarding the amount of iodine/iodide needed for iodine/iodide supplementation, 12.5-37.5 mg elemental iodine from Lugol solution.

Orthoiodosupplementation increased urinary excretion of lead, cadmium, arsenic, aluminum, and mercury. Urinary bromide and fluoride levels increased markedly and proportionally to the amount of iodine/iodide ingested. At three tablets a day, urinary fluoride and bromide increased up to 20-fold, although the preloading test levels were not elevated. Obesity seems to increase the requirement for iodine/iodide, and this may be due to sequestration of iodine by unsaturated fats. So many factors affect the requirement of iodine/iodide that the best way to assess whole body sufficiency for this element is with the loading test.

Orthoiodosupplementation decreased the need for thyroid hormones in patients on these hormones. In some cases, this occurred during the first months of orthoiodosupplementation. However, in a patient with atrophic autoimmune thyroiditis, 11 months of orthoiodosupplementation was required before decreasing the amount of thyroid hormones. A 54-year-old female patient with atrophic autoimmune thyroiditis (thyroid volume by ultrasound = 2.8 ml) and elevated TPO Ab titers, on 150 µg of T₄ was placed on orthoiodosupplementation with 3-4 tablets/day. The presupplementation loading test revealed 23% iodide excreted. After three months on orthoiodosupplementation, her loading test was 92% of iodide excreted. Her serum T₄ levels progressively increased to reach above normal level (14.6 µg %; normal range 4.5–12) after 11 months on orthoiodosupplementation. T₄ supplementation was decreased from 150 µg to 100 µg/day. She stated that since on orthoiodosupplementation, she feels more energetic with a clearer mind and with an improved sense of well-being.

If indeed, iodine deficiency, that is iodine/iodide intake below orthoiodosupplementation levels, is involved in autoimmune thyroiditis, then diseases that are associated with autoimmune thyroiditis may also be caused by iodine deficiency. In 1996, Giani, et al. reported a significant association of breast cancer with Hashimoto’s thyroiditis. When 100 consecutive patients with breast cancer were compared with 100 match controls, Hashimoto’s thyroiditis was present in 2% of the control group compared with 13.7% in the group with breast cancer. Simple goiter, a sign of iodine deficiency, was present in 11% of controls compared to 27.4% of the patients with breast cancer. Diabetes may also be an iodine-
deficiency disease. Lindberg, et al\textsuperscript{22} compared 52 diabetic children (insulin-dependant) with 386 non-diabetic school children. TPO antibodies were present in 6\% of the control group, compared with 38\% of diabetic children. It seems like thyroldists and nutritionists missed the boat. Such a simple, safe, inexpensive way to heal so many medical conditions! An overview of the effects of orthoiodosupplementation on mental performance, resistance to infections, protection of the thyroid gland against radioactive fallout, detoxification of heavy metals and of the toxic halides bromide and fluoride, suggests that orthoiodosupplementation may be the best and safest preventive measure against bioterrorism. The corollary then would be: The worst form of domestic bioterrorism is the dissemination of iodophoric misinformation in order to discourage the use of orthoiodosupplementation.

About the Author

Guy E. Abraham, MD, is a former Professor of Obstetrics, Gynecology and Endocrinology at the UCLA School of Medicine. Some 35 years ago, he pioneered the development of assays to measure minute quantities of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974; the "Medaille d'Honneur" from the University of Liege, Belgium, 1976; the Senior Investigator Award of Pharmacia, Sweden, 1980.

The applications of Dr. Abraham's techniques to a variety of female disorders have brought a notable improvement to the understanding and management of these disorders. Twenty years ago, Dr. Abraham developed nutritional programs for women with premenstrual tension syndrome and post menopausal osteoporosis. They are now the most commonly used dietary programs by American obstetricians and gynecologists. Dr. Abraham's current research interests include the development of assays for the measurement of iodide in biological fluids and the application of this assay to the implementation of orthoiodosupplementation in medical practice.

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Debate between Drs. Alan Gaby and Guy Abraham on Iodine

This editorial by Dr. Alan Gaby in the "Townsend Newsletter" sparked an interesting debate...

Recently, a growing number of doctors have been using iodine supplements in fairly large doses in their practices. The treatment typically consists of 12 to 50 mg per day of a combination of iodine and iodide, which is 80 to 333 times the RDA of 150 mcg (0.15 mg) per day. Case reports suggest that iodine therapy can improve energy levels, overall well-being, sleep, digestive problems, and headaches. People with hypothyroidism who experienced only partial improvement with thyroid hormone therapy are said to do better when they start taking iodine. In addition, fibrocystic breast disease responds well to iodine therapy, an observation that has been documented previously. The reported beneficial effects of iodine suggest that some people have a higher-than-normal requirement for this mineral, or that it favorably influences certain types of metabolic dysfunction.

While iodine therapy shows promise, I am concerned that two concepts being put forth could lead to overzealous prescribing of this potentially toxic mineral. First is the notion that the optimal dietary iodine intake for humans is around 13.8 mg per day, which is about 90 times the RDA and more than 13 times the "safe upper limit" of 1 mg per day established by the World Health Organization. Second is the claim that a newly developed iodine-load test can be used as a reliable tool to identify iodine deficiency.

Is the optimal human requirement 13.8 mg per day?
The argument, developed by one investigator, that the optimal human iodine intake is around 90 times the RDA is based mainly on two points. The first point is that the average iodine intake of adults living in Japan is 13.8 mg per day, and the Japanese are among the healthiest people in the world, with low rates of cancer. The second point is in regard to the amount of oral iodine that it takes to saturate the thyroid tissues.

The idea that Japanese people consume 13.8 mg of iodine per day appears to have arisen from a misinterpretation of a 1967 paper. In that paper, the average intake of seaweed in Japan was listed as 4.6 g (4,600 mg) per day, and seaweed was said to contain 0.3% iodine. The figure of 13.8 mg comes from multiplying 4,600 mg by 0.003. However, the 4.6 g of seaweed consumed per day was expressed as wet weight, whereas the 0.3%-iodine figure was based on dry weight. Since many vegetables contain at least 90% water, 13.8 mg per day is a significant overestimate of iodine intake. In studies that have specifically looked at iodine intake among Japanese people, the mean dietary intake (estimated from urinary iodine excretion) was in the range of 330 to 500 mcg per day, which is at least 25-fold lower than 13.8 mg per day.

The other argument being proposed to support a high iodine requirement is that it takes somewhere between 6 and 14 mg of oral iodine per day to keep the thyroid gland fully saturated with iodine. Whether or not that is true, it is not clear that loading the thyroid gland or other tissues with all the iodine they can hold is necessarily a good thing. Since emerging from the iodine-rich oceans to become mammals, we have evolved in an iodine-poor environment. Our thyroid glands have developed a powerful mechanism to concentrate iodine, and some thyroid glands (or other tissues) might not function as well after a sudden 90-fold increase in the intake of this mineral. As I will explain later, relatively small increases in dietary iodine intake have been reported to cause hypothyroidism or other thyroid abnormalities in some people.

It has also been observed that iodine supplementation promotes the urinary excretion of potentially toxic halogens such as bromide and fluoride. While that effect might be beneficial for some people, it is not clear to what extent it would shift the risk-benefit ratio of megadose iodine therapy for the general population.

© Dr. Harvey Kaltsas, Acupuncture Physician, DOM, Dipl. Ac. (NCCAOM)
Is the iodine-load test valid?

For the iodine-load test, the patient ingests 50 mg of a combination of iodine and iodide and the urine is collected for the next 24 hours. The patient is considered to be iodine-deficient if less than 90% of the administered dose is excreted in the urine, on the premise that a deficient person will retain iodine in the tissues, rather than excrete it in the urine. According to one doctor who uses the test and a laboratory that offers it, 92% to 98% of patients who have taken the iodine-load test were found to be deficient in iodine.

However, the validity of the test depends on the assumption that the average person can absorb at least 90% of a 50-mg dose. It may be that people are failing to excrete 90% of the iodine in the urine not because their tissues are soaking it up, but because a lot of the iodine is coming out in the feces. There is no reason to assume that a 50-mg dose of iodine, which is at least 250 times the typical daily intake, can be almost completely absorbed by the average person. While this issue has not apparently been studied in humans, cows fed supraphysiological doses of iodine (72 to 161 mg per day) excreted approximately 50% of the administered dose in the feces.9

Proponents of the iodine-load test argue that the less-than-90% urinary excretion seen in most patients is probably not due to incomplete intestinal absorption. They point out that the percent urinary excretion increases progressively (usually over a period of months) with continued high-dose iodine administration, and that this increase occurs because the body retains less of each successive dose as it becomes more saturated with iodine. However, an alternative explanation for the progressive increase in urinary iodine excretion is that repeated dosing leads to increases in the percent absorbed. That could conceivably occur in a number of different ways. As an antimicrobial agent, iodine might enhance overall nutrient absorption by killing certain pathogens in the gastrointestinal tract. Supplementing with large doses of iodine might also induce the proliferation of an intestinal iodine-transporter molecule, thereby increasing iodine absorption capacity. A third possibility is that an enterohepatic circulation exists for iodine. Repeated dosing with 50 mg of iodine might overload the enterohepatic circulation system, resulting in less iodine being dumped back into the intestine to be excreted in the feces, and more excreted in the urine. Before the iodine-load test can be considered a reliable indicator of tissue iodine levels, it needs to be demonstrated that only negligible amounts of iodine are excreted in the feces after an oral iodine load.

Potential side effects of iodine

Fairly modest increases in iodine intake have been reported to cause thyroid dysfunction, particularly hypothyroidism. In a study of 33 Japanese patients with hypothyroidism, the median serum TSH level decreased from 21.9 mU/L to 5.3 mU/L (indicating an improvement in the hypothyroidism), and one-third became euthyroid, when the patients stopped eating seaweed and other high-iodine foods for 1–2 months.10 In a survey of 3,300 children aged 6–12 years from 5 continents, thyroid glands were twice as large in children with high dietary iodine intake (about 750 mcg per day), compared with children with more normal iodine intake.11 While the significance of that finding is not clear, it suggests the possibility of iodine-induced goiter. In addition, there is epidemiological evidence that populations with "sufficient" or "high normal" dietary iodine intake have a higher prevalence of autoimmune thyroiditis, compared with populations with deficient iodine intake.12 In a study of children in a mountainous area of Greece with a high prevalence of goiter, public-health measures taken to eliminate iodine deficiency were followed by a three-fold increase in the prevalence of autoimmune thyroiditis.13 In addition, modest increases in dietary iodine have been suspected to cause hyperthyroidism in some people,14 an effect that is known to occur with larger doses of iodine.

Other well-known side effects of excessive iodine intake include acne, headaches, allergic reactions, metallic taste in the mouth, and parotid gland swelling. While the doses of iodine reported to causes those side effects have often been higher than those currently being recommended, some people appear to be especially sensitive to the adverse effects of iodine.

Practitioners who are using iodine therapy report that these side effects, including thyroid problems, are very uncommon. The relative absence of side effects may be due to the use of iodine as part of a comprehensive nutritional program. One might also speculate that the iodine/iodide combination causes fewer adverse effects on thyroid function than does iodide alone (which is the type of iodine present in iodized salt).
Conclusion
The possibility that high-dose iodine/iodide can relieve certain common conditions is intriguing. Considering the positive anecdotal reports, an empirical trial of iodine/iodide therapy, based on the clinical picture, seems reasonable. The case has not been made, however, that the average person should markedly increase his or her iodine intake in an attempt to saturate the tissues with iodine. Nor has the case been made that the iodine-load test can provide reliable guidance regarding the need for iodine therapy. Thyroid function should be monitored in patients receiving more than 1 mg of iodine per day.

Alan R. Gaby, MD

References

Iodine Debate Continues...
Note: Dr. Alan Gaby's response to this rebuttal is online, as well as a second rebuttal by Drs. Abraham and Brownstein.

Editor:
We would like to submit a rebuttal to Dr. Gaby's editorial on iodine, published in the August/September 2005 issue of Townsend Letter. Gaby questioned the safety and efficacy of orthiodosupplementation in medical practice and also the validity of the iodine/iodide loading test we use to assess whole body sufficiency for iodine.

Our rebuttal will cover four topics:

- The safe and effective use of iodine by our medical predecessors
- The computation of the average daily intake of iodide from seaweed by mainland Japanese
- The validation of the iodine/iodide loading test
- The effectiveness and safety of orthiodosupplementation in current medical practice

The safe and effective use of iodine by our medical predecessors
To quote Gaby: "Recently, a growing number of doctors have been using iodine supplements in fairly large doses in their practices. The treatment typically consists of 12 to 50 mg per day of a combination of iodine and iodide, which is 80 to 333 times the RDA of 150 mcg (0.15 mg) per day."

The element iodine was used in daily amounts 2 to 3 orders of magnitude greater than the RDA by physicians for over 150 years. Only 8 years after the discovery of iodine from seaweed by French chemist Bernard Courtois in 1811, Swiss physician J. F. Coindet who previously used successfully burnt sponge and seaweed for simple goiter, reasoned that iodine could be the active ingredient in seaweed. In 1819, he tested tincture of iodine at 250 mg/day, an excessive amount by today's standard, in 150 goiter patients with great success. He published his results in 1820.1 There is no question that the amount of iodine used by Coindet was excessive. But, Coindet was the first physician to use the newly discovered element iodine in medical practice. Since then, the collective experience of a large number of clinicians from the U.S. over the last century has resulted in the recommended daily amount of 0.1 to 0.3 ml of Lugol,2 containing from 12.5 to 37.5 mg elemental iodine, for iodine/iodide supplementation.3 This range of daily intake for iodine supplementation was based on clinical observation of the patient's overall wellbeing.

The Lugol solution was developed by French physician, Jean Lugol in 1829 for treatment of infectious diseases using oral ingestion of his preparation. The Lugol solution contains 5% iodine and 10% potassium iodide in water.2 Iodine is not very soluble in water, with aqueous saturation at 0.33 gm iodine/L. The addition of potassium iodide to an aqueous solution of iodine stabilizes the iodine by forming a complex triiodide I3- and increases the aqueous solubility of iodine in the form of a triiodide complex 150 times. The recommended daily amount of Lugol was 0.1 ml to 0.3 ml, containing 12.5 to 37.5 mg elemental iodine.2 As late as 1995, the 19th Edition of Remington's Science and Practice of Pharmacy,4 continued to recommend between 0.1 to 0.3 ml daily of Lugol 5% solution in the treatment of iodine deficiency and simple goiter.

British physicians recommended a similar range of daily intake of iodine in the form of hydrogen iodide as the ranges of iodine recommended by U.S. physicians in the form of Lugol solution. The recommended daily intake of hydriodic acid syrup was 2 to 4 ml.5 The syrup is prepared by the British apothecary from an aqueous stock solution containing 10% hydrogen iodide (HI), which is diluted 10 fold with syrups of different flavors. When hydrogen iodide is dissolved in water, it forms
hydriodic acid. The syrup would contain 1% hydrogen iodide equivalent. This would compute to 10 mg iodide per ml. So, the recommended daily amount of elemental iodine was from 20 to 40 mg.

As far back as 100 years ago, U.S. physicians used Lugol solution extensively in their practice for many medical conditions. In 1932, physician B.N. Cohn wrote: "...the widespread use of compound solution of iodine, U.S.P., (For the reader's information, that is Lugol solution) is the result of a paper by Plummer and Boothby, published in that year (1923). Since then compound solution of iodine has been used by nearly every clinician..."

Lugol solution was called then Liquor Iodi Compositus, (that is Latin for compound solution of iodine). Marine in 1923 used a daily average of 9 mg iodide in the prevention of goiter in adolescent girls, an amount 60 times the current RDA for iodine. In Marine's study, the prevalence of goiter decreased 100 fold compared to a control group following 2 ½ years of supplementation.

Gaby used the RDA for iodine as his gold standard: "First is the notion that the optimal daily iodine intake for humans is around 13.8 mg per day, which is about 90 times the RDA and more than 13 times the 'safe upper limit' of 1 mg per day established by the World Health Organization."

Physician Henry A. Schroeder who did extensive studies on the dietary requirement for trace elements reported in 1975 that iodine in dog food is 20 times higher than iodine in food consumed by humans. The amount of iodine in the food supply of humans, of pets and laboratory animals, expressed as parts per million (PPM) are: for humans 0.12; for rabbits 0.59; for rats 1.17 and for dogs 2.25. Schroeder commented: "Because it is doubtful that man differs much in his needs from other omnivorous animals, we could build up a good, if very indirect, case that man is not getting enough."

During the period when potassium iodate was used as a dough conditioner (1960-1980), and prior to the introduction of the goitrogen bromate as an alternative to iodate, one slice of bread contained the full RDA for iodine. During this period, Oddie et al reported the results of a nationwide survey of iodine intake in the U.S. at 133 locations comprising of 30,000 euthyroid subjects. The mean iodine intake in these locations ranged from 240 to 740 ug/day. Correlation between iodine intake and mortality rates from thyroid diseases revealed a highly significant inverse correlation between iodine intake and mortality rates. Oddie et al comment: "Despite this high average, there is still a significant negative correlation (r = -080) between iodine intake and mortality rate from thyroid diseases." In other words, the mortality rates would have continued to decrease with higher intake of iodine.

In Tasmania, Clement reported that a daily intake of 1.4 mg of potassium iodide (10 times the RDA) by infants and children for 16 years resulted in reduction in the prevalence of goiter, but in some regions, that amount of iodine did not have a significant effect on the rates of goiter. Different amounts of goitrogens in these different regions may explain this discrepancy. In Marine's study, 9 mg/day of iodide were required to decrease the prevalence of goiter in adolescent girls by 100 fold. Currently, in Tasmania, potassium iodate is added to bread at 2 mg per loaf of bread.

"After a preliminary survey in 1949, tablets containing 10 mg potassium iodide had been made available to infants, preschool children, and schoolchildren through schools and child-health centres for weekly consumption for approximately sixteen years. State-wide surveys at five-year intervals showed a slow steady reduction in the prevalence of goiter, but in some regions the rates remained
Gaby mentioned the "safe upper limit" of 1 mg/day, established by the WHO. As previously mentioned, prior to World War II, U.S. physicians used routinely 12.5 to 37.5 mg elemental iodine daily for iodine supplementation.³ Large numbers of pulmonary patients were treated safely for years with daily amounts of potassium iodide 2 to 3 orders of magnitude greater than 1 mg. Fradkin and Wolff⁴ commented on the safety of relatively large doses of potassium iodide: "Although there are scattered case reports of IIT (iodide-induced thyrotoxicosis) after the use of KI, these must be considered in the light of over 108 tablets of KI prescribed annually in this country. Reports of experience with KI (1.6-6.4 g/day) in large series of pulmonary patients revealed no hyperthyroidism in 2404 and 502 patients."¹³

The requirement for iodine depends on the goitrogen load. The greater the goitrogen load, the greater the need for iodine. Bromide is a goitrogen that interferes with the uptake and utilization of iodide by target cells.³,¹⁸ The U.S. population is exposed to large amounts of the element bromine in its organic and inorganic forms. The United States utilizes two-thirds of the annual world production of bromine.¹⁵ The annual world production of bromine is 280,000 tons. At 909 Kg/ton, we have then an annual world production of bromine of approximately 254,520,000 Kg. The U.S. consumes 167,983,200 Kg of bromine annually. Out of that amount, 45,450,000 Kg are used in agriculture (food supply) and 9,090,000 Kg for water sanitation (water supply). The amount of bromine used in our food and water supplies compute to 21% of the total U.S. utilization of this goitrogenic halogen.¹⁵ It does not take a rocket scientist to figure out that we, in the U.S., are exposed to high amounts of the goitrogen bromine via our food and water supplies in all its inorganic and organic forms, such as methylbromide in agriculture. Bromine competes with iodine for cellular uptake and utilization; and has goitrogenic, carcinogenic and narcoleptic properties.³ Iodine pulls bromine from storage sites¹⁸ and chloride increases its excretion in urine.¹⁵ For detoxification of bromide, the halides iodide and chloride are the most effective.

The annual world production of iodine in 1981 was 12,000 tons or 10,908,000 Kg.¹⁶ Some 20% of the iodine used in the U.S. is for animal feed supplement, and none for human food, except the minimal amount in table salt. Between 1960 and 1980, iodate was used in bread with one slice of bread containing the full RDA of 0.15 mg.³ But some 20 years ago, iodophobia resulted in the removal of iodate from bread, replacing it with...you guessed it...bromate. If you wanted to keep a nation sick and zombified, we cannot think of a better way to achieve this goal.³

Gaby, assuming we evolve from a Big Bang 20 billion years ago, commented: "Since emerging from the iodine-rich oceans to become mammals, we have evolved in an iodine-poor environment."²

Actually, the oceans are very poor in iodine, based on concentration of this element. Although the largest reservoir of iodine is in the oceans, because of their large volume, the concentration of iodate/iodine/iodide in the oceans is only 0.05 PPM, very dilute indeed, compared to bromide at 70 PPM.¹⁷ For example, to obtain the RDA for iodine from seawater, you need 3 liters. Sea salt is very low in iodide, much lower than iodide in iodized table salt. It is understandable why someone who believes in the theory of evolution has a problem with such high requirements for iodine in an environment depleted of this element. Unless sometimes in the distant past, the topsoil of planet earth contains significant levels of iodine and meeting these high requirements for iodine sufficiency could then be achieved with any diet. The theory of evolution does not offer an intellectually satisfying answer to this paradox. However, the Biblical account of the origin of the world through creation 6000 years ago followed by the fall of man and the flood fits very well the current situation. According to the biblical narrative, the Creator declared planet earth and everything in it perfect. Therefore, the original planet earth contained a topsoil rich in iodine, and all elements required for perfect health of Adam, Eve and their descendants. A rebelled archangel was expelled from God's Habitation for attempting a hostile takeover (Isaiah 14:12-15). His name was Lucifer before the attempt (Isaiah 14:12) and Satan after his expulsion (Luke 10:18). Satan deceived Eve into believing that she could become a goddess by disobeying her Creator (Genesis 3:4,5). A sequence of events followed, culminating in the worldwide flood 4500 years ago. Following this episode, the receding
waters washed away the topsoil with all its elements into oceans and seas. The new topsoil became deficient in iodine and most likely other essential elements, whose essentialities are still unknown. Mountainous areas became the most iodine-deficient because the receding waters were the most rapid over the steep slopes, eroding deeper into the soil.

The Biblical account of the flood fits very well with the finding of high concentrations of iodine in brines, which accompany oil wells and natural gas deposits. By 1977, the brines associated with deposits of natural gas in Japan accounted for 56% of the world iodine production. The previous existence of iodine-rich living organisms from which came these iodine-rich degradation products strongly suggests that sometime in the distant past, iodine was plentiful on planet earth, and some catastrophic event resulted in washing away the iodine-rich top soil in the oceans.

The toxicity of iodine depends on the forms of this element. Several forms of iodine prescribed by U.S. physicians are listed in Table I. The manmade organic forms of iodine are extremely toxic, whereas the inorganic non-radioactive forms are extremely safe. However, the safe inorganic non-radioactive forms were blamed for the severe side effects of the organic iodine-containing drugs. For example, in reference #14 of Gaby's editorial, discussing thyrotoxicosis induced by iodine, the form of iodine involved is an iodophore, an organic form of iodine. This iodophore interferes with iodine uptake and utilization by the thyroid gland. From a publication by Philippou, et al, published in 1992, it is obvious that the cytotoxicity of the organic iodine-containing drugs is due to the molecule itself, not the iodine released or present in the molecule. "We can, therefore, conclude that the effect of amiodarone, benziodarone, Na iopanate, and other iodine-containing substances with similar effects is due to the entire molecule and not to the iodine liberated. It should be noted that the cytotoxic effect of amiodarone in all cultures is also due to the entire molecule and not to the iodine present in it."

Table 1
Various forms of iodine/iodide used in clinical medicine and their toxicity levels (from Reference 16)

<table>
<thead>
<tr>
<th>Forms</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>A) Inorganic</td>
<td></td>
</tr>
<tr>
<td>1) Non-radioactive</td>
<td></td>
</tr>
<tr>
<td>a) iodides (i.e. SSKI)</td>
<td>Extremely safe</td>
</tr>
<tr>
<td>b) tincture of iodine</td>
<td></td>
</tr>
<tr>
<td>c) Lugol Solution</td>
<td></td>
</tr>
<tr>
<td>2) Radioactive iodides for diagnostic and therapeutic purposes</td>
<td>Carcinogenic</td>
</tr>
<tr>
<td>B) Organic</td>
<td>Cytotoxic</td>
</tr>
<tr>
<td>1) Natural occurring</td>
<td></td>
</tr>
<tr>
<td>a) thyroid hormones</td>
<td>Safe within physiological ranges</td>
</tr>
<tr>
<td>b) thyroidal iodolipids</td>
<td></td>
</tr>
<tr>
<td>2) Manmade</td>
<td></td>
</tr>
<tr>
<td>a) radiographic contrast media</td>
<td>Extremely toxic</td>
</tr>
<tr>
<td>b) iodine-containing drugs (i.e. amiodarone)</td>
<td></td>
</tr>
</tbody>
</table>

A new syndrome, medical iodophobia, was recently reported with symptoms of split personality, double standards, amnesia, confusion and altered state of consciousness. Medical iodophobia has
reached pandemic proportion and it is highly contagious (iatrogenic iodophobia). A century ago, non-radioactive forms of inorganic iodine were considered a panacea for all human ills, but today, they are avoided by physicians like leprosy.18 We have previously discussed the factors involved in this medical iodophobia.3,18

The computation of the average daily intake of iodide from seaweed by mainland Japanese. Over 95% of the iodine consumed by mainland Japanese comes from seaweed. If you want to prove that the intake of iodine by mainland Japanese is within the same range as consumed by the U.S. population or maybe slightly above, just tell your Japanese study subjects to abstain from seaweed during the study period. It's that easy and this technique has been used effectively in several publications. As a general rule, mainland Japanese living in the coastal areas of Japan, consume more seaweed than inland dwellers.22•24 Among the coastal areas, the inhabitants of Hokkaido ingest the largest amount of seaweed.25 Hokkaido produces 90% of the seaweed consumed in Japan,25 further processed by drying and flattening for sales in food stores. Statistics compiled by the Japanese Ministry of Health is based on the dry form of seaweed.26 Seaweed contains predominantly the inorganic form of the element iodine, mainly iodide.27 Seaweed also concentrates other halides such as bromide, which possess goitrogenic, carcinogenic and narcoleptic properties.3 Seawater is very poor in iodide and relatively rich in bromide with 0.05 PPM iodide and 70 PPM bromide. There is 1400 times more bromide than iodide in seawater.

Mainland Japanese consume large amounts of iodine from seaweed and they are one of the healthiest nations.11 Based on extensive surveys performed by the International Agency for Research on Cancer and published in 1982,28 mainland Japanese, at least up to 1982, experienced one of the lowest incidences of cancer in general. Mainland Japanese have the longest lifespan in the world.29 Although seaweed has been the main source of iodine for the Japanese population, inorganic iodine/iodide in supplements (liquid or tablets) seems a much purer, safer and more accurate form for supplementation of this essential element than seaweed. It is more difficult to titrate the amount of seaweed needed to achieve whole body sufficiency for iodine than the amount of a pure standardized solid dose form of this essential element. The reported seaweed-induced goiter with normal thyroid functions 40 years ago in Hokkaido, Japan,25 was not caused by iodine. This seaweed-induced goiter eventually disappeared.22 Suzuki et al25 questioned whether seaweed itself was the cause of this goiter, since much larger amounts of iodide in pulmonary patients did not induce goiter. Suzuki et al commented: "Considering the paucity of reported cases of iodine goiter with the wide spread usage of iodine medication, we cannot exclude factors other than excessive intake of dietary iodine as a cause of the goiter." Also, residents in Tokyo, Japan, who excreted similar levels of iodide in their urine (around 20 mg/24h) did not experience goiter. Contamination
of seaweed with bromide is the most likely explanation, since bromide is a goitrogen, and there is 1400 times more bromide than iodide in seawater. The presence of excess goitrogens in the diet would require greater amounts of ingested iodine to prevent the goitrogenic effect of these substances.

In assessing the intake of iodine by mainland Japanese based on urinary excretion of iodide, keep in mind that urinary iodide levels are not a good index of intake unless whole body sufficiency for iodine is achieved and the form of iodine consumed is highly bioavailable. For example, only 10% of sodium iodide present in table salt is bioavailable, due to competition with chloride for intestinal absorption. On a molar basis, there is 30,000 times more chloride than iodide in iodized salt. The % of ingested iodine excreted in the 24 hr. urine collection can be as low as 10% of the ingested amount in iodine-deficient subjects, due to body retention of iodine. With this in mind, let us review some published data. Konno et al measured iodide in morning urine samples of 2,956 men and 1,182 women, all normal and healthy, residing in Sapporo, Japan. The 95% confidence limits were from 1.14 to 8.93 mg/L. Assuming an average 24 hr. urine volume of 1.5 liters, the daily iodide excretion would range from 1.7 to 13.4 mg with an average of 5 mg. As discussed previously, these amounts are an underestimate of iodine intake. Yabu et al from Osaka measured iodide levels in morning urine samples obtained from 39 male and 88 female local residents. He reported a range of 0.6 to 17.4 mg/L. If those iodine levels are expressed as mg/24 hr. and assuming an average 24 hr. urine volume of 1.5 liter, the range of iodine excretion per 24 hr. would be from 1 to 25 mg in these 163 Japanese subjects.

Gaby mentioned that the calculation we used to estimate the average daily intake of mainland Japanese was based on dry weight whereas the data in Nagataki's publication on iodine in seaweed was reported per wet weight. Quoting from that article: "For example, the dry weight of such food as "tangle" (Laminaria) contains 0.3% iodine and this may be eaten in quantities as large as 10 g daily. This daily intake would compute to 30 mg of elemental iodine. However, on page 643 of the same article, Nagataki et al misquoted their Reference #13, that is our Reference #26, when they stated: "...according to the statistics of the Ministry of Health and Welfare, the average daily intake of seaweed was 4.6 g (wet weight)," when in fact, that Organization confirmed by a phone interview (6/21/05) that their data on seaweed are always expressed as dry weight.

For example, in table 8 of Nagataki's Reference #13, values for seaweed consumption for several years from 1950 to 1963 are listed in gms of dry weight, confirmed by the Japanese Ministry of Health and Welfare. We have compiled some of these data in our Table II, taken from reference 13 of Nagataki's article. The value of 4.6 g that Nagataki quoted as wet weight was actually expressed as dry weight and Nagataki used the value for the year 1963 only, that is, 4.6 gm. Nagataki et al mentioned correctly dry weight on page 638 at the beginning of their article, and for some unknown
reason, they erroneously mentioned wet weight on page 643 of the same publication, which is confusing. We have relied, therefore, on the original information supplied by the Japanese Ministry of Health and Welfare, that is Nagataki’s Reference #13, and our reference #26.

The average daily intake of iodine by mainland Japanese in 1963 was 13.8 mg, based on information supplied by the Japanese Ministry of Health, which used only dry weight in their calculations, confirmed by a phone interview of one of us (GEA) on June 21, 2005, with officials of this organization (See Table II).

Table II
Annual change of intake of food by food groups in Japan
(Except for the calories, all values below are expressed as gms / per capita / day)

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>2,098</td>
<td>2,109</td>
<td>2,074</td>
<td>2,092</td>
<td>2,118</td>
<td>2,096</td>
<td>2,080</td>
<td>2,083</td>
</tr>
<tr>
<td>Proteins</td>
<td>Total</td>
<td>68</td>
<td>70</td>
<td>69</td>
<td>69.1</td>
<td>70.1</td>
<td>69.7</td>
<td>70.4</td>
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<tr>
<td>Animal</td>
<td>17</td>
<td>23</td>
<td>22</td>
<td>22.6</td>
<td>23.8</td>
<td>24.7</td>
<td>27.3</td>
<td>27.7</td>
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<tr>
<td>Vegetable</td>
<td>51</td>
<td>47</td>
<td>47</td>
<td>46.5</td>
<td>46.4</td>
<td>45.0</td>
<td>43.2</td>
<td>42.9</td>
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<tr>
<td>Fat</td>
<td>18</td>
<td>20</td>
<td>21</td>
<td>21.8</td>
<td>23.7</td>
<td>24.7</td>
<td>28.3</td>
<td>29.2</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>418</td>
<td>412</td>
<td>403</td>
<td>405</td>
<td>406</td>
<td>399</td>
<td>386</td>
<td>382</td>
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<tr>
<td>Sugars</td>
<td>7.2</td>
<td>14.5</td>
<td>15.6</td>
<td>15.6</td>
<td>12.3</td>
<td>12.3</td>
<td>13.4</td>
<td>14.0</td>
</tr>
<tr>
<td>Fats &amp; Oils</td>
<td>2.6</td>
<td>3.9</td>
<td>4.6</td>
<td>5.1</td>
<td>5.7</td>
<td>6.1</td>
<td>7.6</td>
<td>8.1</td>
</tr>
<tr>
<td>Beans</td>
<td>53.7</td>
<td>68.4</td>
<td>68.2</td>
<td>72.7</td>
<td>71.0</td>
<td>71.2</td>
<td>70.8</td>
<td>69.4</td>
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<tr>
<td>Milk</td>
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<td>10.2</td>
<td>12.5</td>
<td>19.4</td>
<td>22.0</td>
<td>29.5</td>
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<tr>
<td>Milk products</td>
<td>0.4</td>
<td>0.6</td>
<td>2.1</td>
<td>2.6</td>
<td>3.4</td>
<td>5.9</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>*Sea weeds (dry weight)</td>
<td>3.0</td>
<td>4.1</td>
<td>4.8</td>
<td>5.0</td>
<td>5.0</td>
<td>4.7</td>
<td>4.5</td>
<td>4.6</td>
</tr>
</tbody>
</table>


* In a phone interview with Guy E. Abraham, M.D., on June 21, 2005, using Miss Hisa Izumi as an interpreter, the interviewees Miss Nichi and Mr. Arai at the Japanese Ministry of Health and Welfare confirm that, in the nutritional surveys published in 1965, the average daily amount of seaweed consumed is expressed as gms of dried seaweed.

One can see that iodine intake was even higher during the years 1954, 1956, 1958 and 1960. The mean value for the 8 amounts of seaweed displayed in Table II is 4.5 gm and at 0.3% iodide, this average daily amount would contain 13.5 mg iodide. During that phone interview (6/21/05), Miss Nichi and Mr. Arai stated that the last survey for which statistics are available was for the year 2001 (Heisei 14), with an average daily intake of 14.6 gm of seaweeds (dry weight). Obviously, the consumption of seaweed by mainland Japanese has increased significantly over the past 40 years. The exact amount of iodine consumed in 2001 would depend on the concentrations of iodine in the
excretion of iodine to balance completely the intake. They estimated that the body retained 1.5 gm of iodine before the ingested iodine in amiodarone is completely excreted, and before therapeutic efficacy.

In 3 patients who eventually died following long-term treatment with amiodarone, the levels of inorganic iodine (not amiodarone) present in various organs and tissues were measured. The total body non-amiodarone iodine content was estimated at approximately 2 gm with the greatest amount found in fat tissues (700 mg) and striated muscle (650 mg). Iodine was present in every tissue examined. The highest concentrations of non-amiodarone iodine were found in descending order: thyroid gland, liver, lung, fat tissues, adrenal glands and the heart. We previously reported a double peak of serum inorganic iodide levels, 8 hours apart, following ingestion of a solid dosage form of Lugol. This pattern is indicative of an enterohepatic circulation of inorganic iodine, which could explain the high iodine content of the liver.

When a tablet form of Lugol is ingested at a daily amount of 50 mg elemental iodine, whole body sufficiency is achieved in approximately 3 months and the estimated amount of iodine retained in the body is approximately 1.5 gm. This is the same amount of iodine retained in patients on amiodarone following 7 weeks at 300 mg/day containing 112.5 mg iodine. Clinical response to amiodarone is observed after the same period of time on amiodarone therapy. Some comparisons between amiodarone, an organic form of iodine, and inorganic iodine/iodide are in order. In the patients who ingested 300 mg amiodarone for 7 weeks, the total amount of iodine ingested is: 112.5 mg x 49 days = 5.5 gm. The patients retained 1.5 gm, that is 1.5 gm / 5.5 gm x 100 = 27% of the total dose. In patients of orthoiodosupplementation at 50 mg elemental iodine/day, sufficiency is achieved usually in 3 months and 1.5 gm of iodine is retained. The total amount of iodine ingested during 3 months at 50 mg/day = 50 mg / day x 90 days = 4.5 gm. The patients retained 1.5 gm, that is 1.5 gm / 4.5 gm x 100 = 33% of the total dose. Roughly 30% of the total dose of iodine is retained at iodine sufficiency in both cases, but the time required to achieve sufficiency decreases as the daily amount of iodine increases. Whether this inverse relationship between the daily dose of iodine and time required for whole body iodine sufficiency will persist with daily intake of iodine greater than 100 mg would require further investigation.

Since iodine mobilizes toxic metals and goitrogenic halides from their storage sties, it may not be wise to achieve whole body sufficiency for iodine too rapidly since mobilization of these toxic substances may increase their peripheral levels high enough to cause symptoms. A complete nutritional program combined with increased fluid intake will help the body eliminate these toxic elements more safely. To be discussed later, in cases of increased mobilization of bromide from storage sites by orthoiodosupplementation and elevated serum bromide levels high enough to cause bromism, the administration of sodium chloride (6-10 gm/day) increases the renal clearance of bromide by 10 fold and minimizes the side effects of bromism. If orthoiodosupplementation results in elevated urine lead levels, together with increased bromide, ammonium chloride is preferable to sodium chloride since it is the chloride that increases renal clearance of bromide. The ammonium is metabolized to urea and has an acidifying effect, which increases renal clearance of lead also.

The above comparison of the data obtained from amiodarone administration and orthoiodosupplementation is suggestive of an important role of inorganic iodine released from amiodarone in the therapeutic effect of this drug, and that whole body sufficiency for iodine is a requirement for optimal cardiac function. Since the amount of iodine used in the amiodarone study is twice the amount of iodine used in orthoiodosupplementation, the time required for whole body iodine sufficiency was only 7 weeks for amiodarone and 12 weeks for orthoiodosupplementation. In order to achieve whole body sufficiency for iodine in 6 weeks using orthoiodosupplementation, the daily intake required would be 100 mg.

One more argument in support of the validity of the iodine/iodide loading test follows. Serum inorganic iodide levels measured under steady state conditions are a good index of bioavailability of the iodine preparation. We have previously calculated that the serum levels of inorganic iodide at equilibrium would be the daily amount of iodine ingested divided by 43.5 liters if the form of iodine
ingested was completely bioavailable. At 50 mg iodine/day, the expected serum inorganic iodide level at equilibrium would be: 50 mg/43.5 L = 1.15 mg/L. In 8 normal subjects who achieved whole body iodine sufficiency, the fasting serum inorganic iodide levels 24 hrs after the last intake of iodine, ranged from 0.85 to 1.34 mg/L.

The effectiveness and safety of orthoiodosupplementation in current medical practice

Physicians who use holistic therapies are always on the search for safe and effective natural therapies that have minimal adverse effects. The experience of several physicians with iodine/iodide in daily amounts from 6.25 to 50 mg, using a solid dosage form of Lugol (Iodoral®) for over three years in several thousands of patients has shown it to be safe and effective, with minimal adverse effect.

Effectiveness

The Center for Holistic Medicine in West Bloomfield, MI (office of D. Brownstein, M.D.) has tested over 500 patients for iodine deficiency using the iodine/iodide loading test, developed by one of us. Based on the experience of the Center, the loading test provides an accurate and reproducible picture of the iodine status in the body. Retesting many of these patients has shown the changes in the test correlates with the changes in the clinical picture. In other words, as the loading test improves, the clinical picture improves.

Our experience at the Center for Holistic Medicine has shown that patients with the lowest urinary iodide levels on the loading tests are often the most ill. Many of these patients with very low urine iodide levels following the loading test have severe illnesses such as breast cancer, thyroid cancer or autoimmune thyroid disorders. All of these conditions have been shown in the literature to be associated with iodine deficiency. Positive clinical results were seen in most of these patients after supplementation of orthoiodosupplementation within the range of 6.25-50 mg of iodine/iodide (1/2 to 4 tablets of Lugol in tablet form).

One of the most satisfying effects of orthoiodosupplementation has been in the treatment of fibrocystic breasts and thyroid nodules. The treatment of fibrocystic breasts with iodine has been reported for over 100 years. Iodine/iodide supplementation has resulted in significant improvement in fibrocystic breast illness for nearly every patient treated. Thyroid nodules also respond positively to iodine/iodide supplementation. Serial ultrasounds usually show decrease in the size of the thyroid cysts and nodules and eventual resolution of the lesions. When orthoiodosupplementation is combined with a complete nutritional program, it is rare not to see improvement in the palpation and radiological examination of thyroid nodules and cysts following iodine/iodide therapy as described here.

The effectiveness of orthoiodosupplementation has not been limited to the very ill. In fact, most patients treated with orthoiodosupplementation have quickly experienced positive results although optimal responses are observed when whole body iodine sufficiency is achieved based on the iodine/iodide loading test. Our experience has shown that a wide range of disorders have responded to orthoiodosupplementation including thyroid disorders, chronic fatigue, headaches, fibromyalgia and those with infections. Additionally, our clinical experience has shown that iodine/iodide supplementation has resulted in lower blood pressure in hypertensive patients. The blood pressure-lowering effect is seen when sufficiency of iodine is achieved.

Occasionally, individuals on thyroid medication will develop signs and symptoms of hyperthyroidism on orthoiodosupplementation. This situation has been easily rectified by lowering or discontinuing the thyroid medication. Of those individuals taking thyroid medication, approximately 1/3 of them will need to discontinue or lower their thyroid medication upon taking iodine/iodide due to increased thyroid function and improved receptor responsiveness. The remaining 2/3 of the thyroid treated patients will maintain their thyroid dosages while taking...
iodine/iodide without side effects.

Safety
Dr. Gaby’s editorial claims that the relatively high doses of iodine/iodide used in orthoiodosupplementation may lead to hypothyroidism, goiter or autoimmune thyroid problems. This just is not the case. A review of the literature revealed that the organic forms of iodine were involved in most of these complications. Iodine intake has fallen over 50% in the U.S. over the last 30 years. During this same time, increases in diabetes, hypertension, obesity, breast and thyroid cancer, and other thyroid disorders, have been reported. It appears to us that iodine deficiency, not iodine excess may be responsible for the increase of these conditions.

As of this writing (7/12/05), the clinical experience with orthoiodosupplementation in approximately 4,000 patients at the Center for Holistic Medicine has clearly shown that orthoiodosupplementation at daily dose of 6.25 to 50mg elemental iodine has not been associated with increases in hypothyroidism, goiter and autoimmune thyroid problems. On the contrary, the use of iodine/iodide has been effective at treating the above conditions with minimal adverse effects.

Dr. Gaby points out that "some people are especially sensitive to the adverse effects of iodine." He is correct. Just as some people are sensitive to Vitamin C, some are sensitive to iodine/iodide. Few holistic physicians would deny the effectiveness of mega doses of Vitamin C, in amounts thousands of times greater than the RDA for Vitamin C, in the treatment of wide range of illnesses. Just as with Vitamin C therapies, individualized doses and proper follow-up visits can help minimize adverse effects of iodine/iodide therapies.

Dr. Gaby writes, "The relative absence of side effects may be due to the use of iodine as part of a comprehensive nutritional program." He is correct. With orthoiodosupplementation the best results do occur when used as part of a comprehensive nutritional program, as do all holistic therapies. We favor a magnesium emphasized total nutritional approach.

The most common adverse effects of iodine/iodide supplementation observed at the Center for Holistic Medicine has been metallic taste in the mouth and acne. Based on the experience of three clinicians at that Center, with a combined patient population of some 4,000, the prevalence of these side effects is about 1%. This is probably due to a detoxification reaction. The release of bromide may be one cause of this detoxification reaction. Clinical experience has continually shown that iodine/iodide supplementation results in a large urinary excretion of bromide. When bromide levels begin to decline, the above mentioned adverse effects begin to decline as well. Chloride increases renal clearance of bromide and the use of NaCl or ammonium chloride shortens the time required for bromide detoxification with orthoiodosupplementation. Oral administration of sodium chloride (6 to 10 gm/day) increased the renal clearance of bromide by 10 fold with mean serum half-life of 290 hrs in control subjects and 30-65 hrs after chloride administration. Intravenous sodium chloride gives the same results as the oral route.

In the practice of medicine, we have seen very few natural therapies as safe and effective as orthoiodosupplementation. In the proper forms of iodine (inorganic non-radioactive forms), in daily amounts of iodine for whole body sufficiency and properly monitored, orthoiodosupplementation is not only safe, it is an effective tool for the clinician. Prior to the availability of assays for thyroid hormones and without any test for assessing whole body sufficiency for iodine, our medical predecessors recommended a range of daily iodine intake from Lugol solution (12.5-37.5 mg) exactly within the range required for achieving whole body sufficiency for iodine. Relying on clinical observation of the patient's overall wellbeing, our predecessors have given us useful information, which we have discarded in favor of preconceived opinions of self-appointed pseudopseudoexperts. This has resulted in pandemic iodine deprivation. Iodine deficiency is misdiagnosed and treated with toxic drugs. Orthoiodosupplementation may be the simplest, safest, most effective and least expensive way to help solve the health care crisis crippling our nation.
Correspondence
Guy E. Abraham, M.D.
Optimox Corporation, Torrance, California
1-800-223-1610 / Fax: 1-310-618-8748
optimox@earthlink.net

David Brownstein, M.D.
Center for Holistic Medicine, West Bloomfield Michigan
1.248-851-1600 / Fax: 1-248-851-0421
info@drbrownstein.com

Financial Disclosure
Guy E. Abraham, M.D. is the owner of the company that developed and distributes Iodoral®, a tablet form of Lugol solution, to healthcare professionals. Although he developed the iodine/iodide loading test at his own expense, including the procedure to measure urine iodide levels and the positive displacement manifold, which allows semi automation of this procedure, he has no financial interest in the Lab that performs the loading tests. Neither did he receive remuneration for passing this technology to others. He serves as a consultant to this Lab without pay.

David Brownstein, M.D. has no financial interest in Iodoral® or the Lab that performs the loading test.

References


Alan R. Gaby, MD's Response to:
A Rebuttal of Dr. Gaby's Editorial on Iodine

More on High-dose Iodine
by Alan R. Gaby, M.D.

In an editorial in the Aug/Sept issue of the Townsend Letter, I expressed concern about potential adverse effects that might occur with the routine use of megadose iodine therapy, which is currently being advocated by some practitioners. I cited research indicating that even modest increases in dietary iodine intake might increase the incidence of hypothyroidism, autoimmune thyroiditis, and possibly hyperthyroidism. In the following issue of the Townsend Letter, Drs. Abraham and Brownstein wrote a rebuttal to my editorial. They stated that, in Brownstein's experience with 4,000 patients at the Center for Holistic Medicine in West Bloomfield, Michigan, these side effects have not occurred; on the contrary, high-dose iodine has been effective in some cases as a treatment for these conditions. Although high-dose iodine therapy has a definite place in clinical medicine, I believe that some of their remarks warrant comment.

First, it does not seem appropriate to use the term "orthoiodosupplementation" to describe the treatment they are recommending. That term is borrowed from Linus Pauling's "orthomolecular medicine," which refers to the concept of creating the optimal molecular environment in the body ("orthomolecular" means "the right molecules"). Defining the optimal dosage range as an amount that is 40 to 320 times the usual dietary intake obfuscates any debate about whether such a high intake is desirable or safe. Therefore, until iodine doses of 6.25-50 mg per day are proven to be optimal, it would be more logical to refer to these doses as "high-dose iodine therapy."

Drs. Abraham and Brownstein stated that the thyroid disorders I mentioned that resulted from iodine supplementation occur mainly with "organic forms" of iodine, such as amiodarone and certain iodine-containing dyes used in radiology. However, all but one of the references I cited discussed the adverse effects of inorganic iodine. The other article concerned the use of an iodophore, which is a surfactant molecule that slowly releases inorganic iodine. As surfactants would not by themselves be expected to affect thyroid function, one might presume that the released inorganic iodine was responsible for the reported adverse effects.

I would also question the statement that our medical predecessors recommended daily iodine intake of 12.5 to 37.5 mg from Lugol's solution. While Dr. Lugol did use those doses, they were recommended primarily to treat infections (iodine is a broad-spectrum antimicrobial agent) and...
hyperthyroidism, not as routine nutritional support for the average person.

Regarding the safety data from the Michigan clinic, Dr. Brownstein learned about high-dose iodine only about two years ago, from a letter written by Dr. Abraham in the Townsend Letter. For a three-doctor practice to initiate high-dose iodine therapy on 4,000 patients over a two-year period seems like a daunting endeavor, and one wonders how meticulously these patients were monitored for adverse effects. How many patients discontinued the treatment because of side effects and never returned to the clinic to report their experiences? How many patients who did return were questioned in detail about potential side effects, including fatigue and other symptoms of hypothyroidism? How many patients showed a decline in their serum thyroxine level that was judged to be clinically insignificant because it remained in the normal range? Abraham has in fact, observed such decreases in thyroid hormone levels in patients receiving iodine therapy. One should not automatically assume that these changes are benign. Research has shown that each person has a unique "set point" for serum concentrations of T4, T3, and TSH. Any iodine-induced deviation from these set points may be result in suboptimal thyroid function for that person, even if all measurements remain within the normal range.1 How many patients were tested serially to identify the appearance of thyroid antibodies during treatment with iodine? Before one could confidently conclude that high-dose iodine is safe for 99% of the population (as stated by Abraham and Brownstein), it seems that a systematic toxicity study would be necessary.

It is also worth considering that the positive results observed in Michigan might not be reproducible in other geographical areas. Drs. Abraham and Brownstein hypothesized that the beneficial effect of iodine is due in part to removal of bromine from the body. In 1973-4, several thousand Michigan dairy farms were contaminated by polybrominated biphenyls (PBBs) from an industrial accident. This bromine-containing pollutant is known to persist in the body for long periods of time. Five years after the accident, 97% of adipose tissue samples taken from Michigan residents had detectable levels of PBBs,2 and 96% of breast milk samples from women in densely populated areas of the state contained this chemical up to three years after the accident.3 Because of its exceptionally long half-life, it is reasonable to assume that many Michigan residents still have a body burden of PBBs. As thyroid dysfunction is known to occur in people exposed to PBBs, it is possible that some of the beneficial effects attributed to iodine therapy were due to a reduction of the body burden of PBBs.4

High-dose iodine therapy is of great value in some circumstances. We should not forget, however, that this treatment was abandoned in the past, because it caused many deaths from heart failure, as well as a long list of other side effects. The doses used then were higher than those currently being advocated. However, it is premature to assert that more modest doses do not cause more modest side effects.

References

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Iodine Debate Continues:
Rebuttal #2
by Guy E. Abraham, MD and David Brownstein, MD
We would like to submit a second rebuttal to Gaby's response to our first rebuttal which was in response to Alan Gaby's editorial on iodine. In his editorial, Gaby questioned the validity of the iodine/iodide loading test we use to assess whole body sufficiency for iodine and the safety of our orthoiodosupplementation program, which is currently used safely and effectively by thousands of physicians and other health care professionals nationwide. Our first rebuttal covered the main objections by Gaby and also questioned the scientific validation of the theory of evolution.

On the Townsend Letter web site, (www.townsendletter.com), in December 2005, Alan R. Gaby, MD posted a sequel to his editorial on iodine. This time, Gaby did not defend his belief in evolution and the origin of man from the "iodine-rich" oceans. This time, he did not question the validity of our iodine/iodide loading test. This time, he did not debate the method we used to calculate the average daily intake of iodine by mainland Japanese. This time, Gaby concentrated his attention on the safety of iodine as used in the orthoiodosupplementation program. Running out of scientific arguments, Gaby resorted to personal attacks. We will respond in a scientific manner, point-by-point and with references, including definitions of words from an English dictionary.

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Gaby:
"First, it does not seem appropriate to use the term 'orthoiodosupplementation' to describe the treatment they are recommending. That term is borrowed from Linus Pauling's 'orthomolecular medicine,' which refers to the concept of creating the optimal molecular environment in the body ('orthomolecular' means 'the right molecules'). Defining the optimal dosage range as an amount that is 40 to 320 times the usual dietary intake obfuscates any debate about whether such a high intake is desirable or safe. Therefore, until iodine doses of 6.25-50 mg per day are proven to be optimal, it would be more logical to refer to these doses as 'high-dose iodine therapy.'"

Comment:
The prefix "ortho" is not borrowed from Linus Pauling. The English dictionary contains hundreds of words starting with "ortho." For Gaby's erudition, the daily amount of iodine needed for whole body sufficiency was named orthoiodosupplementation from ortho = the right amount; iodo = for inorganic non radioactive iodine; and supplementation = for oral intake of this essential nutrient.

To find the definition of "obfuscate," we consulted the Etymological Dictionary of the English Language by Reverend Walter W. Skeat. It derives from two Latin words:

ob (prefix) = over, toward, before, about, near, above
fusate = to darken
obfuscate = to darken over
The endpoint in optimizing a nutritional program is the clinical response. The optimal amount of a nutrient is reached when it results in optimal mental and physical health. Having a test that confirms the optimal amount of a nutrient that achieves whole body sufficiency, concomitant with optimal physical and mental health in the absence of significant side effects, is what we strive to do. In fact, it is what all holistic physicians strive to achieve.

Gaby:
"Drs. Abraham and Brownstein stated that the thyroid disorders I mentioned that resulted from iodine supplementation occur mainly with 'organic forms' of iodine, such as amiodarone and certain iodine-containing dyes used in radiology. However, all but one of the references I cited discussed the adverse effects of inorganic iodine. The other article concerned the use of an iodophore, which is a surfactant molecule that slowly releases inorganic iodine. As surfactants would not by themselves be expected to affect thyroid function, one might presume that the released inorganic iodine was responsible for the reported adverse effects."

Comment:
To support his contention that iodine supplementation is associated with thyroid disorders, Gaby list five references:


In reference 10, the authors studied the effect of restricting seaweed on thyroid functions, not iodine. Seaweed contains more that just iodine. In reference 11, the authors of this publication reported that urine iodide concentrations greater than 0.5 mg/L were associated with increased thyroid volume in multiethnic groups of children between six and 12 years old. Analysis of the data in Table I of that publication revealed only children from Hokkaido, Japan showed increased thyroid volumes of significance compared to the other groups: 2.16 to 2.59 ml for all the other groups; and 2.86 and 4.91 ml for the two groups from Hokkaido. This area of Japan is known to have a high incidence of...
euthyroid goiter. Suzuki et al., who first reported this finding in 1965 did not think that iodine was the cause of this goiter. He commented: "Considering the paucity of reported cases of iodine goiter with the wide spread usage of iodine medication, we cannot exclude factors other than excessive intake of dietary iodine as a cause of the goiter."

In reference 12 and 13, the authors reported an increased incidence of autoimmune thyroiditis following iodization of salt. This is a common observation worldwide. As we have previously reported, autoimmune thyroiditis cannot be induced in laboratory animals in the absence of a goitrogen. The goitrogen used in these experiments is an anti-thyroid drug. We previously discussed the mechanism involved in the induction of thyroiditis following ingestion of iodized salt containing on a molar basis 30,000 more chloride than iodide. Magnesium and iodine deficiencies are the causes of autoimmune thyroiditis, not excess iodide.

In reference 14, an organic iodine-containing drug, polyvinylpyrolidone, induced thyrotoxicosis, not inorganic non-radioactive iodine. This drug was shown to interfere with uptake and utilization of iodine, similar to the effect of amiodarone. We discussed this drug in our first rebuttal.

Gaby:
"I would also question the statement that our medical predecessors recommended daily iodine intake of 12.5 to 37.5 mg from Lugol's solution. While Dr. Lugol did use those doses, they were recommended primarily to treat infections (iodine is a broad-spectrum antimicrobial agent) and hyperthyroidism, not as routine nutritional support for the average person."

Comment:
Gaby claimed that iodine was used only in infectious diseases and hyperthyroidism. Nobel Laureate Albert Szent Györgyi, the physician who discovered Vitamin C in 1928, commented 50 years ago:

When I was a medical student, iodine in the form of KI was the universal medicine. Nobody knew what it did, but it did something and did something good. We students used to sum up the situation in this little rhyme:

If ye don't know where, what, and why
Prescribe ye then K and I.

Our medical predecessors, ...were keen observers and the universal application of iodide might have been not without foundation.
To quote F.C. Kelley:

In the first flush of enthusiasm for the newcomer, physicians and surgeons tested it and tried it for every conceivable pathological condition. The variety of diseases for which iodine was prescribed in the early years is astonishing - paralysis, chorea, scrofula, lacrimal fistula, deafness, distortions of the spine, hip-joint disease, syphilis, acute inflammation, gout, gangrene, dropsy, carbuncles, whitlow, chilblains, burns, scalds, lupus, croup, catarrh, asthma, ulcers, and bronchitis – to mention only a few.


The following is a list of the principal conditions in which iodides are recognized to be of definite value: metallic poisonings, as by lead and mercury, asthma, aneurism, arteriosclerosis, angina pectoris, gout, goiter, syphilis, haemophilia, Bright's disease (nephritis), and bronchitis.

Gaby:

"How many patients showed a decline in their serum thyroxine level that was judged to be clinically insignificant because it remained in the normal range? Abraham has, in fact, observed such decreases in thyroid hormone levels in patients receiving iodine therapy. One should not automatically assume that these changes are benign. Research has shown that each person has a unique 'set point' for serum concentrations of T4, T3, and TSH. Any iodine-induced deviation from these set points may be result in suboptimal thyroid function for that person, even if all measurements remain within the normal range."

Comment:

We have previously reported a statistically significant decrease in total T4 in ten Caucasian women following three months on iodine at 12.5 mg/day. The results are displayed in Table 1.

Table 1: Effect of iodine supplementation in daily amount of 12.5 mg for three consecutive months on thyroid volume and thyroid function tests in ten Caucasian normal women (From reference 11)

<table>
<thead>
<tr>
<th>Subjects #</th>
<th>Thy. Vol. (mL)</th>
<th>TSH (mIU/L)</th>
<th>T4 (ug/dL)</th>
<th>FT4 (ng/dL)</th>
<th>FT3 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>X</td>
<td>7.7</td>
<td>8.1</td>
<td>4.4</td>
<td>3.2</td>
<td>8.8</td>
</tr>
</tbody>
</table>
There was a drop from a mean T4 of 8.8 ug/dL before to a mean of 7.1 ug/dL after three months on iodine. No change occurred in Free T3 and Free T4. In the Discussion section, we stated:

The significant decrease in serum T4 observed in the present study, concomitant with the absence of significant changes in the mean values for TSH, FT3 and FT4, following one supplementation at 12.5 mg/day (Table VII), could be due to either a decreased secretion of T4 by the thyroid gland; or it could be due to lower levels of thyroxine binding globulin (TBG). The synthesis of TBG occurs in the liver and this synthesis is stimulated by estrogens. In the female rat, I-deficiency increases the sensitivity of mammary tissue to estrogens. I-supplementation to these female rats in amounts equivalent, based on body weight, to amounts of I required in women with FDB for subjective and objective improvement of FDB had an attenuating effect on estrogen stimulation of the mammary tissue in those female rats, decreasing their response to estrogens. Therefore, the decreased T4 levels following I-supplementation could be due to a similar mechanism on hepatic synthesis of TBG, by decreasing the sensitivity of hepatic receptors to estrogens, resulting in decreased synthesis and release of TBG by the liver and decreased T4 levels. Since we did not include serum TBG levels in our thyroid profile, the explanation for this decrease of serum T4 levels must await future research.

The subjects studied above did not exhibit any adverse effects to the change in thyroid levels. In fact, they experienced a significant clinical improvement in many of their symptoms, including symptoms commonly associated with hypothyroidism such as fatigue, headaches, etc. It is well known that relying solely on thyroid function tests to diagnose and treat hypothyroidism will often lead to a suboptimal outcome.
Gaby:
"For a three-doctor practice to initiate high-dose iodine therapy on 4,000 patients over a two-year period seems like a daunting endeavor, and one wonders how meticulously these patients were monitored for adverse effects."

Comment:
Let's do the math. We see patients 4.5 days per week. On average, we each see approximately 15-20 patients per day. Let's take 15 patients/day x four days per week = 60 patients per week/doctor. 60 patients/week x 50 weeks/year = 3,000 patients/year/doctor. If we multiply that number by three doctors, we see approximately 9,000 patients per year. These numbers are very similar to most busy family practice offices throughout the country. We started using orthoiodosupplementation approximately three years ago. Not such a daunting endeavor.

Not every patient was treated with orthoiodosupplementation. As with any therapy, a history and exam were completed, and a clinical diagnosis was made. As all good clinical physicians, we not only monitor our patients, we see them back in follow-up. We are always looking for adverse effects of any therapy, just as we are looking for positive effects. To insinuate poor medical care was given is not appropriate, nor is it fair.

Gaby:
"It is also worth considering that the positive results observed in Michigan might not be reproducible in other geographical areas."

Comment:
These positive results are observed nationwide by many physicians and other health care professionals. In fact, elevated toxic halogen levels have not been found to be solely associated with Michiganders. We have seen elevated toxic halides nationwide.

Gaby:
"High-dose iodine therapy is of great value in some circumstances. We should not forget, however, that this treatment was abandoned in the past, because it caused many deaths from heart failure, as well as a long list of other side effects. The doses used then were higher than those currently being advocated. However, it is premature to assert that more modest doses do not cause more modest side effects."

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effects."

Comment:
Where is the reference(s) to support the above statements? We are not aware that iodine, even in gram amounts, has been reported to be associated with fatal outcomes. The literature shows that iodine used in gram amounts to treat lung disorders was not associated with serious complications. 12 We have previously quoted 8-10 our predecessors extolling the widespread use of iodine in several clinical conditions. The past literature does not support Gaby's claim that deaths have been associated with the use of gram amounts of iodine.

Guy E. Abraham, MD and David Brownstein, MD
5821 W. Maple Road
Suite 192
W. Bloomfield, Michigan 48322

References
This is Alan Gaby’s reply to the April 2006 rebuttal.

Drs. Abraham and Brownstein argue that it is seaweed, not the iodine in it, that causes thyroid disorders. However, a main aspect of their iodine hypothesis is that Japanese people are healthy because they eat a lot of iodine, which in the Japanese diet comes mainly from seaweed. This seems like a contradiction.

Questioning whether Drs. Abraham and Brownstein have meticulously monitored their patients for adverse effects is completely different than suggesting that poor medical care was given, which I did not suggest. What I said was, "Before one could confidently conclude that high-dose iodine is safe for 99% of the population (as stated by Abraham and Brownstein), it seems that a systematic toxicity study would be necessary." I suggested that such a study should include serial testing of all patients to identify the appearance of thyroid antibodies during treatment with iodine, since iodine supplementation has been reported to increase the incidence of thyroiditis. Thyroid-antibody measurements may not be necessary as a component of routine medical care, but they would seem to be necessary before one could confidently claim that high-dose iodine supplementation does not increase the incidence of autoimmune thyroiditis. I asked in my rebuttal how many of the iodine-treated patients had had thyroid-antibody tests, but Drs. Abraham and Brownstein did not answer my question.

Concerning the report of deaths due to high-dose iodine, here is the pertinent reference:

In this review article, the authors state that in the 1920s and 1930s, when potassium iodide (KI) was widely used, many patients died of KI-induced side effects, particularly pulmonary edema and associated heart failure.

Alan R. Gaby, MD replies:

"Iodophobic bioterrorism?" Methinks the gentlemen doth protest too much.

If Dr. Brownstein has done before-and-after thyroid antibody tests on all his patients, then his data might resolve the question of whether short-term treatment with high-dose iodine increases the incidence of thyroiditis. I urge him to publish his results. His data would not appear, however, to answer the question of whether long-term iodine therapy increases the incidence of thyroiditis, particularly since Dr. Brownstein only started using high-dose iodine routinely about three years ago.

Aside from my comments above, I see no value in continuing this debate. My concerns about iodine toxicity were stated in my editorial and in the rebuttals that followed. Those who have an interest in resolving these issues are urged to read the original research cited by Abraham/Brownstein and by me, and to reach their own conclusions.

I cannot accept Abraham/Brownstein's analogy between iodine and the Myers cocktail, with respect to the need for toxicity studies. While I am an advocate of the Myers cocktail, I have never stated that it is entirely safe. Indeed, I have described adverse reactions and potential toxicities and have recommended that it be administered with caution. I use the Myers cocktail to treat chronic fatigue, fibromyalgia, heart failure, acute asthma, and several other conditions. I do not recommend that the entire human race receive Myers cocktails, as Abraham and Brownstein seem to be recommending for megadose iodine.