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Orthoiodosupplementation in a Primary Care Practice

by Jorge D. Flechas, MD

This article will focus on my experience with the use of inorganic, non-radioactive iodine/iodide, hereafter referred to as iodine in a primary care practice. My medical practice is situated in the Appalachian Mountains close to Asheville, North Carolina. This area is considered to be a goiter belt. One of the major problems that we encounter in this location is a problem with hypothyroidism.

Back in 1997, hypothyroidism involved 11.7% of the US population.[1] By 1994, severe iodine deficiency also involved 11.7% of the population.[2] Both of these studies were done at separate times by separate groups showing the exact number of 11.7%. This reinforces what we were taught, that iodine deficiency goes hand in hand with the manifestation of hypothyroidism. On a weekly basis, I have at least one phone call from a health care practitioner questioning whether the intake of iodine causes hypothyroidism and goiter. I often have to go back over the basics of thyroid physiology with these practitioners and explain to them that iodine is essential for normal thyroid function and that it is the manmade organic forms of iodine that are toxic.[3]

My practice is family medicine with an integrative medicine twist. I have been using iodine supplementation in my practice over the last four years in amounts needed for whole body sufficiency (orthoiodosupplementation). Orthoiodosupplementation is the daily amount of iodine required for whole body sufficiency.[3,4,5] Whole body sufficiency for iodine is assessed by an iodine/iodide loading test.[3] Prior to implementing orthoiodosupplementation, I perform a complete history and physical examination.

During a physical examination, I always check the patient's thyroid. If a mass is picked up on physical, then another test that I order is an ultrasound of the thyroid. While doing the ultrasound to evaluate the mass, I will have my technician measure the thyroid volume. Each lobe will have its length, width, and height measured in centimeters. All three measurements are multiplied by each other, and this gives the volume in cubic centimeters. Due to the non-spherical shape of each lobe a correctional factor of 0.52 is used. The two lobe volumes are added together for the total thyroid size. A total volume of 18 cm^3 or more is considered a goiter.[6] A volume size of 5 cm^3 or less is suggestive of thyroid atrophy, another manifestation of iodine deficiency.

Any solid mass that is picked up on ultrasound and shows itself to be greater in size than one centimeter by one centimeter will require a radioactive I^{-123} uptake and scan. This test should be done previous to starting any patient on iodine if a nodule is suspected. A nodule that does not pick up radioactive iodide is considered to be a cold nodule and would suggest the presence of thyroid cancer. A needle biopsy of the cold nodule should be done by an ear, nose and throat specialist (ENT), general surgeon, or endocrinologist. If cancer is present, the thyroid gland should be surgically removed. Thyroid carcinoma is the most common malignancy of the endocrine system. Malignant tumors derived from the follicular epithelium are classified according to histological features.

The incidence of thyroid cancer is approximately nine per 100,000 in the population per year, and this usually increases with age plateau after about age 50. Age is also an important prognostic factor. Thyroid cancer at a young age (less than 20) or in older people (greater than 65) is usually associated with a worse prognosis. Thyroid cancer is twice as common in women as men, but the prognosis is worse in men. Additional important risk factors include a history of childhood head or neck irradiation, large nodule size greater than four centimeters, evidence for local tumor fixation or invasion into lymph nodes, and the presence of metastasis.[7] In my small practice of around 5,000 patients, I have found five thyroid cancers in one year. If multiple nodules of the thyroid gland are found at the time of ultrasound, then the diagnosis of multinodular thyroid goiter is considered even if the gland is normal in size.

I request serum T_4 (the main hormone produced by the thyroid), free T_3 (the biologically active thyroid hormone at the cellular level) and a thyroid stimulating hormone (TSH) level. The T_3 level inside the cell correlates very well with the free T_3 that is in the serum.[7] Following orthoiodosupplementation, serum T_4 and TSH levels usually go down while free T_3 stays steady.[6] I have seen TSH sometimes go up rather than down while T_4 and free T_3 did not change or elevated slightly. This does not mean that the patient was developing hypothyroidism but that the brain was stimulating the body to make more sodium iodide symporters (NIS).

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The NIS are channels in the cell membrane that transport atoms into a cell as compared to calcium, sodium, or chloride channels where the channel only allows one atom to go through. The NIS transports sodium iodide into cells and has been found in all cell lines tested so far. Thyroid stimulating hormone, prolactin, and oxytocin have been found to stimulate the making of NIS.[8] While taking iodide, one may see an elevated TSH, but we have to recognize that this is not a bad thing. TSH has many actions outside the thyroid that have been discovered.[7] While taking iodine, the vast majority of patients lose fat and gain muscle weight.[4,5] Very rarely does weight gain occur. Often a check of the patient's T_4, free T_3, and TSH shows the T_4 to go down, free T_3 going down, and TSH going up. Iodide is an essential nutrient that is absorbed by all cell lines. Its highest concentration is seen in the thyroid.

The nutritional status of the patient will determine the response to orthoiodosupplementation.[3] It is crucial that the thyroid gland has plenty of antioxidants, as well as other nutrients, in its cells. We have found that giving a multivitamin for women with PMS (Optivite®) improves the response to orthoiodosupplementation. One of my patients is a classic example of the above scenario. She is a CNA and is 5'1". At the time she started taking iodine, she experienced an increase in appetite. Within a short period of time (6-8 weeks), she gained about 15 pounds. She then was started on this supplementation. Within six weeks the patient's appetite decreased, and she lost 15 pounds.

Breast tissue has an affinity for iodine.[4,9,10,11,12,13,14] Iodine deficiency causes fibrocystic breast disease (FBD) with nodules, cyst enlargement, pain, and scar tissue.[13,14] FBD can be characterized by a lumpy, painful breast, generally in women of reproductive age. Initially, this syndrome occurs in the premenstrual phase of a cycle or involves the whole cycle. These symptoms can also occur in menopausal women on estrogen therapy. In 1928, an autopsy series reported a 3% incidence of FBD, whereas in 1973, an autopsy report quoted an 89% incidence.[7] A review by the American Academy of Pathology gives a minimum incidence for FBD of 50% but suggests that 80% of North American women are afflicted with the syndrome during their reproductive lifetime.[15]

Ghent, *et al*, in 1993, presented data showing that iodine works great to reduce FBD.[14] He was able to develop a protocol and a scoring system that helps doctors assess how severe a woman's FBD is. I would recommend that this scoring system be utilized by physicians in their own medical practice. A precise method of recording the patient's data will help both physicians and patients see the improvement that occurs following orthoiodosupplementation. This simple method numbers the quadrants of each breast one to four. The pathological changes that can occur in FBD are noted as micronodularity, tenderness, fibrous tissue plaques, macrocysts, and turgidity. The presence or the absence of changes is recorded. For example, if the micronodularity of macrocysts disease was present in the upper half of the breasts, the numerical score would be one for micronodularity and two for the two breast quadrants scoring a total of three. If all five changes occurred in all quadrants in one breast, the score would be 4 (all four breast quadrants) x5 (all five changes) equals 20 and for both breasts would be 40.

Patients are also encouraged to evaluate their own symptomology as expressed by a score of zero equals symptoms worse, one equals symptoms unchanged, two equals less pain only premenstrual discomfort, three equals no pain unable to predict menstruation. The subjective scoring system was employed and graded as follows. Zero equals no palpable abnormalities normal, one equals is score of less than 7.2 and a score greater than 7 but less than the pretreatment score and three equals a score greater than the pretreatment score (See Table 1).

Over the last four years in my practice, I have worked with some 200 women who have FDB. On average, patients come to my office with a mean Ghent score of 15.7 and an average age of 41.4 years. On 12.5 mg of iodine, the score after six months will drop from a mean score of 15 down to about 12.8. On 25 mg, the score will drop down to a mean score of 10.2. On 37.5 mg the score was 8.6. When we prescribe 50 mg of Iodoral® (4 tablets) for 3-6 months, the average patient will have a score of 7.6 with a p-value less than 0.001 compared to baseline scores. After a full year at 50 mg iodine per day (4 tablets of Iodoral®), the patients' mean score dropped to 3.8. We saw many patients with a score of zero, meaning no evidence of FBD. We often see patients' breast pain disappear in 1-30 days at a dose of 50 mg. At lower doses, the pain persisted for a much longer time. The other findings of micronodularity, tenderness, fibrous tissue plaques, macrocysts, and turgidity will take almost a full year to completely go away. Ghent felt that a score of seven or below was normal. We did not see any of the patients reach the score of zero, meaning the absence of all of the pathological symptoms and physical findings of fibrocystic breast disease while taking 12.5-37.5 mg/day.

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Table 1

Ghent's Scoring System for Fibrocystic Disease of the Breast

Right Breast	Quadrants				Score	Left Breast	Quadrants				Score
	1	2	3	4			1	2	3	4	
Micronodularity						Micronodularity					
Tenderness						Tenderness					
Fibrous Tissue (Plaques)						Fibrous Tissue (Plaques)					
Macrocysts						Macrocysts					
Turgidity						Turgidity					
Total Score				=		Total Score				=	
Sum of both Total Scores = _____											

Once FBD is gone, a patient may opt to drop iodine intake to 12.5-25 mg/day. There is a chance that the cysts will return. Optimum amount for most patients with FBD is 50 mg (4 tablets) per day continued indefinitely. Monitoring the patient's serum TSH, T_4, and free T_3 is done every 3-6 months. We did not see any major changes in serum T_4, TSH, and free T_3 in these patients.

It was while treating a 320-pound woman with insulin dependent diabetes that we learned a valuable lesson regarding the role of iodine in hormone receptor function. This woman had come in via the emergency room with a very high random blood sugar of 1,380 mg/dl. She was then started on insulin during her hospitalization and was instructed on the use of a home glucometer. She was to use her glucometer two times per day.

Two weeks later on her return visit for a checkup of her insulin dependent diabetes, she was informed that during her hospital physical examination she was noted to have FBD. It was recommended that she start taking 50 mg of iodine (4 tablets) at that time. One week later she called us requesting to lower the level of insulin due to having problems with hypoglycemia. She was told to continue to drop her insulin levels as long as she was experiencing hypoglycemia and to monitor her blood sugars carefully with her glucometer. Four weeks later during an office visit, her glucometer was downloaded to my office computer, which showed her to have an average random blood sugar of 98. I praised the patient for her diligent efforts to control her diet and her good work at keeping her sugar level under control with the insulin. She then informed me that she had come off her insulin three weeks earlier and had not been taking any medications to lower her blood sugar. When asked what she felt the big change was, she said that she felt that her diabetes was under better control due to the use of iodine. Two years later and 70 pounds lighter, this patient continues to have excellent glucose control on iodine 50 mg per day.

We have since done a study of 12 diabetics, and in six cases we were able to wean all of these patients off of medications for their diabetes and were able to maintain a hemoglobin A1C of less than 5.8 with the average random blood sugar of less than 100. To date, these patients continue to have excellent control of their Type 2 diabetes. The range of daily iodine intake was from 50-100 mg/day. All diabetic patients were able to lower the total amount of medications necessary to control their diabetes. Two of the 12 patients were controlled with the use of iodine plus one medication. Two patients have control of diabetes with iodine plus two medications. One patient had control of her diabetes with three medications plus 50 mg iodine. The one insulin dependent diabetic was able to reduce the intake of Lantus insulin from 98 units to 44 units per day within a period of a few weeks.

In the Type 1 diabetics that we have been following, we have noted that if C-peptide is measurable, this would

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

When patients take 12.5-50.0 mg/day of iodine, it seems that the body becomes increasingly more responsive to thyroid hormones.[3,4,5] T_3 and steroid hormones show the same family of receptors as hydrophobic small molecules.[16] Clur[17] has postulated that iodization of tyrosine residues in the hydrophobic portion of these receptors normalize their response to the corresponding hormone. Optimal intake of iodine in amounts two orders of magnitude greater than iodine levels needed for goiter control may be required for iodization of these receptors.[4] Insulin resistance is on the increase. The insulin receptor tyrosine kinase plays a major role in signal transduction distal to the receptor as the primary event leads to subsequent phosphorylation of cytoplasmic proteins, called insulin receptors substrate proteins (IRS). The IRS proteins are cytoplasmic proteins, with multiple tyrosine phosphorylation sites, and phosphorylation of IRS proteins has been implicated as the first post receptor step in insulin signal transmission. The IRS proteins have been referred to as the metabolic switch of the cell.[18]

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

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

Ideally, all patients should have an iodine loading test prior to orthoiodosupplementation. This test is administered by giving 50 mg of iodine after discard of the first morning void. All urine is collected for the next

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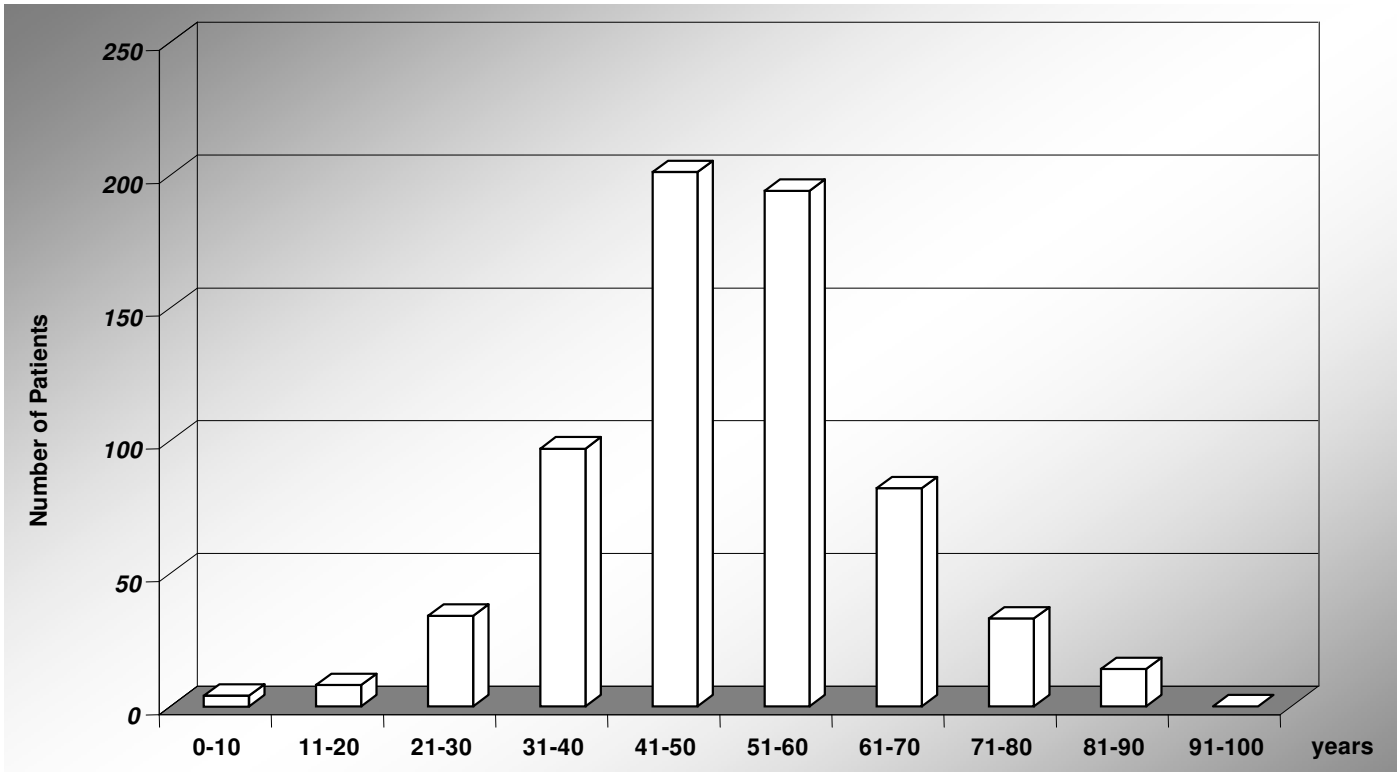
Figure 1

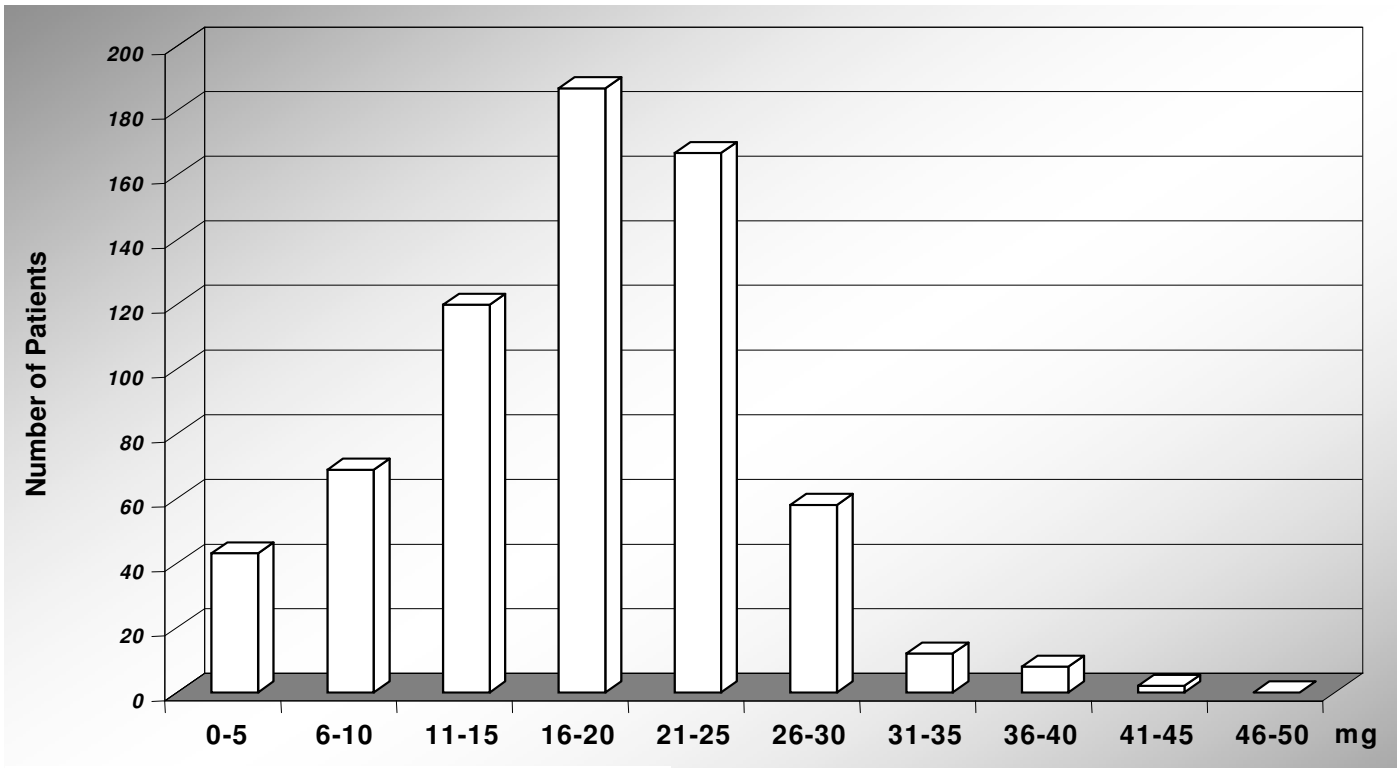
Age Distribution of 667 Patients* Who Underwent the Iodine Loading Test with 4 Tablets of Iodoral® (50 mg)



*78 were male, and 589 were female.

Figure 2

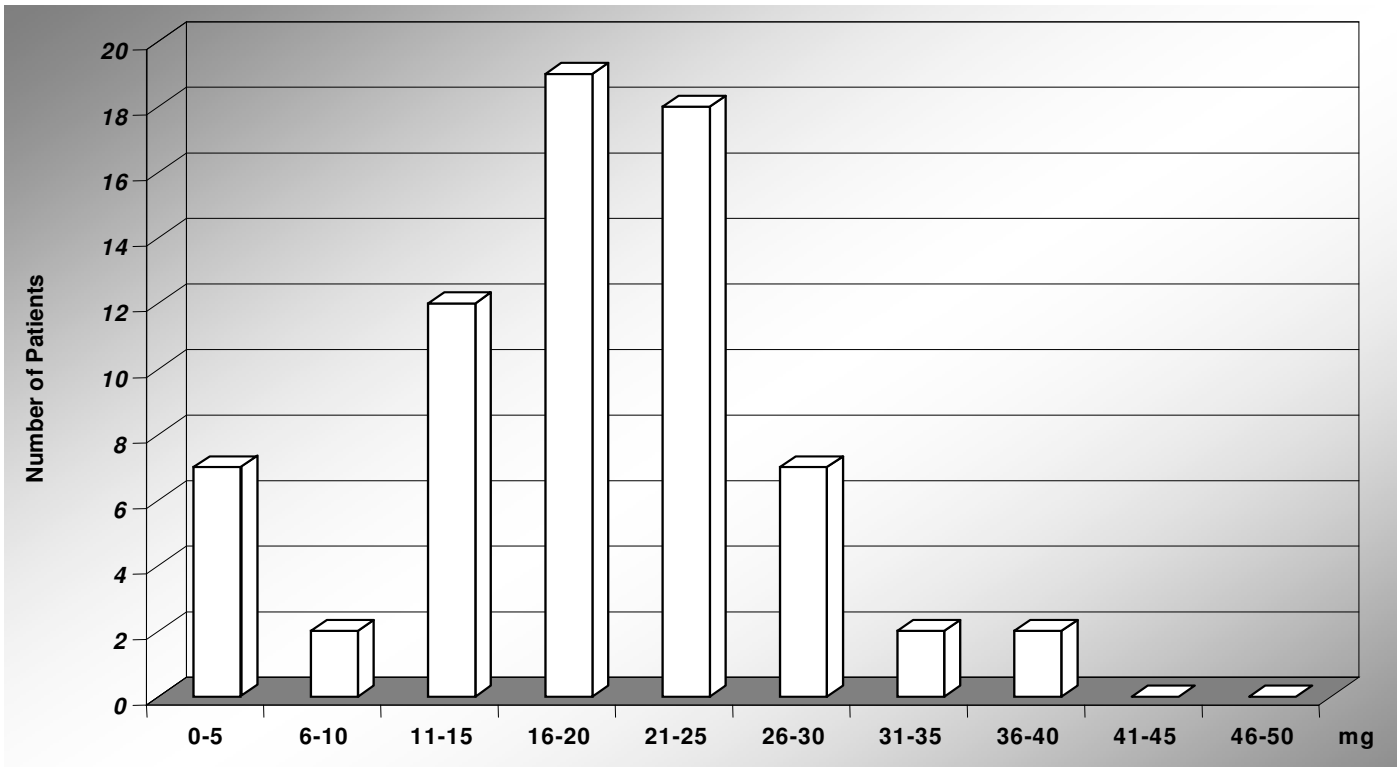
Iodide Measured* in 24-hour Urine Collection in 667 Patients Following the Loading Test with 4 Tablets of Iodoral® (50 mg)



*Mean: 17.9; Standard Deviation: 7.2

Figure 3

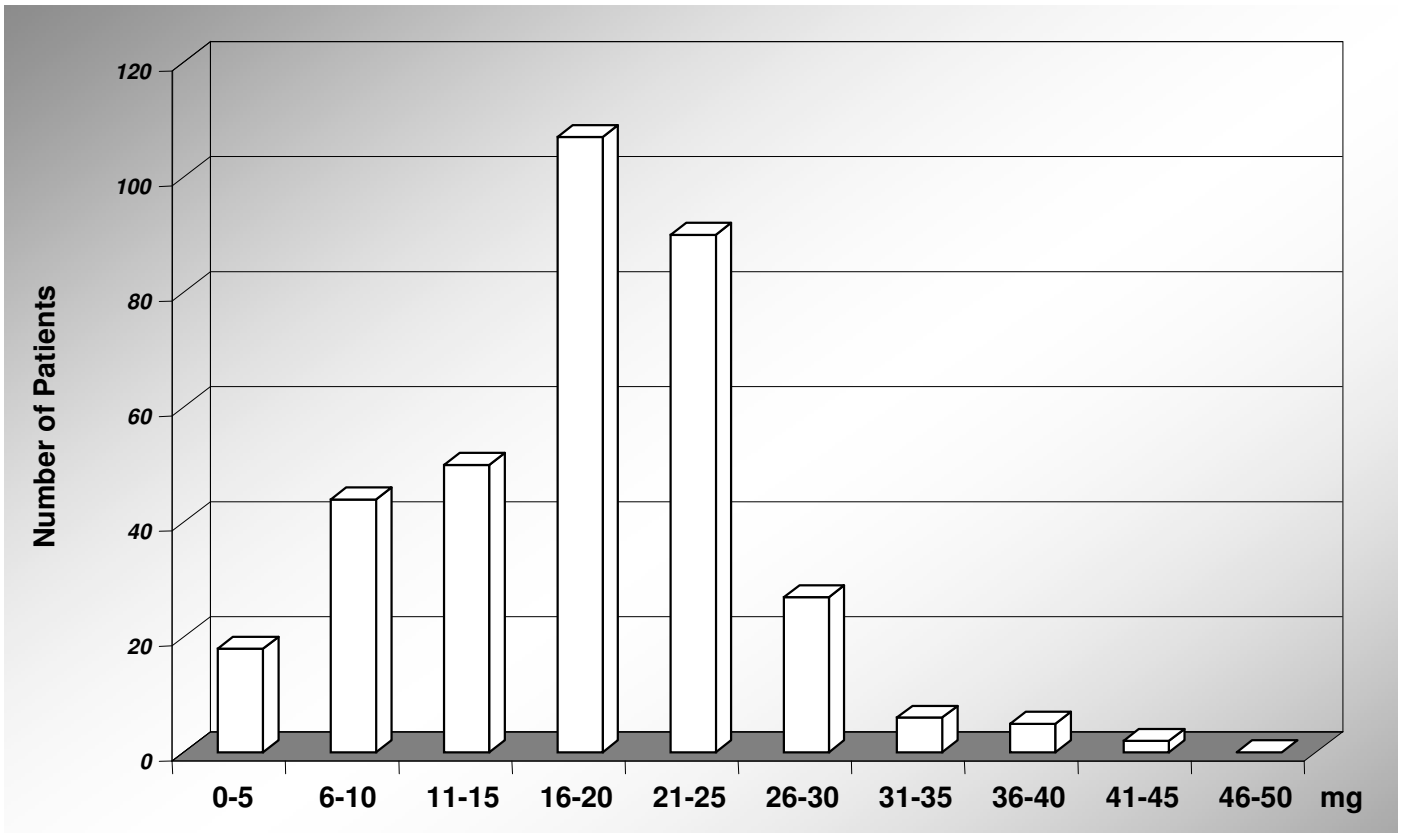
Iodide Measured* in 24-hour Urine Collection in 69 Female Patients Age 34 Years or Less Following the Loading Test with 4 Tablets of Iodoral® (50 mg)



*Mean: 18.9; Standard Deviation: 8.0

Figure 4

Iodide Measured* in 24-hour Urine Collection in 349 Female Patients Age 36-55 Years Following the Loading Test with 4 Tablets of Iodoral® (50 mg)



*Mean: 18.9; Standard Deviation: 7.2

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

We have received many comments over the last two years. Following orthoiodosupplementation, patients have described vivid dreams, dissipated depression, no more cold extremities, more energy, and less fatigue. Patients have noticed an overall feeling of well-being, and some have lost weight. One patient, after taking four pills of iodine, lost eight pounds of fluid weight in 24 hours. We have had patients note better bowel function. Patients who have been constipated for over 10 years now note daily bowel movements. We have also had patients describe relief from leg cramps at night. In less than 1% of all the patients treated with I, we have seen an allergic reaction. More often than not, the allergic reaction is hives. After treating over 1,000 patients with iodine, I have at no time seen the Wolff-Chaikoff effect.

Iodine induces apoptosis and inhibits cells from forming cancer. The absence of iodine in the thyroid causes goiter.[3,4] Goiter is associated with breast cancer, stomach cancer, esophageal cancer, ovarian cancer, and endometrial cancer.[22,23,24] It is felt by many researchers that the absence of iodine is a promoter of cancer. I feel that those patients with the lowest excretion rates and the

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highest absorption of iodine on the iodine loading test are the ones with the highest risk for development of cancer. From literally hundreds of phone interviews with patients over the last two years, the levels of iodine excretion that seem to raise the highest alarm are those in which the excretion is somewhere around 10 mg or less per 24 hours in patients age 35 and up. My observations at this point show that there is a definite increase in the incidence of breast cancer, stomach cancer, ovarian cancer, or thyroid cancer. If a patient has the iodine loading test and has an iodine excretion of 10 mg or less in a 24-hour period, I initiate a cancer workup. In 1976, a *JAMA* article showed that 6% of the female population was at risk for breast cancer.[25] Women who received thyroid supplementation doubled their risk of breast cancer to 12%. The age groups we used to separate the patients in Figures 1-6 were based on this article. As women get older, the risk of breast cancer increases. In Figures 2-6 the iodine/iodide loading test shows that the older the women are, the lower the rate of iodine excretion.

About the Author

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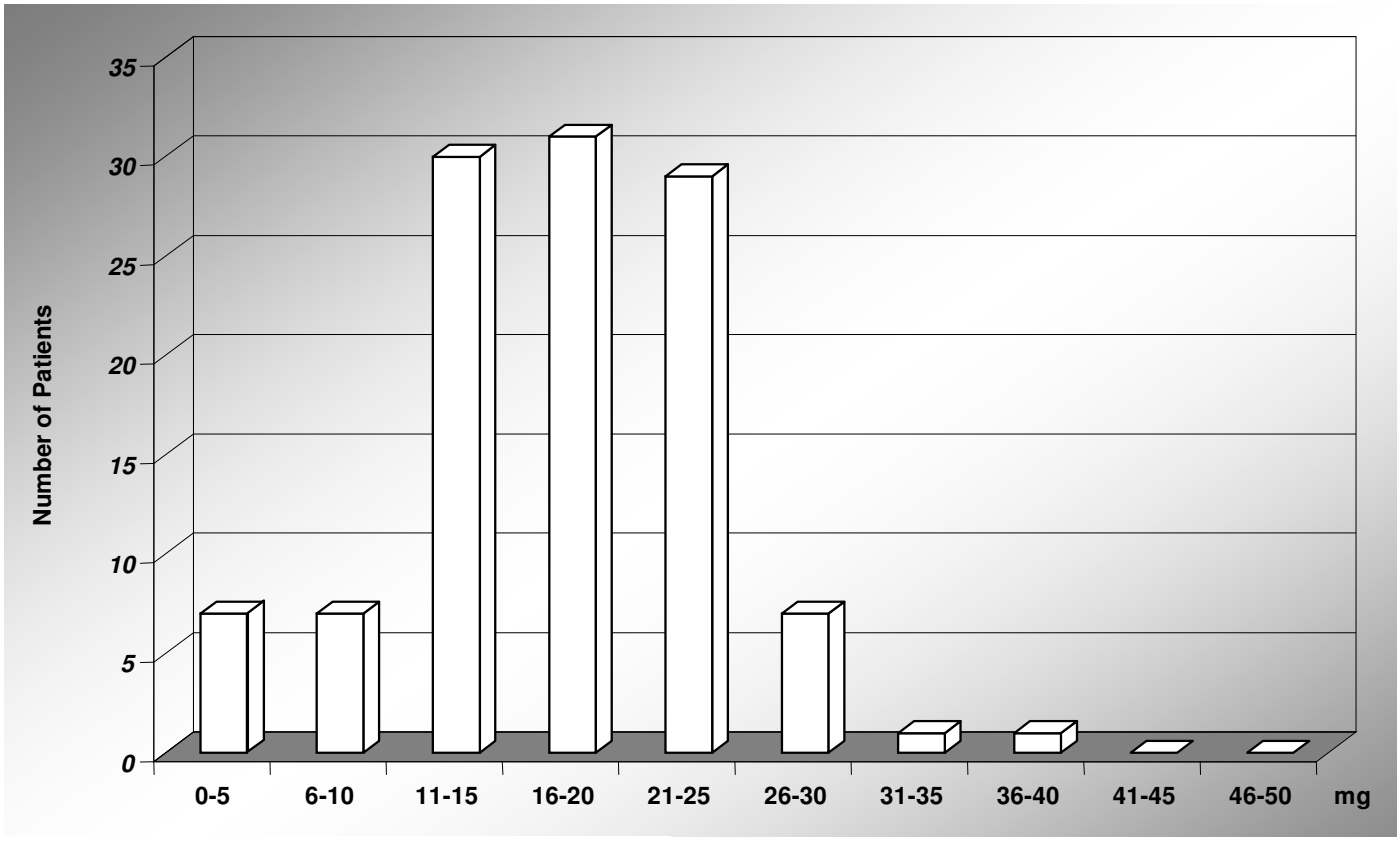
Figure 5

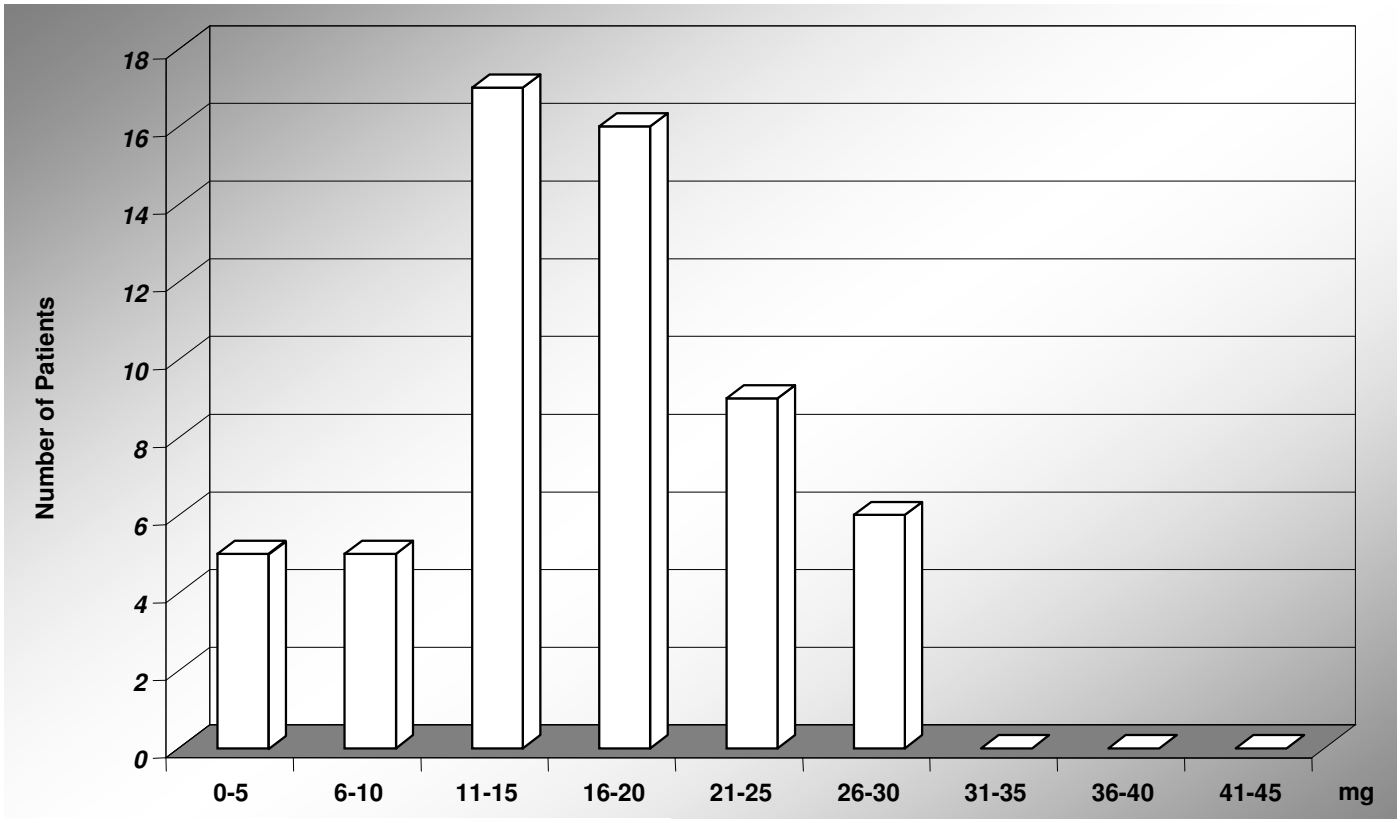
Iodide Measured* in 24-hour Urine Collection in 113 Female Patients Age 56-68 Years Following the Loading Test with 4 Tablets of Iodoral® (50 mg)



*Mean: 17.2; Standard Deviation: 6.6

Figure 5

Iodide Measured* in 24-hour Urine Collection in 58 Female Patients Age 66-100 Years Following the Loading Test with 4 Tablets of Iodoral® (50 mg)



*Mean: 16.5; Standard Deviation: 6.5

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