

The Safe and Effective Implementation of Orthiodosupplementation In Medical Practice

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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 Phillippou, *et al.*:⁴ "We can, therefore, conclude that the effect of amiodarone, benziodarone, Na iopante, 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 orthiodosupplementation 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.)

Medicoiodophobes suffer from: A) a split personality which results in iodophobia within the orthiodosupplementation range previously used safely and successfully in medical practice and iodophilia 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 France⁵ 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

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Table 1

Various Forms of Iodine/Iodide Used in Clinical Medicine

- A) Inorganic
 - 1) Non-radioactive
 - a) Iodides (i.e., SSKI)
 - b) Tincture of iodine
 - c) Lugol solution
 - 2) Radioactive iodides for diagnostic and therapeutic purposes
- B) Organic
 - 1) Naturally occurring
 - a) Thyroid hormones
 - b) Thyroid iodolipids
 - 2) Man-made
 - a) Radiographic contrast media
 - b) Iodine-containing drugs (I.e., amiodarone)
 - c) Iodinated lipids for goiter prevention

because it is incorporated into some very important hormones of the thyroid gland.¹⁰⁻¹³ Starting out as a panacea for all human ills,¹⁴ iodine, as an essential element, eventually became associated exclusively with the thyroid gland.¹⁵ This **thyroid fixation** resulted in endocrinologists dictating the human needs for this nutrient. All human applications of iodine became eventually subservient 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.¹⁶⁻¹⁹ However, unfounded concern about the adverse effects of iodine at these levels on the thyroid gland,²⁰⁻²² and *vide infra* 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."¹⁹ "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."¹⁷ "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."¹⁹ "No evidence of iodine-induced allergic phenomena was detected during this study."¹⁷ "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."¹⁹ **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,¹⁹ 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.^{23,24} 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 al²⁵** 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."⁷ Reference 7 of their manuscript is a study published in **1949 by Stanley²⁶** one year after the Wolff-Chaikoff Effect was reported in rats.²⁷ The first paragraph of Stanley's manuscript stated the objective, "The interest of thyroidologists 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 thyroidologists could not have been aroused so quickly by the publication of Wolff and Chaikoff in *The Journal of Biological Chemistry*,²⁷ a journal involved in publishing research in the basic sciences, not clinical medicine. The thyroidologist with aroused inter-

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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, Wolff²⁸ 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*²⁹ 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,³⁰ 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 (orthoiodosupplementation) serves as a preventive measure against unexpected exposure to radioactive iodide/iodine.³⁰ 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 orthoiodosupplementation, amounted to 100 times the RDA.³⁰

In the 1980s, thanks to iodophobia, iodine was replaced with bromine in the bread-making process.³¹ Bromide is a goitrogen and interferes with iodide utilization by the thyroid gland,³²⁻³⁴ and possibly by the mammary gland also.³⁵ Iodine has an anticarcinogenic effect on the breast.³⁰ The last national nutritional survey showed a trend of decreasing iodine intake by the US population.^{30,31} 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.³⁰ 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.³⁰

Velicky, *et al*³³ 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 al*³⁶ observed that bromine enhances the biological activity of a tumor promoter. Sangster, *et al*³⁷ 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 al*³⁸ 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-

scribing to iodine-deficient female patients with hypothyroidism and simple goiter the hormone thyroxine (T₄), which increases the risk of breast cancer in those patients (discussed in Section III). In Graves' disease, the non-physiological use of goitrogens and radioiodide has replaced iodine/iodide resulting in hypothyroidism of these unfortunate patients. It seems that no matter what your thyroid problem is, you always end up getting T₄. In the discussion of published data on iodine-induced hypothyroidism and hyperthyroidism, a clear distinction will be made between inorganic versus organic forms, in order to demonstrate that adverse effects attributed to iodine in most publications were the result of ingestion and injection of organic forms of iodine-containing drugs. A review of some historical events combined with some physiological aspects of iodide metabolism by the thyroid gland will be discussed in order to demonstrate that inadequate iodine/iodide intake combined 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.

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Table 2

The Halides: Discovery in Chronological Order

Halide	Discovery		
	Year	Discoverer	Country
Chloride	1809 1810	Gay-Lussac H. Davy	France Great Britain
Iodide	1811	B. Courtois	France
Bromide	1826	A.J. Balard	France
Fluoride	1886	F. Moissan	France
Astatin	1940	Carson, McKenzie, Segre	US

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.

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*,³⁹ 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."³⁹

The history of iodine in medicine and pharmacy was reviewed by F.C. Kelly¹⁴ from its discovery in 1811 up to 1961. The review of the history of iodine by L.E. Braverman,¹⁵ 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*³⁹ 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. Kelly¹⁴ 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 1656.³⁹ 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 esthetical. 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 1820.⁴⁰ He later reported some side effects to iodine, including iodine-induced thyrotoxicosis.⁴¹ "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,⁴² 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 scrofuleuses." 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.³⁹ Orthoiodosupplementation³⁰ 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

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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. Boussingault⁴³ 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, Ohio⁴⁴ wrote, "Iodized salt is now being very much more extensively used by the public than other forms of iodine, such as sodium iodide, iodostarine, 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."¹⁴ 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.⁶ Even after iodine was recognized as an essential element in the 1920s, mainly due to Marine's studies,^{7,8} no attempt was made to assess the optimal daily requirement of this nutrient for sufficiency of the whole human body. Marine⁸ 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*⁴⁵ 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.¹⁴ The number of preparations containing iodine and iodine compounds increased rapidly afterward. To quote Kelly, "In the Great Exhibition at the Crystal Palace in Hyde Park in May 1851, iodine and iodine 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*,⁴⁶ 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 (orthoiodosupplementation). 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

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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. Cohn⁴⁷ 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.⁴⁴ 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 iodophobic 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.⁴⁸ 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."⁴⁹

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 Lar-

sen⁵⁰ 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.³⁰ What happened to inorganic, non-radioactive iodine/iodide? Don't they know that iodine deficiency in women predisposed them to breast cancer,³⁰ and that giving T₄ to iodine-deficient women increases further their risk for breast cancer?⁵¹

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

Since Graves' disease represents up to 90% of hyperthyroidism,⁵² 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 Basedow⁵³ and in 1854 by Stokes.⁵⁴ In 1863, Trousseau inadvertently used tincture of iodine successfully in a patient with exophthalmic goiter.⁵⁵ "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 iodine, I wrote iodine instead of digitalis, so that the patient took from 15 to 20 drops of tincture of iodine a day for a fortnight. (For the reader's information, "tincture of iodine" 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 iodine, but, after another fortnight, the pulse had again gone up to 150, so that I at once returned to the iodine." 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.⁵⁶

Thompson, *et al*,⁵⁷ in a 1930 publication, quoted several
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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 Clinic^{62,63} 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 iodine 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 al*⁵⁷ 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

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the mid 1940s, coincident with the appearance of iodophobic 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 continuously 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 exceptions (all unsatisfactory responses to iodine) the patients pursued their daily work throughout the period of observation, 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 iodophobic attitude, "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 hyperthyroid 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 hyperthyroidism, and with most of them the administration of iodine has been a part of the treatment. There is no danger 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 al*⁶⁵ from the Massachusetts General Hospital used 15 drops (90 mg) of Lugol daily for the treatment of exophthalmic goiter, with a 92% success rate, eliminating the need for surgery. "Of these 25 cases, 20 (80%) responded to iodine by a more or less extensive remission of the disease. Of these 20, 12 (48%) responded with the acute iodine remission resembling the effect produced by subtotal thyroidectomy. In the remaining eight (32%) the remission occurred, but was less extensive. In five unsuccessful cases (20%) two of the patients were pregnant, and one had cardiac decompensation. If these are omitted from the calculation, iodine 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 approach 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 nutritional 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 thyroid 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 between micronutrients in their overall effects on biological systems. We have incorporated a total nutritional program with orthoiodosupplementation, emphasizing magnesium instead of calcium (discussed further in Section 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 exophthalmia. After researching the medical literature, she refused treatment with radioiodides, goitrogens and surgery. She was placed on the nutritional program, including 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 μ U/ml. Total T₄ was 18 μ g/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 μ U/ml; Total T₄ dropped to 16 μ g/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 μ U/ml; Total T₄, Total T₃ and Free T₄ were all within the normal range at 8.0 μ 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 μ g/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. Astwood⁶⁷ 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 lower-

ing the recommended dosage.⁷⁰

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 al*⁷³ failed to realize that iodization of bakery products started several years before the second study by Astwood, *et al*⁷² published in 1966, which reported a very high success rate. In 1965, London, *et al*²⁵ reported an estimated iodine intake of 1 mg/day with 726 µg 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 remis-

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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**

I. Before Supplementation

TSH < 0.01 µU/ml
Total T₄ = 18 µg/dL
Total T₃ = 442 ng/dL
Free T₄ = 5 ng/dL

**II. After One Month on Complete Nutritional
Supplementation with 1,200 mg Magnesium/day**

TSH < 0.03 µU/ml
Total T₄ = 16 µg/dL
Total T₃ = 299 ng/dL
Free T₄ = 5.6 ng/dL

III. After One Month on Iodoral® — 1 Tablet/Day

TSH = 2.3 µU/ml
Total T₄ = 8.0 µg/dL
Total T₃ = 195 ng/dL
Free T₄ = 1.2 ng/dL

IV. After Three Months on Iodoral® — 1 Tablet/Day

TSH not measured
Total T₄ = 9.0 µg/dL
Total T₃ = 156 ng/dL
Free T₄ = 1.6 ng/dL

Table 4

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

Iodophobic Publications

1944 Inorganic iodide blocks synthesis of thyroid hormones *in vitro* using sheep thyroid.

Morton ME, Chaikoff IL, and Rosenfled S. "Inhibiting effect of inorganic iodide on the formation in vitro of thyroline and diiodotyrosine by surviving thyroid tissue." *J Biol Chem*, 1944; 154:381.

1948 Inorganic iodide blocks synthesis of thyroid hormones *in vivo*, (rats). Known as the Wolff-Chaikoff Effect.

Wolff J and Chaikoff IL. "Plasma inorganic iodide as a homeostatic regulator of thyroid function." *J Biol Chem*, 1948; 174:555-564.

1949 The Wolff Chaikoff Effect "extended to humans."

Stanley MM. "The direct estimation of the rate of thyroid hormone formation in man. The effect of the iodide ion on thyroid iodine utilization." *J Clin Endocr*, 1949; 9:941-954.

Publications testing and promotin goitrogens in the treatment of Graves' disease

1943 Introduction of goitrogens in the treatment of Graves' disease by EB Astwood.

Astwood EB. "Treatment of hyperthyroid with thiourea and thiouracil." *JAMA*, 1943; 122:78-81.

1944 Goitrogens block the conversion of radioactive inorganic iodide to thyroxine — *in vitro*.

Franklin AL, Chaikoff IL, and Lerner SR. "The influence of goitrogenic substances on the conversion in vitro of inorganic iodide to thyroxine and diiodotyrosine by thyroid tissue with radioactive iodine as indicator." *J Biol Chem*, 1944; 153:151-162.

1946 Goitrogens block the uptake of radioiodide by the thyroid gland *in vivo* (rats).

Wolff J, Chaikoff IL, *et al.* "The disturbance of iodine metabolism produced by thiocyanate: The mechanism of its goitrogenic action with radioactive iodine as indicator." *Endocrinology*, 1946; 39:140-148.

1947 Evaluation of several goitrogens in normal subjects using radioiodide as a marker.

Stanley MM and Astwood EB. "Determination of the relative activities of antithyroid compounds in man using radioactive iodine." *Endocrinology*, 1947; 41:66-84.

1949 Evaluation of goitrogens in the treatment of Graves' disease, tested in 2 groups of 34 and 30 patients, respectively.

Stanley MM and Astwood EB. "Notes and comments. 1-methyl-2-mercaptimidazole: An antithyroid compound highly active in man." *Endocrinology*, 1949; 44:588-589.

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 Association⁷⁵ 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:⁷⁶ "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 preconditioned to be in an iodophobic mode when he goes to Chapter 13, an ominous number, with "excess iodide" in the title and where inorganic iodine/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 iodine/iodide like leprosy. However, if he is inquisitive and searches the literature carefully, he may read the publication by Phillipou, *et al.*,⁴ 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-

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ziodarone, Na iopodate, 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 iodine/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 inor-

ganic 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 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 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-

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lar trend was reported. In 1966 and 1968, Weaver, *et al*^{81,82} 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*⁸³ 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,⁸⁴ 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.^{71,81} 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*,^{81,82} 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.⁸⁵⁻⁸⁸ These goitrogens induced thyroid hyperplasia and **iodide deficiency**. **Antioxidants either reduced or prevented the acute iodide-induced thyroiditis in chicks⁸⁹ and mice.⁹⁰** Bagchi, *et al*⁸⁹ and Many, *et al*⁹⁰ 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 peroxydase (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.⁸⁹** 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-

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ence of H_2O_2 and organic substrate reverts to its peroxydase function which is the primary function of haloperoxidases, causing oxidative damage to molecules nearest to the site of action. TPO and the substrate thyroglobulin (Tg). Oxidized TPO and Tg elicit an autoimmune 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 manifestations 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 tyrosine 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 inhibited by certain iodinated lipids⁹²⁻⁹⁵ and is enhanced by cytosolic free calcium Ca^{++} .⁸⁹ and vide infra

The equation for organification of iodide by TPO is displayed in Figure 1, together with the feedback system controlling the production of

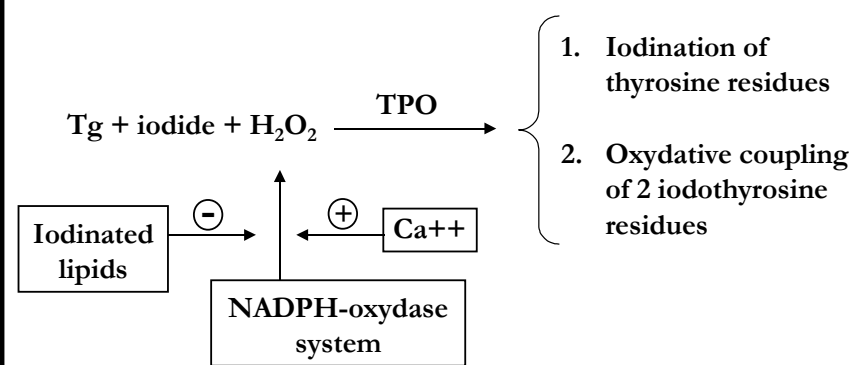
H_2O_2 . The logical deduction from this equation is that increased cytosolic free calcium will cause an excess of H_2O_2 . Increased levels of iodinated lipids, on the other hand, would limit the production of H_2O_2 . How much iodide is required for the production of iodinated lipids? In 1976, Rabinovitch, *et al*⁹⁶ reported their results regarding the effect of three levels of iodide supplementation 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 subjects? In 1994, Dugrillon, *et al*⁹⁷ reported for the first time the presence of 5-hydroxy-6-iodo- 8,11,14-eicosatrienoic delta lactone (delta iodolactone) in a human thyroid, following the ingestion of 15 mg iodide/day for 10 days in the host. It was the first time this biologically active iodolipid was isolated from human thyroid glands. The amount of iodide the host received was 100 times the RDA, but it is the amount of iodine/iodide we recommended for orthoiodosupple-

mentation.³⁰ Dugrillon, *et al*⁹⁷ stated, "These results demonstrate for the first time that delta-iodo-lactone is present in iodide-treated human thyroid."

Magnesium deficiency, which is prevalent in the US population, results in increased levels of cytosolic free calcium.⁹⁸ Intracellular free calcium levels above the normal range are cytotoxic causing calcification of mitochondria and cell death. The cell membrane possesses an ATP-dependant calcium pump that keeps intracellular levels of free ionized calcium within narrow limits. This calcium pump is magnesium-dependent for normal function. Magnesium deficiency results in a defective calcium pump and intracellular accumulation of ionized calcium. Inadequate iodine/iodide intake below or-

Figure 1

Iodination of Tg by TPO Using H_2O_2 and Iodide



The NADPH-oxidase system which generates H_2O_2 is modulated by free cytosolic calcium and iodinated lipids.

1. Iodination of tyrosine residues
2. Oxydative coupling of 2 iodothyrosine residues

we now know that TPO and the liver need selenium as well as zinc.

thoiodosupplementation results in decreased levels of delta-iodo-lactone. Combined magnesium and iodine/iodide deficiency based on the concept of orthoiodosupplementation 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, orthoiodosupplementation,³⁰ combined with magnesium intake between 800-1,200 mg/day, a daily amount this author recommended 21 years ago⁹⁸ for magnesium sufficiency, should reverse autoimmune thyroiditis. This nutritional approach is also effective in Graves' autoimmune thyroiditis as previously discussed.

VII. Implementation of Orthoiodosupplementation as Part of a Total Nutritional Program

The thyroid gland, like the rest of the body needs adequate amounts of all the macro- and micronutrients to function optimally. Ideally, besides orthoiodosupplementation and magnesium in adequate amounts, a complete nutritional program would be most appropriate since other essential nutrients are important for thyroid

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function and are involved in overall well-being. Since thyroid disorders occur predominantly in women,³⁰ 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.⁹⁹⁻¹⁰³ This nutritional program, combined with orthiodosupplementation, 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.⁷⁶ The use of radioiodide in the treatment of Graves' disease has been associated with leukemia and other forms of cancer.¹⁰⁴ Fever and arthralgia are reported in 1-5% of patients on goitrogens (antithyroid drugs).⁷⁶ 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.¹⁰⁵

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.¹⁰⁶ It catalyses the oxidation of iodide, bromide, and chloride in the presence of H₂O₂ to yield products that oxidize and halogenate microbial components.^{107,108} Chloride, due to its high concentration in leukocytes¹⁰⁹ is believed to be the main halogen used by myeloperoxydase. However, leukocytes have the ability to concentrate iodide 300-fold during phagocytosis¹¹⁰ and even deiodinate thyroid hormones to generate inorganic iodide when iodide supply is inadequate.¹¹¹ 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 µg/100 ml).¹¹⁰ 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.¹¹¹ Klebanoff and Green¹¹¹ 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,³⁰ the concentration of iodide used by Stole¹¹⁰ (i.e., 10 µg/100ml, roughly 10⁻⁶ Molar) is equivalent to the expected serum levels of inorganic iodide in patients on orthiodosupplementation and also in mainland Japanese who consume an average daily amount of 13.8 mg of elemental iodine,³⁰ the only population in the world on orthiodosupplementation and one of the healthiest based on cancer statistics.³⁰ From data available in published studies regarding the effect of increasing amounts of iodide on serum inorganic iodide levels at steady state conditions,^{112,113} we have calculated the expected serum levels of inorganic iodide at steady state conditions, when a patient is on orthiodosupplementation (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 2×10^{-6} M, which is the serum level reported by Wolff-Chaikoff,²⁷ 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 hypothyroxinemia in patients with chronic infections, such as chronic active hepatitis.¹¹⁴ Accelerated thyroid hormone degradation during bacterial infection has been reported in man¹¹⁵ and rhesus monkeys.^{116,117} Such findings would not be expected in mainland Japanese and in patients on orthiodosupplementation because the calculated serum levels of iodide in those subjects would approximate the concentration of iodide in Stole's incubation media.^{26,110} Wartofsky and Burman¹¹⁴ 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
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would obviously be the administration of thyroid hormones, it would be more physiological to implement orthiodosupplementation 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 orthiodosupplementation? Thyroid hormones are very expensive forms of the element iodine, which is what these patients really need to start with.

The concept of orthiodosupplementation³⁰ 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,¹¹⁸ 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, orthiodosupplementation was administered with Lugol solution 0.1-0.3 ml containing 12.5-37.5 mg of iodine/iodide.⁴⁶ 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.¹¹⁹ 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 \pm 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

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Figure 2

Effect of Iodine/Iodide on Serum Inorganic Iodide Level at Equilibrium

Population consuming this range of intake	Average daily intake (mg iodine/iodide per day)	Expected serum level of inorganic iodide at equilibrium
USA Range	0.01	10^{-8} M (0.0013 PPM)
"Endocrinologist's excess"	0.5	10^{-7} M (0.013 PPM)
Orthiodo-supplementation	12.5	2×10^{-6} M (0.25 PPM)
	37.5	6×10^{-6} M (0.75 PPM)
Loading test	50	8×10^{-6} M (1 PPM)
Range of daily intake as expectorant	1000.0	2×10^{-4} M (20 PPM)
	6000.0	1.2×10^{-3} M (120 PPM)

W-C Effect

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.¹²⁰ 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.³⁰ However, in a patient with atrophic autoimmune thyroiditis, 11 months of orthoiodosupple-

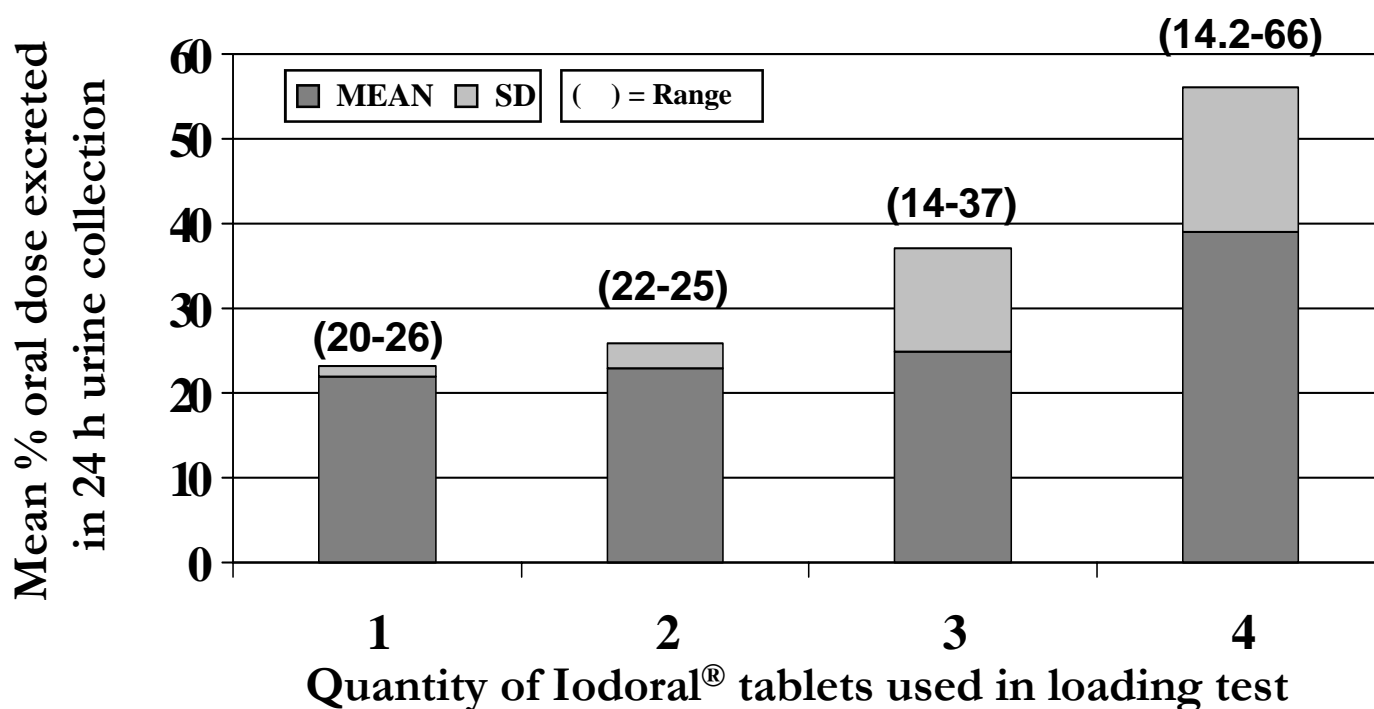
mentation was required before decreasing the amount of thyroid hormones. A 54-year-old female patient with atrophic autoimmune thyroiditis (thyroid volume by ultrasound = 2.8 ml) and elevated TPO Ab titers, on 150 µg of T₄ was placed on orthoiodosupplementation with 3-4 tablets/day. The presupplementation 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*¹²¹ 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-

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Figure 3

Mean Percent Excretion of Iodide in 24-hour Urine Collections with Increasing Amount of Iodine/Iodide Ingested in Six Normal Subjects on a Western Diet



deficiency disease. Lindberg, *et al*¹²² 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 thyroidologists 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 iodophobic 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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