

# CLINICAL THYROIDOLOGY FOR PATIENTS



AMERICAN  
THYROID  
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Clinical Thyroidology for Patients

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# CLINICAL THYROIDOLOGY FOR PATIENTS

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## EDITOR'S COMMENTS

Welcome to the one year anniversary of the current format of *Clinical Thyroidology for Patients*! We are celebrating with a double issue. In the last 12 months, we have brought to you summaries of the most important research articles published in the field of thyroidology. There have been 26 articles on thyroid cancer, 7 on hyperthyroidism, 7 on nodules and goiter, 6 on TSH and hypothyroidism, 5 on thyroid and pregnancy, 3 on thyroid and the heart and 1 on autoimmune thyroid disease. These articles were published in *Clinical Thyroidology*, a publication of the American Thyroid Association for physicians. This means that you, the patients, are getting the latest information on thyroid research and treatment at the same time as your physicians. Within each article summary there are links to the relevant ATA Educational Brochures on our website.

We have also brought you summaries of the annual meetings of the patient advocacy groups *ThyCa: Thyroid Cancer Survivors Association*, *Graves' Disease Foundation* and the *Light of Life Foundation*. Along with the *American Thyroid Association*, these outstanding patient advocacy groups also make up **ATA Alliance for Thyroid Patient Education**. The **Calendar of Events** brings you up-to-the-minute notice of local and national meetings and educational forums for thyroid patients sponsored by the Alliance groups.

### In this issue, studies ask the following questions:

- Is there an association between thyroid disease, heart disease and death?
- Does recombinant TSH have a role in the treatment of nodular goiters?
- Is recombinant TSH effective in treating metastatic thyroid cancer?
- Is recombinant TSH effective in thyroid remnant ablation with low dose radioactive iodine?
- Does spread of thyroid cancer to the lymph nodes predict cancer recurrence?
- What is the role of PET scans in the management of thyroid cancer?
- Can Vitamin C decrease exposure of salivary glands to I-131 after radioactive iodine treatment for thyroid cancer?
- Should all pregnant women be screened for thyroid disease?
- Can molecular analysis improve the diagnostic accuracy of thyroid nodule biopsies?

Our goal with these educational offerings is to empower you to take control of your thyroid health by providing you with the latest accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases. We welcome your feedback and suggestions. Let us know what you want to see in this publication. I hope you find these summaries interesting and informative.

— Alan P. Farwell, MD

**HOW TO NAVIGATE THIS DOCUMENT:** The Table of Contents and the Bookmarks are linked to the articles. To navigate, move your cursor over the article title you wish to see (either in the Contents or in the Bookmarks panel) and the hand will show a pointing finger, indicating a link. Left-click the title and the article will instantly appear. To return to the Contents, move the cursor to the bottom of the page and left-click **Back to Table of Contents**.



## THYROID CANCER

### Patients with spread of papillary thyroid cancer to the lymph nodes at the time of their diagnosis are more likely to experience return of their cancer to lymph nodes over time

#### WHAT IS THE STUDY ABOUT?

When papillary thyroid cancer spreads outside of the thyroid, it initially spreads into the lymph nodes in the neck around the thyroid. The spread of thyroid cancer into lymph nodes occurs frequently and is often detected at the time of initial surgery. Return of thyroid cancer after the initial surgery also is not uncommon. Despite these observations, neither factor changes the generally good prognosis of thyroid cancer and the low mortality rates. Because of this, it is unclear whether extensive lymph node surgery has any effect on recurrence of thyroid cancer in the lymph nodes of the neck. Understanding risks associated with cancer recurrence will help physicians and patients determine the best treatment for thyroid cancer. This study was done to identify diagnostic features of papillary thyroid cancer associated with recurrence of the cancer to lymph nodes in the neck.

#### THE FULL ARTICLE TITLE:

Baek et al. Clinical risk factors associated with cervical lymph node recurrence in papillary thyroid carcinoma. *Thyroid* 2010;20:147-52.

#### WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to identify diagnostic features of papillary thyroid cancer associated with recurrence of the cancer to lymph nodes in the neck.

#### WHO WAS STUDIED?

The study reviewed 189 patients with papillary thyroid cancer who had undergone surgical removal of the thyroid from 1992 through 2003 and had at least 2 years of follow-up. Within this group were 33 patients (17%) found to have recurrence of the cancer to neck lymph nodes and 156 (83%) that did not have any spread to neck lymph nodes.

#### HOW WAS THE STUDY DONE?

The patients' medical records were reviewed. Patients who had been diagnosed with spread of the cancer to the neck lymph nodes either prior to thyroidectomy or who were

suspected to have spread during the surgery underwent more extensive surgery that removed lymph nodes from the neck along with the thyroid gland. After the initial surgery, patients were monitored every 3 to 6 months for any return of thyroid cancer. On average, patients were followed for 81 months after the initial surgery.

#### WHAT WERE THE RESULTS OF THE STUDY?

Only 11 of the 189 patients were treated initially with a partial thyroidectomy and none of these patients had recurrence of the thyroid cancer. Of the 178 patients treated with a total thyroidectomy, 18.5% had recurrence of the cancer to the neck lymph nodes over time. Characteristics associated with recurrence of thyroid cancer to the neck lymph nodes included: 1) cancer size > 2 cm, 2) presence of spread of cancer beyond the thyroid gland at the time of initial surgery and 3) spread of cancer to neck lymph nodes at the time of initial surgery. Only 10% of 130 patients without initial spread of cancer to neck lymph nodes ultimately developed spread of cancer to neck lymph nodes. The return of cancer in these cases involved multiple regions of the neck on the side of the neck where the cancer was removed.

#### HOW DOES THIS COMPARE WITH OTHER STUDIES?

The authors of this study conclude that if there is no spread of papillary thyroid cancer to the neck lymph nodes at the time of initial surgery, extensive surgery to remove neck lymph nodes may not be needed. Several studies have found a similar result, while others suggest that routine, more extensive removal of neck lymph nodes is warranted at the time of initial surgery. Other studies have found additional risk factors for neck lymph node papillary thyroid cancer recurrence, including the number of lymph nodes with cancer at the time of initial study, spread of the thyroid cancer initial tumor beyond the thyroid gland, cancer size > 4 cm and elevations of blood thyroid cancer markers.

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## **THYROID CANCER**, continued

### **WHAT ARE THE IMPLICATIONS OF THIS STUDY?**

This study emphasizes the challenge that patients and physicians currently face in choosing the best surgery for papillary thyroid cancer. Most patients do well and do not die from papillary thyroid cancer. More extensive initial surgery may be associated with more surgical risk but also may benefit patients who are more likely to have return of their cancer. Also, more extensive initial surgery may provide important information guiding future therapy decisions. Future well-designed studies could clarify how to help patients remain free of disease with targeted, personalized therapy.

— Ruth Belin, MD

### **ATA THYROID BROCHURE LINKS**

Thyroid cancer: [http://www.thyroid.org/patients/patient-brochures/cancer\\_of\\_thyroid.html](http://www.thyroid.org/patients/patient-brochures/cancer_of_thyroid.html)

Thyroid surgery: <http://www.thyroid.org/patients/patient-brochures/surgery.html>

### **ABBREVIATIONS & DEFINITIONS**

**Papillary thyroid cancer** — the most common type of thyroid cancer.

**Thyroidectomy** — surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a total thyroidectomy. When less is removed, such as in removal of a lobe, it is termed a partial thyroidectomy.

**Lymph node** — bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

**Cancer recurrence** — return of cancer after an initial treatment that was successful in destroying all detectable cancer at some point



## SUBCLINICAL HYPOTHYROIDISM

### Reanalysis of the Whickham Survey shows an association of subclinical hypothyroidism and heart disease

#### WHAT IS THE STUDY ABOUT?

Hypothyroidism occurs when the thyroid gland is underactive and doesn't produce enough thyroid hormone. Subclinical hypothyroidism occurs when an increased TSH level is the only abnormality and the thyroid hormone levels are normal. Subclinical hypothyroidism has been associated with increasing several cardiac risk factors, including cholesterol, homocystine levels and blood pressure. It is unclear whether these changes are associated with an increased risk for heart disease in this group. Indeed, a [study by Andrees](#) that was summarized in the January issue (*Clinical Thyroidology for Patients* 3(1):3-4 Jan. 2010) suggested a decrease in heart disease if subclinical hypothyroidism is treated with thyroid hormone while a [study by Boekholt](#) in the February issue (*Clinical Thyroidology for Patients* 3(2): 5-6 Feb. 2010) suggested that subclinical hypothyroid has no risk for heart disease. One of the largest studies of thyroid problems in a population is the Wickham Survey, which studied the thyroid levels of adults living in the town of Wickham in England. Initially, the Wickham Survey did not find an association between thyroid disease and heart disease over a 20 year follow-up period. The current study looked at the Wickham Survey data more closely to examine the association between heart disease and death related specifically to subclinical hypothyroidism.

#### THE FULL ARTICLE TITLE:

Razvi et al. The incidence of ischemic heart disease and mortality in people with subclinical hypothyroidism: Reanalysis of the Whickham survey cohort. *J. Clin. Endocrinol. Metab.* 2010; 95:00-00 [Epub February 11, 2010].

#### WHAT WAS THE AIM OF THE STUDY?

The aim of the study was to examine the association between heart disease and death related specifically to subclinical hypothyroidism in the Whickham Survey.

#### WHO WAS STUDIED?

The Whickham Survey is a study of adults living in Wickham, an urban area in northern England. A randomly selected group of 2779 adults were first studied

in 1972-1973 and have subsequently been followed for 20 years. For this re-analysis, the study group included a total of 2376 adults who had been followed for 20 years.

#### HOW WAS THE STUDY DONE?

The study group was divided into two groups based on their TSH level at the original entry into the Whickham survey. Subjects were considered to have normal thyroid function if their TSH was between 0.3 and 5.9 mIU/L and considered to have subclinical hypothyroidism if their TSH was between 6 and 15 mIU/L. The incidence of heart disease and death was determined in each group over the 20 year time of follow up.

#### WHAT WERE THE RESULTS OF THE STUDY?

Most of the participants in the study had a normal TSH (95.9%, average TSH 1.6) with only 4.1% having subclinical hypothyroidism (average TSH 13.2). There were more women than men in the study. Women with subclinical hypothyroidism had significantly higher baseline levels of blood pressure, cholesterol, LDL cholesterol ("bad" cholesterol), and homocysteine than women with normal thyroid function. Over the 20 years of follow-up, there were 165 deaths due to heart disease. The mortality rate of heart disease was higher in the individuals with subclinical hypothyroidism than in the individuals with normal thyroid function. Overall, there were 24 deaths in the group with subclinical hypothyroidism. Levothyroxine therapy was started in 20 of the 91 individuals with subclinical hypothyroidism. Mortality was significantly lower in the levothyroxine-treated group as compared with untreated individuals with subclinical hypothyroidism.

#### HOW DOES THIS COMPARE WITH OTHER STUDIES?

Numerous studies have linked subclinical hypothyroidism with increasing cardiac risk factors such as blood pressure, cholesterol and homocysteine and the current study supports these observations. Many studies have shown a decrease in these cardiac risk factors with thyroid hormone replacement therapy. However, the association between

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## SUBCLINICAL HYPOTHYROIDISM, continued

subclinical hypothyroidism with heart disease and death remains unclear. This study is one of the few that shows a link between subclinical hypothyroidism and the risk for cardiac disease and death.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that there is an increased risk of cardiac disease and death in those with subclinical hypothyroidism. Further, this study suggests that thyroid hormone therapy may decrease this risk to that of an individual with normal thyroid function. While more

studies need to be done to confirm these results, this study gives physicians more of a reason to treat individuals with thyroid hormone to restore their thyroid levels to the normal range.

— Whitney Woodmansee, MD

### ATA THYROID BROCHURE LINKS

Thyroid Function Tests: [http://thyroid.org/patients/patient\\_brochures/function\\_tests.html](http://thyroid.org/patients/patient_brochures/function_tests.html)

Hypothyroidism: [http://thyroid.org/patients/patient\\_brochures/hypothyroidism.html](http://thyroid.org/patients/patient_brochures/hypothyroidism.html)

### ABBREVIATIONS & DEFINITIONS

**Hypothyroidism** — a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

**Subclinical Hypothyroidism** — a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH.

**Thyroxine (T<sub>4</sub>)** — the major hormone secreted by the thyroid gland. Thyroxine is broken down to produce Triiodothyronine which causes most of the effects of the thyroid hormones.

**TSH** — Thyroid stimulating hormone – produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

**Cardiac risk factors** — these are factors that are associated with an increase risk of having heart disease. These include increased cholesterol, increased homocystine levels, high blood pressure, diabetes and smoking.



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## GOITER

### Recombinant Human Thyrotropin (rhTSH) use in the treatment of nontoxic multinodular goiter

#### WHAT IS THE STUDY ABOUT?

A multinodular goiter is an enlarged thyroid that contains more than one thyroid nodule. Multinodular goiters are very common as we get older. They are also common in areas that have low amounts of iodine in their diet, such as parts of Europe and Asia. In the United States, anywhere from one-third to one-half of people over the age of 50 will have one or more nodules in their thyroid. While multinodular goiters can be overactive or contain a thyroid cancer, most function normally and do not include a cancer. Occasionally, multinodular goiters can enlarge and put pressure on structures in the neck, causing choking and difficulty swallowing. When this occurs, the usual treatment is surgery. Recently, some studies have suggested that large multinodular goiters can shrink if treated with radioactive iodine. Further, some studies have shown that the radioactive iodine can be more effective if the thyroid is turned on first by treatment with recombinant human TSH (rhTSH). However, this therapy can have some side effects and has been shown to increase thyroid size and potentially cause hyperthyroidism. At present, rhTSH is mainly used for treating patients with thyroid cancer and has not yet been approved by the Food and Drug Administration for this reason. The aim of this study was to determine which dose of rhTSH is the most effective with the least side effects.

#### THE FULL ARTICLE TITLE:

Fast et al. Dose-dependent acute effects of recombinant human TSH (rhTSH) on thyroid size and function: comparison of 0.1, 0.3 and 0.9 mg of rhTSH. Clin Endocrinol (Oxf) 2010;72:411-6.

#### WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to determine which dose of rhTSH is the most effective with the least side effects.

#### WHO WAS STUDIED?

Nine men with an average age of 33 years were studied. All of them had normal thyroid size and normal thyroid function tests.

#### HOW WAS THE STUDY DONE?

The study participants were injected with increasing doses of rhTSH (0, 0.1, 0.3, and 0.9 mg) over four study rounds. They evaluated thyroid volume by ultrasound and thyroid hormone levels in the blood 1, 2, 3, 7 and 28 days after injection of each dose.

#### WHAT WERE THE RESULTS OF THE STUDY?

This study showed that rhTSH did cause enlargement of the thyroid gland on a dose dependent basis. The thyroid enlarged to 35-45% with the 0.3 mg and the 0.9 mg dose, but not with the 0.1 mg dose of rhTSH. Thyroid hormone levels also increased in a dose-dependent fashion, with peak levels observed 24-48 h after the injection. Most of the study participants developed mild hyperthyroid symptoms for a few days following the injections, more often at the higher doses. Only one participant reported hyperthyroid symptoms after the 0.1 mg dose. No permanent abnormalities in thyroid function were seen in the patients for up to 2 years after the study.

#### HOW DOES THIS COMPARE WITH OTHER STUDIES?

Several studies have looked at the use of rhTSH to increase that amount of radioactive iodine taken up by goiters. The initial concerns were that rhTSH stimulation would increase the release of T<sub>4</sub> and T<sub>3</sub> from the thyroid and possibly cause some problems. The early studies showed this was not a problem. Older studies found that with higher doses of rhTSH (0.3, 0.9) there was thyroid enlargement with multinodular goiter. However, this study differs from other studies in that the same subjects were given repeat rhTSH doses to determine the effects. The dose of rhTSH used was also examined and the most safe and effective dose was found to be 0.1 mg, as it was in this study. This dose is 1/3 of the dose used in thyroid cancer.

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## GOITER, continued

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Doses of rhTSH of 0.1 mg or less are likely to cause fewer adverse effects in patients. If side effects occur, they usually go away quickly.

— Heather Hofflich, MD

### ATA THYROID BROCHURE LINKS

Thyroid Nodules: [http://thyroid.org/patients/patient\\_brochures/nodules.html](http://thyroid.org/patients/patient_brochures/nodules.html)

### ABBREVIATIONS & DEFINITIONS

**Goiter:** a thyroid gland that is enlarged for any reason is called a goiter. A goiter can be seen when the thyroid is overactive, underactive or functioning normally. If there are nodules in the goiter it is called a nodular goiter; if there is more than one nodule it is called a multinodular goiter.

**TSH:** Thyroid stimulating hormone – produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

**Recombinant human TSH (rhTSH)** - human TSH that is produced in the laboratory and used to produce high levels of TSH in patients after an intramuscular injection. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan. The brand name for rhTSH is Thyrogen™.

**Radioactive iodine (RAI)** – this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

**Thyroid Ultrasound:** a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.



## THYROID CANCER

### PET scans are very effective at finding spread of thyroid cancer to the lymph nodes in the neck

#### WHAT IS THE STUDY ABOUT?

Thyroid cancer is common and is the fastest rising cancer in women. It is known that as many as 1/3 of patients will have spread of the thyroid cancer to the lymph nodes in the neck at the time of the initial thyroid surgery. However, as we develop more sensitive means of finding thyroid cancer, doctors are learning that this is actually more common than initially thought. Further, these patients frequently have persistent thyroid cancer in the neck lymph nodes after treatment with radioactive iodine. Fortunately, thyroid cancer has a good prognosis, even for those patients that have spread of the cancer to the lymph nodes in the neck. One sensitive way of examining patients for thyroid cancer is an imaging study known as Positron-Emission Tomography (PET) Scan. Importantly, PET scans can identify thyroid cancer that does not take up the radioactive iodine and that cannot be seen on thyroid scans. This study examines how effective PET scans are at finding residual thyroid cancer remaining after radioactive iodine therapy.

#### FULL ARTICLE TITLE:

Kaneko et al. Detection of residual lymph node metastases in high-risk papillary thyroid cancer patients receiving adjuvant I-131 therapy: the usefulness of F-18 FDG PET/CT. Clin Nucl Med 2010;35:6-11.

#### WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to examine how effective PET scans are at finding residual thyroid cancer remaining after radioactive iodine therapy.

#### WHO WAS STUDIED?

The study group included 37 patients at a Japanese university hospital with high-risk papillary thyroid cancer who were treated between 2006 and 2008. All patients had a total thyroidectomy and removal of lymph nodes in the neck followed by radioactive iodine therapy.

#### HOW WAS THE STUDY DONE?

The records of the patients were examined for the initial pathology of the thyroid cancer, the amount of radioactive iodine received and the number of lymph nodes that contained thyroid cancer. All patients also had PET scans.

#### WHAT WERE THE RESULTS OF THE STUDY?

A total of 9 patients were found to have residual thyroid cancer in the lymph nodes. A total of 33 lymph nodes were involved with cancer in these 9 patients. PET scans identified all 33 lymph nodes that contained thyroid cancer. Only 14 (42%) of these lymph nodes were identified on the radioactive iodine whole body scan.

#### HOW DOES THIS COMPARE WITH OTHER STUDIES?

It has been known for many years that when papillary thyroid cancer spreads from the thyroid, it spreads to the lymph nodes in the neck. Recent studies indicate that cancers that have a specific gene mutation (BRAF) are more aggressive and often do not take up radioactive iodine.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Despite the excellent prognosis for most patients with thyroid cancer, it appears that residual thyroid cancer in the lymph nodes in the neck after radioactive iodine therapy is more common than initially thought. PET scanning is very sensitive to identify spread of thyroid cancer to the lymph nodes, including thyroid cancer that does not take up iodine. Thus, a PET scan may be a very valuable tool to identify thyroid cancer patients that may benefit from more aggressive treatment.

— Henry Fein, MD

#### ATA THYROID BROCHURE LINKS

Thyroid cancer: [http://thyroid.org/patients/patient\\_brochures/cancer\\_of\\_thyroid.html](http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html)

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## **THYROID CANCER**, continued

### **ABBREVIATIONS & DEFINITIONS**

**Papillary thyroid cancer** — the most common type of thyroid cancer.

**Radioactive iodine (RAI)** — this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

**Thyroglobulin** — a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker.

**Lymph node** — bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

**Cancer recurrence** — this occurs when the cancer comes back after an initial treatment that was successful in destroying all detectable cancer at some point.



## THYROID CANCER

### The first administration of radioiodine following total thyroidectomy for thyroid cancer can destroy metastatic thyroid cancer

#### WHAT IS THE STUDY ABOUT?

After surgery, many patients with thyroid cancer are treated with radioactive iodine. The main reason to treat with radioactive iodine is to destroy any normal thyroid tissue remaining in the thyroid bed (thyroid remnant) as well as thyroid cancer remaining after surgery. After the radioactive iodine treatment, a whole body scan (post-RAI WBS) is done to identify any thyroid cancer that has spread outside the thyroid bed (ie become metastatic). In order for radioactive iodine to be effective, the patient's TSH levels need to be increased to stimulate the thyroid cells to take up the radioactive iodine and be destroyed. There are two ways to increase TSH: 1) withdraw the patient from thyroid hormone (THW), making the patient hypothyroid for a short period of time or 2) use recombinant human TSH (rhTSH) to allow patients to stay on their thyroid hormone and avoid the short term hypothyroidism. It is clear that metastatic thyroid cancer can be identified on the post-RAI WBS following THW. It is not entirely clear if this also occurs with radioactive iodine after rhTSH. There is also uncertainty if the initial radioactive iodine treatment after surgery effectively destroys the metastatic thyroid cancer. The aims of this study were: 1) to determine if radioactive iodine therapy after rhTSH could identify metastatic thyroid cancer outside the neck on the post-RAI WBS and 2) to determine if the initial radioactive iodine treatment, either by rhTSH or THW, is effective in destroying the metastatic thyroid cancer.

#### THE FULL ARTICLE TITLE:

Tuttle RM. et al. Radioactive iodine administered for thyroid remnant ablation following recombinant human thyroid stimulating hormone preparation also has an important adjuvant therapy function. *Thyroid* 2010;20:257-63.

#### WHAT WAS THE AIM OF THE STUDY?

The aims of this study were: 1) to determine if radioactive iodine therapy after rhTSH could identify metastatic thyroid cancer outside the neck on the post-RAI WBS and

2) to determine if the initial radioactive iodine treatment, either by rhTSH or THW, is effective in destroying the metastatic thyroid cancer.

#### WHO WAS STUDIED?

The study subjects were 394 patients treated with radioactive iodine for papillary or follicular thyroid cancer at the Memorial Sloan-Kettering Cancer Center from 1997 through 2005.

#### HOW WAS THE STUDY DONE?

The medical records and radioactive iodine post-RAI WBS of the 394 study patients were reviewed. Some of these patients were prepared for the radioactive iodine by THW while others received rhTSH before the radioactive iodine. In all patients who were found to have metastatic thyroid cancer in the lungs, a computed tomography (CT) of the chest was also obtained for comparison. Patients had follow up at 6-12 months intervals and most patients also had a diagnostic rhTSH-WBS 12 to 18 months after the initial radioactive iodine treatment. Patients who had negative diagnostic WBS and thyroglobulin (Tg) levels < 2 ng/ml were considered to have no evidence of disease.

#### WHAT WERE THE RESULTS OF THE STUDY?

Of the 394 patients, 84 had spread of the thyroid cancer outside of the thyroid bed diagnosed on the post-RAI WBS. Of these 84 patients, 64 were treated after rhTSH and 20 were treated after THW. Most of these patients (76) had thyroid cancer limited to the neck while 8 patients either had lung metastases only, or cancer in both the neck region and lungs. Of these 8 patients, 4 were treated after rhTSH and 4 after THW.

After approximately 2.7 years from the initial radioactive iodine treatment, 56 of the 84 patients (67%) no longer had evidence of the thyroid cancer. Of the patients with persistent thyroid cancer, 19 were treated with radioactive iodine after rhTSH (30%) while 9 were treated after THW (45%).

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## THYROID CANCER, continued

### HOW DOES THIS COMPARE WITH OTHER STUDIES?

A recent study of 72 patients with thyroid cancer evaluated whether patients had similar results after receiving either low dose or high dose radioactive iodine after rhTSH. The study found that both doses had similar success rates (approximately 75%), even in patients with metastatic thyroid cancer limited to the neck.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that initial radioactive iodine treatment after surgery is effective for metastatic thyroid cancer that

has spread outside the thyroid bed and outside the neck (ie to the lungs). Similar results were obtained by radioactive iodine after either rhTSH or THW.

— M. Regina Castro, MD

### ATA THYROID BROCHURE LINKS

Thyroid cancer: [http://thyroid.org/patients/patient\\_brochures/cancer\\_of\\_thyroid.html](http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html)

### ABBREVIATIONS & DEFINITIONS

**Radioactive iodine (RAI)** — this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

**Post- Radioactive iodine Whole Body Scan (post-RAI WBS)** — the scan done after radioactive iodine treatment that identifies what was treated and if there is any evidence of metastatic thyroid cancer.

**Thyroid Hormone Withdrawal (THW)** — this is used to produce high levels of TSH in patients by

stopping thyroid hormone pills and causing short-term hypothyroidism. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan.

**Recombinant human TSH (rhTSH)** — human TSH that is produced in the laboratory and used to produce high levels of TSH in patients after an intramuscular injection. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan. The brand name for rhTSH is Thyrogen™.

**Papillary thyroid cancer** — the most common type of thyroid cancer.

**Follicular thyroid cancer** — the second most common type of thyroid cancer.



## THYROID AND THE HEART

### Subclinical Thyroid Dysfunction: Relationship to death from all causes and from cardiovascular disease

#### WHAT IS THE STUDY ABOUT?

Subclinical thyroid disease occurs when the TSH is the only abnormality and the thyroid hormone levels are normal. Subclinical hypothyroidism occurs when an increased TSH level is the only abnormality and subclinical hyperthyroidism occurs when a decreased TSH level is the only abnormality. While subclinical hypothyroidism has been associated with increasing several cardiac risk factors, it is unclear whether these changes are associated with an increased risk for heart disease in this group. Several articles published in *Clinical Thyroidology for Patients* this year, including one in this issue ([Razvi et al, page 5](#)) have reported evidence both for and against such an association. This study takes the risk of cardiac disease one step further and looks at death rates in patients with subclinical thyroid disease. The aim of the study was to determine if the risk of death is higher in patients with either subclinical hypothyroidism or subclinical hyperthyroidism as compared to individuals with normal thyroid function.

#### THE FULL ARTICLE TITLE:

Sgarbi et al. Subclinical thyroid dysfunctions are independent risk factors for mortality in a 7.5 year followup: The Japanese-Brazilian thyroid study. *European Journal of Endocrinology*, 2010. Vol. 162, Issue 3, pp 569-577.

#### WHAT WAS THE AIM OF THE STUDY?

The aim of the study was to determine if the risk of death is higher in patients with either subclinical hypothyroidism or subclinical hyperthyroidism as compared to individuals with normal thyroid function.

#### WHO WAS STUDIED?

A total of 1110 Japanese-Brazilian subjects living near Sao Paulo, Brazil were studied as part of a larger investigation of the prevalence of many diseases in this population.

#### HOW WAS THE STUDY DONE?

The 1110 subjects aged 30 and above who had no known thyroid disease and were not taking thyroid medication were studied. A survey was completed in 1999-2000 by the participants as to the presence of a variety of medical conditions such as heart disease, high blood pressure and diabetes. Blood tests, including cholesterol and thyroid

tests, were performed in the participants. The survey and blood tests were repeated 7.5 years later.

#### WHAT WERE THE RESULTS OF THE STUDY?

At baseline, 913 individuals (82%) had normal thyroid tests, 99 (8.7%) had subclinical hypothyroidism and 69 (6.2%) had subclinical hyperthyroidism. The risk of death from all causes was 3 times higher in individuals with subclinical hyperthyroidism and 2.3 times higher in individuals with subclinical hypothyroidism as compared to the 913 subjects with normal thyroid tests. The risk of death from heart disease was 3.3 times higher in individuals with subclinical hyperthyroidism. There was no increased risk of death from heart disease in individuals with subclinical hypothyroidism.

#### HOW DOES THIS COMPARE WITH OTHER STUDIES?

There are several studies over the years that have reported evidence both for and against an association between subclinical thyroid disease and cardiac disease and mortality. Some studies suggest that treatment of subclinical hypothyroidism with thyroid hormone may improve cardiac risk factors but there is no information on a change in mortality with treatment. There is no information on the effects of treatment of subclinical hyperthyroidism on cardiac disease or mortality.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests individuals with subclinical thyroid disease have a higher risk of death than those with normal thyroid function. What is unknown is whether treatment of subclinical thyroid disease would have any effect on the increased risk of death. As such, while there is no consensus on the benefits of treating patients with subclinical thyroid disease, close monitoring would appear to be appropriate.

— Jerrold Stock, MD

#### ATA THYROID BROCHURE LINKS

Hypothyroidism: [http://thyroid.org/patients/patient\\_brochures/hypothyroidism.html](http://thyroid.org/patients/patient_brochures/hypothyroidism.html)

Hyperthyroidism: [http://thyroid.org/patients/patient\\_brochures/hyperthyroidism.html](http://thyroid.org/patients/patient_brochures/hyperthyroidism.html)

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## **THYROID AND THE HEART, continued**

### **ABBREVIATIONS & DEFINITIONS**

**TSH:** Thyroid stimulating hormone – produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

**Hypothyroidism** — a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

**Subclinical Hypothyroidism:** a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH.

**Hyperthyroidism:** a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

**Subclinical Hyperthyroidism:** a mild form of hyperthyroidism where the only abnormal hormone level is a decreased TSH.



## THYROID CANCER

### Salivary stimulation with vitamin C at any time after I-131 therapy has no major effect on salivary uptake of I-131

#### WHAT IS THE STUDY ABOUT?

After surgery for thyroid cancer, most patients are treated with radioactive iodine (I-131). This serves two functions: 1) destroy any remaining cancer cells anywhere in the body and 2) destroy any remaining normal thyroid tissue, thus allowing patients to be followed more easily for thyroid cancer return or persistence. I-131 is taken up not only by thyroid tissue, but also some other tissues in the body such as salivary glands. As a result, I-131 can damage the salivary glands, which are very sensitive to radiation. Because of this, the radiation sialadenitis (salivary gland inflammation) and xerostomia (dry mouth) are the most common complications of I-131 therapy, which can even occur with small amounts of I-131. One treatment to reduce the damage of radiation to the salivary glands has been to stimulate salivary flow by sour candies. The aim of this study was to examine if the use vitamin C as a sour stimulant can decrease damage to the salivary glands by the I-131.

#### THE FULL ARTICLE TITLE:

Liu et al. Influence of vitamin C on salivary absorbed dose of I-131 in thyroid cancer patients: a prospective, randomized, single-blind, controlled trial. *J Nucl Med* 2010;4:618-23.

#### WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to examine the use of vitamin C as a sour stimulant to decrease the effect of I-131 to the salivary glands.

#### WHO WAS STUDIED?

The study group included 72 patients referred to the West China Hospital Department of Nuclear Medicine for radioactive iodine therapy. Patients with extensive thyroid cancer, history of salivary-gland disease, previous I-131 therapy or radiation to the head or neck were excluded from the study.

#### HOW WAS THE STUDY DONE?

All patients were treated with surgery then were allowed to become hypothyroid in preparation for the radioactive iodine treatment. All patients were treated with 100 mCi

I-131. The patients began sucking on lozenges of 100 mg of vitamin C every 6 hours during the day starting 1, 5, 13 and 25 hours after the I-131 treatment. The amount of I-131 taken up by salivary glands was measured and calculated at 1 to 48 hours after I-131 therapy.

#### WHAT WERE THE RESULTS OF THE STUDY?

There was no significant difference between the amount of I-131 taken up by salivary glands in any of the 4 groups after I-131 therapy.

#### HOW DOES THIS COMPARE WITH OTHER STUDIES?

One prior study suggested that the use of lemon candies after I-131 treatment may make the damage worse. However, the group that did not use the candies initially also received other treatment to decrease salivary gland damage. The current study clearly shows that sour stimulation is not harmful; neither does it help. A previous study showed similar results regarding the high frequency of salivary-gland injury after I-131 therapy.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While this study shows that salivary stimulation with vitamin C at any time after I-131 therapy had no significant effect on I-131 uptake of the salivary glands, more controlled studies are needed to determine whether the use of sour stimulation after I-131 is necessary and if yes, when and what amount should be used. Further, because this study included only patients that were allowed to become hypothyroid before I-131 treatment, similar studies should be done on patients prepared with recombinant human TSH for I-131 therapy.

— Jamshid Farahati, MD

#### ATA THYROID BROCHURE LINKS

Thyroid cancer: [http://thyroid.org/patients/patient\\_brochures/cancer\\_of\\_thyroid.html](http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html)

Thyroid Surgery: [http://thyroid.org/patients/patient\\_brochures/surgery.html](http://thyroid.org/patients/patient_brochures/surgery.html)

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## **THYROID CANCER**, continued

### **ABBREVIATIONS & DEFINITIONS**

**Thyroidectomy** — Surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a total thyroidectomy. When less is removed, such as in removal of a lobe, it is termed a partial thyroidectomy.

**Radioactive iodine (RAI)** — this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

**mCi** — millicurie, the units used for I-131.

**Recombinant human TSH (rhTSH)** — human TSH that is produced in the laboratory and used to produce high levels of TSH in patients after an intramuscular injection. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan. The brand name for rhTSH is Thyrogen™.

**Sialadenitis** — inflammation of salivary gland.

**Xerostomia** — dry mouth due to lack of saliva, frequently observed after radiation to the head and neck and after I-131 therapy.



## THYROID AND PREGNANCY

### Effects of detection and treatment of hypo- and hyperthyroidism in pregnancy

#### WHAT IS THE STUDY ABOUT?

Thyroid disease during pregnancy may be associated with a number of complications including miscarriage, preterm delivery, brain abnormalities in the children and postpartum thyroid inflammation in the mother. There are known risk factors for developing thyroid disease during pregnancy, including: a family history of autoimmune thyroid disease, presence of a goiter, signs and symptoms of thyroid disease, known thyroid dysfunction, history of type 1 diabetes mellitus or other autoimmune diseases, prior neck irradiation, or previous miscarriages or preterm deliveries. Pregnant women with these known risk factors are easily screened for thyroid disease with blood tests of TSH and thyroid peroxidase antibody (TPO AB, a marker of autoimmune thyroid disease). However, screening all pregnant women for the presence of thyroid disease regardless of risk factors is controversial and is not currently done on a routine basis. This study was designed to compare screening for thyroid disease in pregnant women with known risk factors for thyroid disease (case-finding group) as compared to screening all pregnant women for thyroid disease (universal screening group).

#### THE FULL ARTICLE TITLE:

Negro et al. Universal screening versus case finding for detection and treatment of thyroid hormonal dysfunction during pregnancy. *J Clin Endocrinol Metab* 2010. doi:10.1210/jc.2009-2009.

#### WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to determine the impact of universal screening for thyroid dysfunction on adverse outcomes in pregnant women.

#### WHO WAS STUDIED?

The study group included a total of 4562 women without a history of thyroid disease who were in their first trimester of pregnancy and attending pregnancy programs in Italy.

#### HOW WAS THE STUDY DONE?

The women were randomized into two groups: a case-finding group and the universal screening group. Within each group, women were divided into high risk (one or

more thyroid risk factors) or low risk (no risk factors). All women had blood tests for FT<sub>4</sub>, TSH and TPO AB done.

**Case-finding group:** The blood tests in the high risk women were done immediately and, if they were abnormal, the women were treated according to guidelines. The blood tests in the low risk women were frozen and done after the pregnancy.

**Universal screening group:** The blood tests in all of the women were done immediately and if they were abnormal, the women were treated according to guidelines. Both groups were compared in regards to pregnancy outcomes.

#### WHAT WERE THE RESULTS OF THE STUDY?

Approximately 20% of women in both groups were classified as high risk.

**Case-finding group:** High risk patients: 95% had normal thyroid function, 4.4% were hypothyroid and 0.4% were hyperthyroid. Those with thyroid disease were treated. Low risk patients: 98% had normal thyroid function, 1.9% were hypothyroid and 0.2% were hyperthyroid. These latter patients were not treated because their blood was not analyzed until after delivery.

**Universal screening group:** 97% had normal thyroid function, 2.8% had hypothyroidism and 0.4% had hyperthyroidism. All patients with thyroid disease in this group were treated.

In the entire study, 59.5% of the women had no adverse outcomes, 25.6% had one, 6.6% had two and 3.5% had four or more. There was no difference in overall adverse outcomes between the Case Finding and Universal Screening groups. An adverse event was not significantly different for the women in the high risk as compared to the low risk universal-screening group (as all of those with abnormal results were treated), but it was higher for the low risk case-finding group, since those with hypothyroidism or hyperthyroidism were not detected or treated during the pregnancy.

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## THYROID AND PREGNANCY, continued

### HOW DOES THIS COMPARE WITH OTHER STUDIES?

This represents the first prospective, randomized trial to compare case-finding with universal screening in the detection of thyroid disease in pregnant women.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While universal screening did not result in a decrease in overall adverse outcomes, it did identify and allow treatment of thyroid dysfunction in a group of women with no thyroid risk factors which resulted in a significant

decrease in adverse outcomes in that group. The study also confirms that case-finding alone fails to detect the majority of pregnant women with thyroid disease. Further analysis needs to be performed to see if universal screening for thyroid disease in pregnancy is cost-effective.

— Glen Braunstein, MD

### ATA THYROID BROCHURE LINKS

Thyroid and Pregnancy: [http://thyroid.org/patients/patient\\_brochures/pregnancy.html](http://thyroid.org/patients/patient_brochures/pregnancy.html)

### ABBREVIATIONS & DEFINITIONS

**Hypothyroidism** — a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

**Hyperthyroidism** — a condition where the thyroid gland is overactive and produces too much thyroid

hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

**Miscarriage** — this occurs when a baby dies in the first few months of a pregnancy, usually before 22 weeks of pregnancy.



## THYROID CANCER

### Cancer-associated gene mutation detection in fine needle aspiration biopsies increases the accuracy for diagnosing cancer

#### WHAT IS THE STUDY ABOUT?

Thyroid nodules are very common and can be found in up to 50% of the population. Most thyroid cancers are discovered by fine needle aspiration biopsy (FNAB) of thyroid nodules. While FNAB is a very accurate test, there are occasional cancers that are missed with the initial biopsy cytology reading. Further, FNAB cannot diagnose follicular or hurtle cell cancer; it can only state that the results are indeterminate. Up to 15-20% of FNABs are read as indeterminate. When these nodules are removed, only 15-20% are cancerous and the rest are noncancerous follicular or hurtle cell adenomas. This means that many patients are operated on for non-cancerous thyroid nodules. A lot of research has been done in trying to do a better job at identifying follicular or hurtle cell cancer with FNAB. In particular, examining FNAB specimens for the presence certain cancer-associated gene mutations that are related to thyroid cancer might be able to improve the diagnostic accuracy of FNAB. The study examined whether molecular analysis of cancer-associated gene mutations in addition to cytology improved the accuracy of FNAB in patients with thyroid nodules.

#### THE FULL ARTICLE TITLE:

Cantara s, et al. Impact of proto-oncogene mutation detection in cytological specimens from thyroid nodules improves the diagnostic accuracy of cytology. J Clin Endocrinol Metab 2010;95:1365-9.

#### WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to determine whether molecular analysis of cancer-associated gene mutations in addition to cytology improved the accuracy of FNAB in patients with thyroid nodules.

#### WHO WAS STUDIED?

This study examined 174 patients with thyroid nodules that were already scheduled to undergo surgery.

#### HOW WAS THE STUDY DONE?

The study group of 174 patients were already scheduled for thyroid surgery, either on the basis of an abnormal

FNAB results or on the basis of the patient's clinical condition. Within the group 40.2% had a FNAB suspicious (22) or positive (48) for cancer, 28.7% (50) had a FNAB showing follicular or hurtle lesions and 31.1% (54) had a goiter or nodule that was causing choking or difficulty swallowing with noncancerous or inadequate results on FNAB. All patients had a repeat FNAB prior to surgery with molecular analysis looking for the cancer-associated gene mutation. At the time of surgery, all nodules were again sampled for molecular analysis.

#### WHAT WERE THE RESULTS OF THE STUDY?

Cancer-associated gene mutations were identified in 67 of 235 FNAB samples (28.5%). The two most common mutations were in the BRAF and RET/PTC genes. In all cases, the presence of either of these mutations was indicative of thyroid cancer. Another cancer-associated gene mutation (RAS) was associated with thyroid cancer 74% of the time and with noncancerous follicular adenoma 26% of the time. Looking specifically at indeterminate FNAB results, there were 7 mutations (17%) found. On final pathology 6 were thyroid cancer and 1 was a noncancerous follicular adenoma. Among the 34 indeterminate nodules without mutations, only 1 was thyroid cancer. Thus, adding the cancer-associated gene mutation analysis increased the accuracy of the FNAB diagnosis.

#### HOW DOES THIS COMPARE WITH OTHER STUDIES?

Numerous earlier studies have laid the groundwork for the present study. From previous studies it is known that the presence of BRAF mutations is highly specific for thyroid cancer – there has been only one false positive result in 2766 samples reported in the literature. The present study shows that screening FNAB for multiple cancer-associated gene mutations can be done.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The present study demonstrates that combining FNAB result with new techniques for molecular analysis

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## THYROID CANCER, continued

significantly improves the accuracy of thyroid FNAB. Further studies will be needed to determine the most cost-effective use of molecular analysis in actual clinical practice.

— Frank Cranz, MD

## ATA THYROID BROCHURE LINKS

Thyroid cancer: [http://thyroid.org/patients/patient\\_brochures/cancer\\_of\\_thyroid.html](http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html)

### ABBREVIATIONS & DEFINITIONS

**Thyroid nodule** — an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

**Thyroid fine needle aspiration biopsy (FNAB)** — a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

**Indeterminate thyroid biopsy** — this happens usually when the diagnosis is a follicular or hurtle cell lesion.

Follicular and hurtle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurtle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

**Cancer-associated genes** — these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC and RAS.



## THYROID CANCER

### Preparation of thyroid remnant ablation using recombinant human TSH and 30 mCi of I-131 is as effective as thyroid hormone withdrawal

#### WHAT IS THE STUDY ABOUT?

After surgery, many patients with thyroid cancer are treated with radioactive iodine. The main reason to treat with radioactive iodine is to destroy any normal thyroid tissue remaining in the thyroid bed (thyroid remnant) as well as thyroid cancer remaining after surgery. After the radioactive iodine treatment, a whole body scan (post-RAI WBS) is done to identify any thyroid cancer that has spread outside the thyroid bed (i.e. become metastatic). In order for radioactive iodine to be effective, the patient's TSH levels need to be increased to stimulate the thyroid cells to take up the radioactive iodine and be destroyed. There are two ways to increase TSH: 1) withdraw the patient from thyroid hormone (THW), thus making the patient hypothyroid for a short period of time or 2) use recombinant human TSH (rhTSH) to allow patients to stay on their thyroid hormone and avoid the short term hypothyroidism. In general, there has been a trend toward using lower amounts of radioactive iodine, with previous studies suggesting that a 50 mCi dose is as effective as a 100+ mCi dose. This study goes further in examining an even lower dose (30 mCi) in low risk patients. This dose is aimed at destroying any remaining normal thyroid tissue (Thyroid Remnant Ablation) rather than ensuring that all remaining thyroid cancer cells are destroyed. The aims of this study were: 1) to determine if treatment with 30 mCi I-131 after preparation with rhTSH was comparable 30 mCi I-131 after THW in thyroid remnant ablation and 2) to compare the quality of life of patients with thyroid cancer who were prepared with rhTSH versus those prepared with THW.

#### THE FULL ARTICLE TITLE:

Lee et al. Quality of life and effectiveness comparisons of thyroxine withdrawal, triiodothyronine withdrawal, and recombinant thyroid-stimulating hormone administration for low-dose radioiodine remnant ablation of differentiated thyroid carcinoma. *Thyroid* 2010;20:173-9.

#### WHAT WAS THE AIM OF THE STUDY?

The aims of this study were: 1) to determine if treatment with 30 mCi I-131 after preparation with rhTSH was comparable 30 mCi I-131 after THW in thyroid remnant

ablation and 2) to compare the quality of life of patients with thyroid cancer who were prepared with rhTSH versus those prepared with THW.

#### WHO WAS STUDIED?

The study group included 281 patients who were treated for thyroid cancer from February 2006 through March 2007. After surgery, all patients were started on 2 µg/kg of levothyroxine (L-T<sub>4</sub>).

#### HOW WAS THE STUDY DONE?

At least 30 days after surgery, patients were randomly assigned to one of three groups:

- 1) T4 THW - L-T<sub>4</sub> was discontinued for 4 weeks prior to radioactive iodine
- 2) T3 THW - L-T<sub>4</sub> was discontinued for 4 weeks followed by 2 weeks on and 2 weeks off L-T<sub>3</sub> prior to radioactive iodine
- 3) rhTSH – patients remained on L-T<sub>4</sub> and treated with rhTSH prior to radioactive iodine.

All patients were on a 2-week low-iodine diet prior to the radioactive iodine therapy. The patients also completed a seven-item written quality-of-life questionnaire after the radioactive iodine therapy. The success of the radioactive iodine therapy in thyroid remnant ablation was assessed at 12 months with a whole-body I-131 scan, serum thyroglobulin measurement and neck ultrasonography.

#### WHAT WERE THE RESULTS OF THE STUDY?

Effective thyroid remnant ablation was achieved in >91% of patients in all three groups, as judged by a negative whole-body I-131 scan and low/undetectable thyroglobulin levels one year after the radioactive iodine therapy. There was no difference between the T4-THW, T3-THW or rhTSH groups. In all 3 groups, patients with lymph node metastases were identified with the 30 mCi dose. There was a highly significant difference in quality-of-life status between the two THW groups (T4-THW and T3-THW) and the rhTSH group.

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## THYROID CANCER, continued

### HOW DOES THIS COMPARE WITH OTHER STUDIES?

This is one of the few prospective, randomized studies that analyze the efficacy of 30 mCi of I-131 for thyroid remnant ablation. Other studies have shown that THW and rhTSH are equally effective in thyroid remnant ablation using higher I-131 doses (50 mCi) and the [article by Tuttle et al in this issue](#) shows that THW and rhTSH are equally effective in treating metastatic thyroid cancer.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that rhTSH can be used with low dose I-131 for effective thyroid remnant ablation after surgery

in patients that have low-risk thyroid cancer. The use of lower doses of I-131 decreases total-body irradiation and decreases damage to nonthyroidal tissues.

— Alan Farwell, MD

### ATA THYROID BROCHURE LINKS

Thyroid cancer: [http://thyroid.org/patients/patient\\_brochures/cancer\\_of\\_thyroid.html](http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html)

### ABBREVIATIONS & DEFINITIONS

**Radioactive iodine (RAI)** — this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

**Thyroid Remnant Ablation** — destruction of the small amount of thyroid tissue that remains after surgery (thyroidectomy) with the use of radioactive iodine.

**Thyroid Hormone Withdrawal (THW)** — this is used to produce high levels of TSH in patients by stopping thyroid hormone pills and causing short-term hypothyroidism. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan.

**Recombinant human TSH (rhTSH)** — human TSH that is produced in the laboratory and used to produce high levels of TSH in patients after an intramuscular injection. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan. The brand name for rhTSH is Thyrogen™.

**Thyroglobulin** — a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker.

**Thyroid Ultrasound** — a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.



## ATA Alliance for Thyroid Patient Education

### GOAL

The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases.

### WHO WE ARE

#### AMERICAN THYROID ASSOCIATION

[www.thyroid.org](http://www.thyroid.org)

ATA Patient Resources: <http://www.thyroid.org/patients/>

Find a Thyroid Specialist: [www.thyroid.org](http://www.thyroid.org)

Phone (toll-free): 1-800-THYROID

e-mail: [thyroid@thyroid.org](mailto:thyroid@thyroid.org)

**ATA Mission:** The ATA leads in promoting thyroid health and understanding thyroid biology.

**ATA Vision:** The ATA is the leading organization focused on thyroid biology and the prevention and treatment of thyroid disorders through excellence and innovation in research, clinical care, education, and public health.

**ATA Values:** The ATA values scientific inquiry, clinical excellence, public service, education, collaboration, and collegiality.

To further our mission, vision and values the ATA sponsors “Friends of the ATA” online to advance the information provided to patients and the public such as this publication, *Clinical Thyroidology for Patients*. We welcome your support.

#### GRAVES' DISEASE FOUNDATION

[www.ngdf.org](http://www.ngdf.org)

Phone (toll-free): 1-877-NGDF-123 or 643-3123

e-mail: [Gravesdiseasefd@gmail.com](mailto:Gravesdiseasefd@gmail.com)

Founded in 1990, the Graves' Disease Foundation offers support and resources to Graves' disease patients, their families, and health care professionals. Their mission is to find the cause of and the cure for Graves' thyroid disease through research, to improve the quality of life for persons with Graves' disease and their caregivers and to educate persons with Graves' disease, their caregivers, healthcare professionals, and the general public about Graves' disease and its treatment. The web site features a monitored bulletin board.

#### LIGHT OF LIFE FOUNDATION

[www.checkyourneck.com](http://www.checkyourneck.com)

email: [info@checkyourneck.com](mailto:info@checkyourneck.com)

The Light of Life Foundation, founded in 1997, is a nonprofit organization that strives to improve the quality of life for thyroid cancer patients, educate the public and professionals about thyroid cancer, and promote research and development to improve thyroid cancer care.

#### THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

[www.thyca.org](http://www.thyca.org)

Phone (toll-free): 877 588-7904

e-mail: [thyca@thyca.org](mailto:thyca@thyca.org)

ThyCa: Thyroid Cancer Survivors' Association, Inc., founded in 1995, is an international nonprofit organization, guided by a medical advisory council of renowned thyroid cancer specialists, offering support and information to thyroid cancer survivors, families, and health care professionals worldwide.





## **ATA Alliance for Thyroid Patient Education CALENDAR OF EVENTS**

Educational forums, patient support groups and other patient-oriented meetings

### **ATA Conferences** [www.thyroid.org](http://www.thyroid.org)

### **Graves' Disease Conferences** [www.ngdf.org](http://www.ngdf.org)

Fall 2010 — San Diego, CA  
**Annual Meeting**

### **Light of Life Foundation** [www.checkyourneck.com](http://www.checkyourneck.com)

Saturday, June 12, 2010, 8:30 am – 3:30 pm — Memorial Sloan Kettering Cancer Center, New York, NY  
**Light of Life Foundation Patient Education Day**

### **ThyCa Conferences** [www.thyca.org](http://www.thyca.org)

Saturday, May 29, 2010 — St. John's, Newfoundland, Canada  
**Newfoundland and Labrador Thyroid Cancer Survivors' Workshop**  
Free one-day educational event. Sponsored by ThyCa: Thyroid Cancer Survivors' Association, Inc.

June 4–5, 2010 — Rockville, Maryland  
**Hypoparathyroidism Association Patient Conference**  
At the Rockville Hilton Hotel, Rockville, Maryland; Details at [www.hypoparathyroidism.org](http://www.hypoparathyroidism.org).

Saturday, June 26, 2010 — Houston, TX  
**Multiple Endocrine Neoplasias Patient Education Conference**  
The University of Texas M. D. Anderson Cancer Center

September 2010  
**Thyroid Cancer Awareness Month**  
Sponsored by ThyCa: Thyroid Cancer Survivors' Association, Inc. Plus year-round awareness campaigns. Visit the Raise Awareness Page to download free flyers, or request free awareness materials.

October 15–17, 2010 — Dallas, Texas.  
**The 13<sup>th</sup> International Thyroid Cancer Survivors' Conference**  
Sponsored by ThyCa: Thyroid Cancer Survivors' Association, Inc.

October 16, 2010 — Dallas, Texas  
**The 8<sup>th</sup> Annual Dinner/Auction Fundraiser for Thyroid Cancer Research**  
Thyroid Cancer Survivors' Conference. Sponsored by ThyCa: Thyroid Cancer Survivors' Association, Inc.

### **M. D. Anderson Cancer Center** [www.mdanderson.org/departments/ccg](http://www.mdanderson.org/departments/ccg)

Saturday, June 26, 2010 — Houston, TX  
**Multiple Endocrine Neoplasias Patient Education Conference**  
The University of Texas M. D. Anderson Cancer Center



# What's New in Thyroid Cancer?

## A Day for Patients and Their Families

### June 12, 2010

Rockefeller Research Laboratories Building  
 430 East 67th Street (between First & York Avenue)  
 New York, NY

#### AGENDA

9:00 – 9:15 am	<b>Welcome: Joan Shey, President &amp; Founder, The Light of Life Foundation</b>	
9:15 – 9:45 am	<b>Overview, Thyroid Cancer: Introduction to Thyroid Cancer, Increasing Incidence, Diagnosis</b>	<i>R. Michael Tuttle, MD</i>
9:45 – 10:15 am	<b>Ultrasound Evaluation of the Thyroid</b>	<i>Lucy Hann, MD</i>
10:15 – 10:45 am	<b>Surgical Decision in Thyroid Cancer</b>	<i>Julie Sosa, MD</i>
10:45 – 11:15 am	<b>Post Op Endocrine Issues: Managing Calcium and Thyroid Hormone Replacement</b>	<i>Rebecca Leboeuf, MD</i>
11:15 – 11:30 am	<b>BREAK</b>	
11:30 am – 12 pm	<b>Pathology of Thyroid Cancer</b>	<i>Ronald Ghossein, MD</i>
12:00 – 12:30 pm	<b>RAI Ablation: What Should I Expect</b>	<i>Ravinder Grewal, MD</i>
12:30 – 12:45 pm	<b>I<sup>131</sup> treatment: Radiation Safety Issues</b>	<i>Christopher Horan</i>
12:45 – 1:15 pm	<b>Questions &amp; Answers Panel of Speakers</b>	<i>R. Michael Tuttle, MD, Moderator</i>
1:15pm – 2:15 pm	<b>LUNCH</b>	
2:15pm – 2:45 pm	<b>Molecular Characterization of Thyroid Cancer: Clinical Relevance</b>	<i>James Fagin, MD</i>
2:45 – 3:15 pm	<b>Clinical Trials in Thyroid Cancer</b>	<i>Eric Sherman, MD</i>
3:15 – 3:30 pm	<b>Questions &amp; Answers</b>	<i>Tuttle moderator)</i>
3:30 pm	<b>Closing Remarks</b>	<i>Joan Shey</i>

# Please Join Us

## MULTIPLE ENDOCRINE NEOPLASIAS PATIENT EDUCATION CONFERENCE

Saturday, June 26, 2010 • 8:30 am to 3:15 pm



### REGISTRATION IS FREE

For more Information

[www.mdanderson.org/departments/ccg](http://www.mdanderson.org/departments/ccg)

or to Register call 713-745-7391

email [ccg@mdanderson.org](mailto:ccg@mdanderson.org)

*The Clinical Cancer Genetics program offers hereditary cancer risk assessment, genetic counseling and genetic testing based on your needs and your medical and family history.*

### Agenda Items Include:

- Overview of MEN: Historical Perspective
- Update on Genetic Testing
- Prenatal Diagnosis and Preimplantation Genetic Diagnosis Options
- MEN: Pediatric Perspective
- Practical Issues in Living with a Chronic Condition
- Patient and Provider Panel

### Breakout Sessions:

- Pancreatic Tumor Surgery, Treatment, and Clinical Trials
- Long-term Screening and Management of MEN1
- Update on MTC Prevention and Genotype Phenotype Correlations
- Advanced Medullary Thyroid Carcinoma and Targeted Therapies
- Pheochromocytoma Management: What's New?