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# Review: An Examination of <sup>131</sup>I Dosages for Treatment of Graves' Disease

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## Summary

In this review, we examine <sup>131</sup>I treatment options available to patients. Research has shown that Graves' Disease patients who undergo <sup>131</sup>I treatment are cured of hyperthyroidism but have the chance to develop hypothyroidism, depending on the dosage used (4-5). The two different treatment options are high dose (8-14.6 mCi) treatment, and low dose (2 mCi) <sup>131</sup>I treatment. Data from previous studies were collected from patients who had been diagnosed with Graves' Disease and treated with <sup>131</sup>I. The data shows that low dose treatment results in a higher likelihood of euthyroidism. Based on the data, low dose <sup>131</sup>I treatment is a better option for patients that do not have heart related complications due to Graves' Disease.

## Introduction

### History of Graves' Disease

Graves' Disease is an autoimmune disease in which the body produces antibodies that stimulate the thyroid, causing it to produce excess amounts of triiodothyronine (T3) and thyroxine (T4) (1). The disease was recognized by Dr. Robert J. Graves in the 1830s, and is the most common cause of hyperthyroidism in the United States today (1). Research has also found that the disease runs in families and appears to be genetic, although Grave's Disease does occur in patients with no family history. (2). Some studies have found a connection between human leukocyte antigen and the onset of Graves' Disease; however, the complete cause remains unknown (1).

### Typical Patient Profile

Graves' Disease most commonly affects Caucasian women, aged 45-65 (1). After the disease appears, symptoms include anxiety, difficulty sleeping, fatigue, frequent bowel movements, weight loss, and heat sensitivity (1-2). Visual symptoms include goiter (enlarged thyroid gland) and the thickening and reddening of the skin (1-2). Graves' Disease patients also exhibit a phenomenon called Graves' ophthalmopathy, which is manifested as bulging of the eyes (1-2). This is caused by an immune response in which the body attacks eye muscles, causing the tissues to swell (3).

### Normal Physiology of Hypothalamic-Pituitary-Thyroid Axis Compared to Graves' Disease Physiology

The hypothalamic-pituitary-thyroid axis involves the release of four main hormones: thyroid releasing hormone (TRH), thyroid stimulating hormone (TSH), T3 and T4 (3). Normally, the hypothalamus releases TRH, which in turn stimulates the pituitary to release TSH (3). TSH then binds to receptors on the thyroid causing the gland to release T3 and T4 (3). An important component to T3 and T4 is iodine; the thyroid is the only organ in the body that absorbs this element (3). In Graves' Disease, the body produces antibodies that bind to the TSH receptors on the thyroid gland. The binding of these antibodies mimics the binding of TSH, thus causing the release of T3 and T4 (3). Excess amounts of free T3 and T4 are what cause hyperthyroidism (3). T3 and T4 also regulate body metabolism, which is what explains certain symptoms, such as weight loss, increased sensitivity to heat, and anxiety (3).

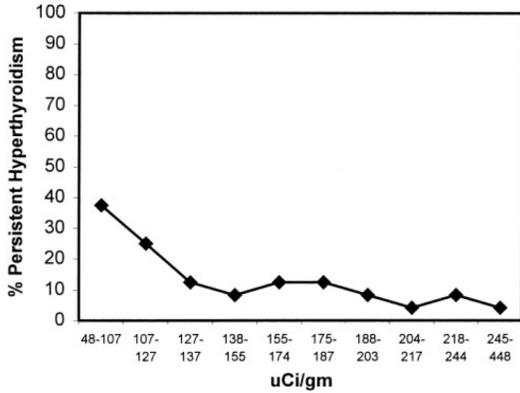
### Treatment Options For Graves' Disease Patients

Several options are available to treat Graves' Disease. The most common and non-invasive treatment involves oral antithyroid (ATD) drugs, such as Tapazole (1). These drugs lower the amount of hormone produced by the thyroid gland (1). Beta-blockers are also given to the patient to treat symptoms, such as increased heart rate (1-2). Beta-blockers function by blocking the effects of epinephrine and norepinephrine on  $\beta$ -adrenergic receptors, decreasing heart rate (3). A second treatment option is surgery to remove the thyroid gland (1). Removal of the thyroid removes the source of T3 and T4, and thus relieves symptoms (2). However, this treatment can also lead to hypothyroidism because the thyroid is no longer producing any T3 or T4 (2). Partial thyroidectomy is another option, as it removes only part of the thyroid and decreases the likelihood of hypothyroidism (2). A third and more recent treatment of the disease involves use of radioactive iodine (1-2). When the thyroid absorbs radioactive iodine, the radiation kills off thyroid cells, shrinking the number of cells that release T3 and T4 (1). Typically, Iodine 131 (<sup>131</sup>I) in millicurie (mCi) amounts is used in this procedure (4). There is some criticism of this method, as excess <sup>131</sup>I can destroy too much thyroid tissue causing a shift into hypothyroidism (1). We have researched treatment options, and hypothesize that low dose <sup>131</sup>I treatment for people with Graves' Disease is the most effective way to return normal thyroid function, or euthyroidism.

### Two Schools of Thought Involving Radioiodine Treatment

There are currently two different approaches to treating Graves' disease involving the use of <sup>131</sup>I. The first approach involves a large dosage of the radioactive iodine (8-14.6 mCi), which quickly destroys almost all of the thyroid tissue (4). An advantage to high dose <sup>131</sup>I treatment is that the subjects quickly leave a hyperthyroid state (4). Figure 1 illustrates the success rate of high dose <sup>131</sup>I treatment in curing hyperthyroidism. The radiation kills a very large portion of the thyroid, leaving the treated patient without the ability to maintain a euthyroid state. One drawback to

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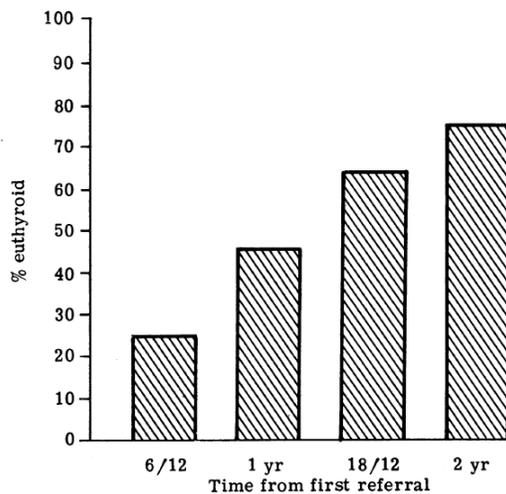


**Figure 1.** Percent of subjects that remain hyperthyroid after various dosages of Iodine-131 (Alexander and Larsen, 2002).

this method is that patients who undergo high dosage radioiodine treatment almost always end up in a hypothyroid state afterwards (4). One study found that 83% of 225 patients became hypothyroid after the treatment (4). The second <sup>131</sup>I method used to treat Graves' disease is low dose therapy. This method involves lower dosages of radioiodine (2 mCi) to achieve an eventual euthyroid state (5). The lower dose of <sup>131</sup>I destroyed the thyroid at a much slower rate than high dosages, resulting in a period of time where the patient was euthyroid. Figure 2 indicates that as time went on, more patients became euthyroid and, after 2 years 75% were euthyroid. However, in one study that followed subjects treated with low dose <sup>131</sup>I treatment, almost all the subjects became hypothyroid after a number of years (5). This study also found that the yearly incidence of hypothyroidism was 4-6% per year (5). It is likely that the <sup>131</sup>I remains in the thyroid for many years after treatment, continually destroying thyroid tissue and thus potentially resulting in hypothyroidism.

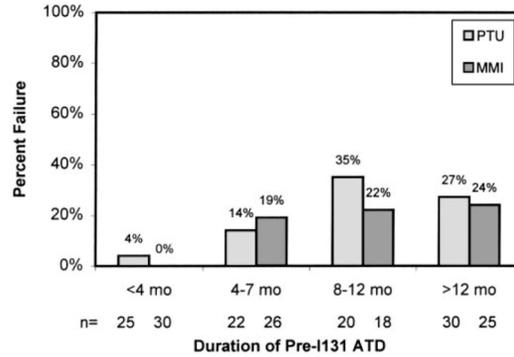
**Effect of ATD on Radioiodine Treatment**

The effect of ATDs on radioiodine treatment is an important component in insuring successful outcome. Figure 3 indicates that patients who took ATDs for more than 4 months before <sup>131</sup>I treatment had an increased treatment failure rate. This failure rate is



**Figure 2.** Percent of patients and time it took for them to become euthyroid after low dose therapy (Hoskin et al., 1985).

thought to be due to the radioresistance caused by ATDs (6). Some ATDs, such as Propylthiouracil (PTU), function by inhibiting the enzyme thyroperoxidase (7). When inhibited, the enzyme cannot add iodine to thyroglobulin, the precursor of T4 (7). When given before <sup>131</sup>I treatment drugs, including PTU, increase failure rate because they block the radioactive iodine from becoming part of the hormone and thus prevent the radiation from destroying tissue (7).



**Figure 3.** Failure rate of High Dose Iodine-131 treatment on patients who previously took ATD drugs for different lengths of time (Cooper, 1994).

**The Best Treatment Options**

Our findings indicate that, in the majority of patients with hyperthyroidism caused by Graves' Disease, the most beneficial treatment is a multiple low dose <sup>131</sup>I program. After undergoing high dose treatment, onset of hypothyroidism is virtually assured with almost no euthyroid period (4). After hypothyroidism occurs, the patient must be on thyroid hormone replacement therapy for the rest of their life (5). Multiple low doses are less likely to cause hypothyroidism than the higher doses, and patients who undergo low dose <sup>131</sup>I treatment are more likely to experience a euthyroid period (4-5). The length of this period varies, but we believe that because there is only a chance for patients to shift into a hypothyroid state after low dose treatment, this is the better option. Despite this, there are some advantages to high dosages. The rapid shift from hyperthyroidism to hypothyroidism is beneficial if the patient has cardiac complications because it removes the strain on the heart faster than low dose treatment (4). Patients who undergo <sup>131</sup>I treatment should also not take ATDs before treatment, as they cause a higher failure rate due to decreased iodine uptake (4).

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**References**

1. Yeung, Sai-Ching Jim (2005, July 28). eMedicine. Retrieved April 14, 2007, from Graves Disease Web site: <http://www.emedicine.com/med/topic929.htm>

2. (2005, December 20). Hyperthyroidism. Retrieved April 14, 2007, from Webmd Web site: <http://www.webmd.com/a-to-z-guides/Hyperthyroidism-Topic-Overview>
3. How Your Thyroid Works: A Delicate Feedback Mechanism. Retrieved April 14, 2007, from EndocrineWeb.com Web site: <http://www.endocrineweb.com/thyfunction.html>
4. Alexander, E. K., & Larsen, P. R., (2002). High Dose <sup>131</sup>I Therapy for the Treatment of Hyperthyroidism Caused by Graves' Disease. *The Journal of Clinical Endocrinology and Metabolism*. 87, 1073-1077.
5. Hoskin, P. J., McCready, V. R., Harmer, C. L., Spathis, G. S., & Cosgrove, D. O. (1985). Low-dose radioiodine given six-monthly in Graves' Disease. *Journal of the Royal Society of Medicine*. 78, 893-898.
6. Cooper, D.S. (1994). Antithyroid Drugs and Radioiodine Therapy: A Grain of (Iodized) Salt. *Annals of Internal Medicine*. 121, 612-614.
7. (2001, February 24). Propylthiouracil. Retrieved April 14, 2007, from MedicineNet.com Web site: <http://www.medicinenet.com/propylthiouracil/article.htm>