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Letter to the Editor:
A Rebuttal of Dr. Gaby's Editorial on Iodine
by Guy E. Abraham, MD and David Brownstein, MD

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 orthoiodosupplementation 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 orthoiodosupplementation 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 triodide I3- and increases the aqueous solubility of iodine in the form of a triodide 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.[3] 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.[3] In 1932, physician B.N. Cohn[6] 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[7] 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."

Does Gaby realize that the RDA for iodine was established very recently in 1980, confirmed in 1989,[8] and based on data supplied by endocrinologists with thyroid fixation ignoring the rest of the body? The goal of the RDA for iodine is the prevention of extreme stupidity (cretinism), iodine-deficiency induced goiter and hypothyroidism, not whole body sufficiency for iodine. In 1930, Thompson et al[9] 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.

Physician Henry A. Schroeder[10] 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,[3] one slice of bread contained the full RDA for iodine.[11] During this period, Oddie et al[12] 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[13] 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.[7] 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 high."[13]

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 Wolff[14] 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."

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 sites[18] and chloride increases its excretion in urine.[15] For detoxificaton 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."

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.[8] By 1977, the brines associated with deposits of natural gas in Japan accounted for 56% of the world iodine production.[16] 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.[18] 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,[19] 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.[20] From a publication by Phillippou, et al, published in 1992,[21] 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)

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

A new syndrome, medical iodophobia, was recently reported[3] 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 al[25] 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,[3] and there is 1400 times more bromide than iodide in seawater.[17] The presence of excess goitrogens in the diet would require greater amounts of ingested iodine to prevent the goitrogenic effect of these substances.[11,18]

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.[8] On a molor 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,[3] due to body retention of iodine. With this in mind, let us review some published data. Konno et al[22] 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[30] 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[23] 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[1] and this may be eaten in quantities as large as 10 g daily."[23] This daily intake would compute to 30mg of elemental iodine. However, on page 643 of the same article, Nagataki et al[23] misquoted their Reference #13, that is our Reference #26, when they stated: "…according to the statistics of the Ministry of Health and Welfare,[13] 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)

Yrs.	1950	1952	1954	1956	1958	1960	1962	1963
Calories	2,098	2,109	2,074	2,092	2,118	2,096	2,080	2,083
Proteins								
Total	68	70	69	69.1	70.1	69.7	70.4	70.6
Animal	17	23	22	22.6	23.8	24.7	27.3	27.7
Vegetable	51	47	47	46.5	46.4	45.0	43.2	42.9
Fat	18	20	21	21.8	23.7	24.7	28.3	29.2
Carbohydrate	418	412	403	405	406	399	386	382
Sugars	7.2	14.5	15.6	15.6	12.3	12.3	13.4	14.0
Fats & Oils	2.6	3.9	4.6	5.1	5.7	6.1	7.6	8.1
Beans	53.7	68.4	68.2	72.7	71.0	71.2	70.8	69.4
Milk	6.8	10.2	12.5	19.4	22.0	29.5	35.9	38.8
Milk products		0.4	0.6	2.1	2.6	3.4	5.9	6.3
*Sea weeds (dry weight)	3.0	4.1	4.8	5.0	5.0	4.7	4.5	4.6

Compiled from tables 6 and 8 of the official publication, *Nutrition in Japan*, 1964, Nutrition Section, Bureau of Public Health, Ministry of Health and Welfare, Tokyo, Japan, March 1965.

* 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 Mister 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 seaweeds involved. Since the surveys performed by this organization do not report the amount of elemental iodine and only tabulate the sum of all seaweeds consumed per capita per day for 2001, it is not possible at this time to calculate exactly the true daily iodine intake by mainland Japanese in 2001. If the concentrations of iodine in seaweeds during the year 2001 remain the same as in the 1960s, the average daily amount of iodine consumed by mainland Japanese in 2001 would be: 3 mg iodine/gm x 14.6 gm = 43.8 mg.

We must emphasize however, that the orthoiodosupplementation program is not based on consumption of iodine by the Japanese population, but on whole body iodine sufficiency assessed by the iodine/iodide loading test, which brings us to our next topic.

The validation of the iodine/iodide loading test

Gaby questions the validity of the iodine/iodide loading test and presents some valid arguments, "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."

Inorganic iodine is an ideal element for an oral loading test. Inorganic forms of iodine are quantitatively absorbed by the gastrointestinal tract and highly bioavailable. Less than 5% of ingested inorganic iodine/iodide are excreted in the feces and sweat,[31] with most of that amount in sweat. The data in reference #9 of Gaby's paper dealing with low bioavailability of ingested iodine in cows, which are ruminants, should not be extrapolated to humans. Since data obtained with the iodine/iodide loading test revealed that 90 to 100% of the ingested iodine/iodide is

recovered in the 24 hr. urine collection when sufficiency is achieved,[3,18] it is obvious that the ingested iodine/iodide in the tablets used for the loading test is highly bioavailable. Serum iodide is rapidly cleared by the kidneys with a daily clearance rate of 43.5 liters.[8] The renal clearance of iodide remains constant with intake from 0.001 mg to 2,000 mg iodide.[32] The gastrointestinal tract has the capacity to absorb quantitatively large amounts of iodine/iodide.[32]

Studies performed with a sustained release form of iodine, amiodarone, give further support for the validity of the iodine/iodide loading test. Amiodarone is a benzofuranic derivative containing 75 mg of iodine per 200 mg per tablet. It is widely used for the long-term treatment of cardiac arrhythmias.[33-35] Broekhuysen et al[36] using balance studies of amiodarone and the non-amiodarone inorganic iodine released from amiodarone, reported the following: In 2 subjects treated with 300 mg of amiodarone/day containing 112.5 mg iodine, the total amount of iodine measured in urine and feces was very low during the first 3 days, with a mean of 19% and 7% of the total iodine ingested, suggesting that as much as 93% of the iodine ingested was retained in the body, or 105 mg iodine per day was retained by the patient. After 25 to 27 days of therapy with 300 mg amiodarone/day, the mean % iodine excretion of combined urine plus feces in these 2 subjects increased 48% and 75%. Therefore, after approximately one month, the percent 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 only inorganic iodide was excreted in urine.

In 2 other subjects treated with 300 mg amiodarone/day for 7 weeks, balance studies revealed that at the end of the study, the total excreted iodine in urine and feces averaged 97.4% and 96.9%. Again, only the organic form amiodarone was found in feces and only the inorganic form in urine. Based on the balance studies, the amount of iodine retained by the body following 7 weeks on amiodarone at 300 mg/day containing 112.5 mg iodine, was estimated at 1.5 gm. 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 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.[37] 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.[8] 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 × 49 days = 5.5 gm. The patients retained 1.5 gm, that is 1.5 gm / 5.5 gm × 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 × 90 days = 4.5 gm. The patients retained 1.5 gm, that is 1.5 gm / 4.5 gm × 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,[3,18] 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.[3] 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.[8] 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.[8] 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.[8]

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.[18]

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.[3] 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.[3] Positive clinical results were seen in most of these patients after supplementation of orthoiodosupplementation within the range of 6.25-50mg 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.[16] 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.[3] Iodine intake has fallen over 50% in the U.S. over the last 30 years.[38] 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.[3,18]

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.[3]

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.[3,18] When bromide levels begin to decline, the above mentioned adverse effects begin to decline as well. Chloride increases renal clearance of bromide[15] 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.[15]

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.[3,16] 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 pseudoexperts. 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.[8]

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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.

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