

# Clinical Thyroidology for the Public

**VOLUME 9** • ISSUE 6 • JUNE 2016

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#### THYROID CANCER.....

#### Thyroid cancer in children near the Fukushima Daiichi Nuclear Power Plant meltdown

It is known that the risk of thyroid cancer is increased for those who are close by a nuclear power plant accident as a result of exposure to radiation emitted from the accident. The thyroid gland in children appears to be acutely sensitive to the results of radiation, as there was a marked increase in thyroid cancer after the Chernobyl nuclear plant meltdown in 1986. This study examined the risks of developing thyroid cancer in children who were nearby the Fukushima Daiichi Nuclear Power Plant meltdown.

Suzuki S et Comprehensive survey results of childhood thyroid ultrasound examinations in Fukushima in the first four years after the Fukushima Daiichi Nuclear Power Plant accident. Thyroid. 2016 Apr 20. [Epub ahead of print]

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While most patients with papillary thyroid cancer do very well, rarely this cancer can be aggressive. Predictors of aggressive cancers are being sought to help decrease this risk for overtreatment. One such predictor may be the presence of a mutation in a common cancer gene. This study was done to determine if the BRAFV600E mutation can predict recurrence in papillary thyroid microcancer, and therefore help to guide treatment decisions.

Chen Y et al BRAF<sup>V600E</sup> is correlated with recurrence of papillary thyroid microcarcinoma: a systematic review, multi-institutional primary data analysis, and meta-analysis. Thyroid 2016;26:248-55. Epub January 11, 2016

#### THYROID CANCER.....

#### Gene mutations and papillary thyroid cancer

Analysis of mutations in cancer-associated genes are helpful in making a diagnosis of cancer on a thyroid biopsy sample as well as predicting the risk of recurrence of the cancer after thyroid surgery. One common cancer-associated gene mutation in thyroid cancer is BRAFV $^{600E}$ . The goal of this study were to determine whether the presence of BRAFV $^{600E}$  is associated with more aggressive types of papillary thyroid cancer.

Lin JD et al. Clinical manifestations and gene expression in patients with conventional papillary thyroid carcinoma carrying the BRAF<sup>V600E</sup> mutation and BRAF pseudogene. Thyroid. March 30, 2016 [Epub ahead of print].

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Obesity and primary hypothyroidism are common conditions. Obese patients usually need higher dose of levothyroxine. The goal of this study was to evaluate the dose of levothyroxine needed to keep normal TSH levels in obese patients with hypothyroidism before and after bariatric surgery.

Fierabracci P et al. Weight loss and variation of levothyroxine requirements in hypothyroid obese patients after bariatric surgery. Thyroid. March 16, 2016 [Epub ahead of print].

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#### **Predicting Graves' Disease recurrence**

Graves' disease is an autoimmune disease where the body produces an antibody that attacks and turns on the thyroid. Graves' disease occasionally can go into remission if the antibody decreases or goes away. This study sought to develop a model for predicting recurrence/remission of Graves' disease.

Vos XG et al. Predicting the Risk of Recurrence Before the Start of Antithyroid Drug Therapy in Patients with Graves' Hyperthyroidism. J. Clin. Endocrinol. Metab. 2016. 101 (4): 1381-1389.

#### ATA ALLIANCE FOR THYROID

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#### CLINICAL THYROIDOLOGY FOR THE PUBLIC

#### A publication of the American Thyroid Association

**VOLUME 9** • ISSUE 6 • JUNE 2016

#### **EDITOR'S COMMENTS**

Welcome to another issue of *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We will be providing summaries of research studies that were discussed in a recent issue of *Clinical Thyroidology*, a publication of the American Thyroid Association for physicians. These summaries are present in lay language to allow the rapid dissemination of thyroid research to the widest possible audience. This means that you are getting the latest information on thyroid research and treatment almost as soon as your physicians. As always, we are happy to entertain any suggestions to improve *Clinical Thyroidology for the Public* so let us know what you want to see.

We also provide even faster updates of late-breaking thyroid news through Twitter at <a href="https://example.com/thyroid/friends">https://example.com/thyroid/friends</a> and on Facebook. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room.

Also check out our friends in the Alliance for Thyroid Patient Education. The Alliance member groups consist of: the American Thyroid Association, Bite Me Cancer, the Graves' Disease and Thyroid Foundation, the Light of Life Foundation, ThyCa: Thyroid Cancer Survivors Association, Thyroid Cancer Canada and Thyroid Federation International.

June is Differentiated Thyroid Cancer Awareness Month.

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

- 1. Do the Japanese children exposed to the Fukushima nuclear accident have an increased risk for developing thyroid cancer?
- 2. Does mutation in the cancer-associated gene BRAF<sup>V600e</sup> predict risk for thyroid cancer recurrence?
- 3. Does mutation in BRAF<sup>V600e</sup> predict recurrence of papillary thyroid microcancer?
- 4. Do thyroid hormone requirements change after bariatric surgery?
- 5. Can we predict remission in patients with Graves disease?

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, FACE









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#### **THYROID CANCER**

# Thyroid cancer in children near the Fukushima Daiichi Nuclear Power Plant meltdown

#### **BACKGROUND**

Thyroid cancer is the fastest rising cancer, especially in women. While the cause of this increase in thyroid cancer is largely unknown, it is know that the risk of thyroid cancer is increased for those who are close by a nuclear power plant accident, as a result of exposure to radiation emitted from the accident. The thyroid gland in children appears to be acutely sensitive to the results of radiation, as there was a marked increase in thyroid cancer after the Chernobyl nuclear plant meltdown in 1986. The Fukushima Daiichi Nuclear Power Plant in Japan experienced a nuclear meltdown on March 11, 2011 following a large earthquake in the area. As a result, there has been concern of increased thyroid cancer risks in the people who were close by at the time. This study examined the risks of developing thyroid cancer in children who were nearby the Fukushima nuclear emergency.

#### THE FULL ARTICLE TITLE

Suzuki S et Comprehensive survey results of childhood thyroid ultrasound examinations in Fukushima in the first four years after the Fukushima Daiichi Nuclear Power Plant accident. Thyroid. 2016 Apr 20. [Epub ahead of print]

#### **SUMMARY OF THE STUDY**

This was study of over 300,000 children (defined as less than 18 years old) who were living close by the Fukushima power plant at the time of the nuclear emergency in 2011. Between 2011-2015, all children received a thyroid ultrasound as part of a mass screening effort. The researchers plan to repeat thyroid ultrasound every 2 years until the children reach age 20, then every 5 years indefinitely. The researchers also asked the children questions related to their exact location and activity level at the time of the nuclear accident, in order to estimate the dose of radiation exposure.

Over this 4-year time period, children who had concerning features on the initial thyroid ultrasound received a more detailed thyroid ultrasound examination, from which some were also recommended to have a thyroid nodule biopsy. Based on the biopsy results, 99 children eventually underwent thyroid surgery, of which over 99% were confirmed to have thyroid cancer. Children with the thyroid cancer results were aged 6-18 years at the time of the nuclear accident. Overall, the researchers found that the rate of new-onset pediatric thyroid cancer following the Fukushima nuclear accident was 37.3/100,000 individuals. In comparison, the rate of new-onset pediatric thyroid cancer in the United States was 0.54/100,000 individuals.

## WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study provides further information regarding the risks of radiation exposure among children after a nuclear accident. The rate of thyroid cancer found in children in the 4 years following the Fukushima accident is much higher than both the general population rates of pediatric thyroid cancer and as well as following other historic nuclear accidents, including the Chernobyl disaster in 1986. This is likely because of the dedicated mass screening effort done in Fukushima, which was not done in such a rigorous way after Chernobyl. It will be important to follow the children in this study through adulthood to see how beneficial mass screening is following a nuclear accident.

- Angela M. Leung, MD, MSc

#### **ATA THYROID BROCHURE LINKS**

Thyroid Cancer: <a href="http://www.thyroid.org/thyroid-cancer/">http://www.thyroid.org/thyroid-cancer/</a> Childhood Head and Neck Irradiation: <a href="http://www.thyroid.org/pediatric-endocrinology/">http://www.thyroid.org/pediatric-endocrinology/</a>

#### **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 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

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#### THYROID CANCER, continued

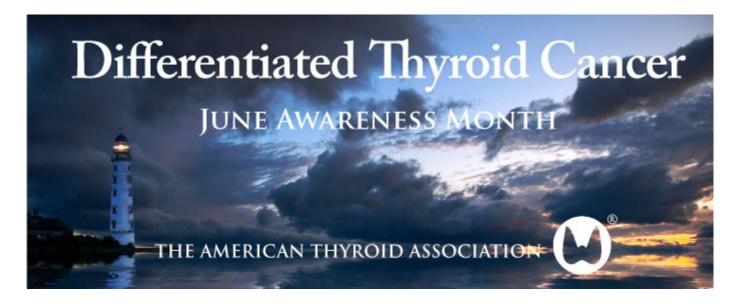


characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

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.

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.





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#### **THYROID CANCER**

# BRAF<sup>V600E</sup> Mutation in papillary thyroid microcarcinoma as recurrence risk factor

#### **BACKGROUND**

The rate of diagnosis of papillary thyroid cancer has increased markedly in the past 20 years. Up to half of these new diagnoses are small (<1 cm) and are termed microcarcinomas. Despite this increase in thyroid cancer, there has not been a corresponding increase in deaths from thyroid cancer, which is ~0.5% over 10 years. While most patients with papillary thyroid cancer do very well, rarely this cancer can be aggressive. Because of this, it is likely that some cancers are overtreated. Predictors of aggressive cancers are being sought to help decrease this risk for overtreatment. One such predictor may be the presence of a mutation in a common cancer gene (BRAFV600E mutation). This mutation has been shown to be common in larger papillary thyroid cancers that are more aggressive. This study was done to determine if the BRAFV600E mutation can predict recurrence in papillary thyroid microcancer, and therefore help to guide treatment decisions.

#### THE FULL ARTICLE TITLE

Chen Y et al BRAF<sup>V600E</sup> is correlated with recurrence of papillary thyroid microcarcinoma: a systematic review, multi-institutional primary data analysis, and meta-analysis. Thyroid 2016;26:248-55. Epub January 11, 2016

#### **SUMMARY OF THE STUDY**

A large search was done for studies that reviewed the correlations between BRAF<sup>V600E</sup> and recurrence of papillary

thyroid microcancer. At total of 431 articles were initially screened, but only 4 met criteria for inclusion. These inclusion criteria were papillary thyroid cancer less than 10mm in size, BRAFV600E studies, documentation of clinical remission, and at least 2 years of follow-up. Also, 2 unpublished series were added to the analysis. The sample size of the combined series was 2247 patients (average age of 45-50, 77-88% women) from 6 different datasets of patients. BRAFV600E rate was 40-69% of the patients depending upon the series, with recurrence rates of 10.0% in the BRAF+ group and 4.5% in the BRAF negative group. BRAFV600E mutation status was directly

correlated this ~2-fold increase in the rate of recurrence.

# WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that the presence of the BRAFV600E mutation is correlated with recurrence or papillary microcancers. If this indeed is true, initial treatment could then be tailored to reduce recurrence in higher risk patients, sparing low risk patients from potential side effects of therapy. Prospective trials from the time of nodule evaluation through long-term follow-up will be helpful in confirming the whether the BRAFV600E mutation analysis can predict cancer recurrence.

- Julie Hallanger Johnson, MD

#### **ATA THYROID BROCHURE LINKS**

Thyroid Cancer: <a href="http://www.thyroid.org/thyroid-cancer/">http://www.thyroid.org/thyroid-cancer/</a>

#### **ABBREVIATIONS & DEFINITIONS**

Papillary microcancer: a papillary thyroid cancer smaller than I cm in diameter.

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

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell.

Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

Mutation: A permanent change in one of the genes.

BRAF gene: this is gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.

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#### **THYROID CANCER**

#### Gene mutations and papillary thyroid cancer

#### **BACKGROUND**

The rate of diagnosis of papillary thyroid cancer has increased markedly in the past 20 years. Many cancers have mutations in cancer-associated genes that are thought to have caused the cancer. Analysis of mutations in cancer-associated genes are helpful in making a diagnosis of cancer on a thyroid biopsy sample as well as predicting the risk of recurrence of the cancer after thyroid surgery. One common cancer-associated gene mutation is BRAFV600E. Identification of this mutation in cells of thyroid nodules that are biopsied is said to ensure that the nodule is cancerous. Further, this mutation has been shown to be common in larger papillary thyroid cancers that are more aggressive. However, not all thyroid cancers have this, or any, mutation. The goal of this study were to determine whether the presence of BRAFV600E is associated with more aggressive types of papillary thyroid cancer.

#### THE FULL ARTICLE TITLE

Lin JD et al . Clinical manifestations and gene expression in patients with conventional papillary thyroid carcinoma carrying the BRAF $^{V600E}$  mutation and BRAF pseudogene. Thyroid. March 30, 2016 [Epub ahead of print].

#### **SUMMARY OF THE STUDY**

This study looked at surgical specimens from 62 women and 16 men and normal appearing tissue from "cancer-free" areas in 48 of the patients. Cancers were graded using a standard system. Patients were treated according to the 2009 ATA cancer management guidelines and

were followed for on average for 77 months. The study assessed the presence of BRAFV600E and numerous other tissue markers.

The authors reported that, in patients with papillary thyroid cancer, there was no significant relationship between the presence of BRAF<sup>V600E</sup> and patient age, sex, cancer size, cancer extending outside of the thyroid, presence of multiple cancers, lymph-node spread, distant spread, clinical stage, "risk category," or the likelihood of remaining disease-free during an average follow-up period of 41 months.

## WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Where the presence of BRAFV600E mutations may be helpful in diagnosing papillary thyroid cancer by a needle biopsy, in this study, the presence of BRAFV600E did not help predict whether a cancer would be aggressive in its appearance, tumor stage, or the likelihood of disease-free survival. This study is in conflict with some other studies, so further research is needed to determine the role of BRAFV600E in the management of papillary thyroid cancer.

- Ronald B. Kuppersmith, MD, FACS

#### **ATA THYROID BROCHURE LINKS**

Thyroid Nodules: <a href="http://www.thyroid.org/thyroid-nodules/">http://www.thyroid.org/thyroid-nodules/</a>

Thyroid Surgery: <a href="http://www.thyroid.org/thyroid-surgery/">http://www.thyroid.org/thyroid-surgery/</a>
Thyroid Cancer: <a href="http://www.thyroid.org/thyroid-cancer/">http://www.thyroid.org/thyroid-cancer/</a>

#### **DEFINITIONS**

Papillary thyroid cancer: the most common type of thyroid cancer. There are 3 variants of papillary thyroid cancer: classic, follicular and tall-cell.

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

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.

BRAF gene: this is gene that codes for a protein that is involved in a signaling pathway and is important for cell

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#### THYROID CANCER, continued



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growth. Mutations in the BRAF gene in adults appear to cause cancer.

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a total thyroidectomy. When less is removed, such as in removal of a lobe, it is termed a partial thyroidectomy.

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.

# Thyroid Awareness Monthly Campaigns

The ATA will be highlighting a distinct thyroid disorder each month and a portion of the sales for Bravelets™ will be donated to the ATA. The month of June is **Differentiated Thyroid Cancer**Awareness Month and a bracelet is available through the ATA Marketplace to support thyroid cancer awareness and education related to thyroid disease.



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#### **HYPOTHYROIDISM**

# Obese patients with hypothyroidism may require adjustments of levothyroxine after bariatric surgery

#### **BACKGROUND**

Obesity and primary hypothyroidism are common conditions. The adequate treatment of hypothyroidism depends on the adequate administration of thyroid hormone, mainly levothyroxine. Measurement of the TSH level is used to determine whether patients are receiving the right amount of medicine to replace thyroid hormones. Obese patients usually need higher dose of levothyroxine. The absorption of levothyroxine may be affected by some medications and the diet. Conditions affecting the intestines and stomach can also affect the absorption of levothyroxine. With the increase in severely obese patient, surgeries aiming to cause weight loss (bariatric surgery) have been used more frequently over time. One of the ways that bariatric surgery works is by disrupting the absorption of food. This can also lead to problems in absorbing other substances, including thyroid hormone pills. The goal of this study was to evaluate the dose of levothyroxine needed to keep normal TSH levels in obese patients with hypothyroidism before and after bariatric surgery.

#### THE FULL ARTICLE TITLE

Fierabracci P et al. Weight loss and variation of levothyroxine requirements in hypothyroid obese patients after bariatric surgery. Thyroid. March 16, 2016 [Epub ahead of print].

#### **SUMMARY OF THE STUDY**

A total of 93 patients with obesity and hypothyroidism were studied (90 women and 3 men), with an average age of 48 years. Patients were treated at the Obesity Center of the University of Pisa, in Italy. They had different causes for hypothyroidism: Surgery (21 patients), treatment with radioactive iodine (6 patients) and autoimmune thyroiditis (66 patients). They had three different procedures to lose weight; fifty-four patients had bypass of the stomach (which decreases intake and decreases absorption of some nutrients), 31 patients banding of the stomach (which decreases food intake), and 8 patients had an operation to decrease the size of the stomach by about 70-80%, called sleeve gastrectomy (also to decreases food intake and some digestion of food). Weight and height, blood levels of thyroid hormones, TSH, and leptin (a hormone made in the fat tissue) were measured after stabilizing TSH level before surgery and 28-36 months after the surgery. Body composition (fat vs. lean body mass) was analyzed in 20 patients.

Results of the study showed that the weight of the patients decreased significantly after bariatric surgery. In the whole study group, weight decreased by 34 kg (75 lbs), with significant improvement in body mass index (weight corrected for body size). Leptin levels also decreased significantly. TSH decreased significantly from 1.56 to 0.84 mU/L and no increase in treatment dose was needed in the immediate period following surgery. The daily dose of levothyroxine decreased by 11%, from 130.6 ± 48.5 μg/day to 116.2 ± 38.6 μg/day, however, when corrected for body weight (µg/kg/day) the dose increased by 27%, from 1.1 to 1.4 mcg/kg/day. The interval between surgery and the first dose change was between 8-13 months. The dose of levothyroxine had to be decreased in 50% of the patients. It remained unchanged in 37% of patients and had to be increased in 13% of patients (all with autoimmune thyroid disease). The final dose per weight was not significantly different among the three groups and no differences were observed among the different surgical procedures. The reduction of levothyroxine dose did not correlate with weight loss or the reduction of leptin levels. Also, the levothyroxine dose per kilogram of fat mass was 63% higher, while the levothyroxine dose per kilogram of lean mass did not change, therefore, the authors conclude that the overall decrease of levothyroxine dose after bariatric surgery is due to the decrease in lean mass which occurs after these types of surgeries.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Bariatric surgery does not seem to cause increase requirement of levothyroxine in most patients. Overall, patients may need a decrease of their levothyroxine dose after surgery, following weight loss and lost of lean body mass. Patients with autoimmune hypothyroidism required higher doses of levothyroxine over time, likely because of progression of their disease. Some patients did not need change in levothyroxine dose following surgery. Although there is no need to do preventive changes in dose of treatment, TSH needs to be monitored, in order to allow adequate adjustments in treatment.

- Liuska Pesce, MD

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#### **HYPOTHYROIDISM**, continued

#### ATA THYROID BROCHURE LINKS

Hypothyroidism: <a href="http://www.thyroid.org/">http://www.thyroid.org/</a>

hypothyroidism/

Thyroid Hormone Treatment: <a href="http://www.thyroid.org/">http://www.thyroid.org/</a>

thyroid-hormone-treatment/

Thyroiditis: <a href="http://www.thyroid.org/thyroiditis/">http://www.thyroid.org/thyroiditis/</a>

Thyroid Function Tests: <a href="http://www.thyroid.org/thyroid-function-tests/">http://www.thyroid.org/thyroid-function-tests/</a>

#### **ABBREVIATIONS & DEFINITIONS**

Obesity: Weight that is higher than what is considered as a healthy weight for a given height is described as overweight or obese. Body Mass Index, or BMI, is used as a screening tool for overweight or obesity. In adults, a BMI > 30 kg/m2 is considered in the obese range

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

Primary hypothyroidism: the most common cause of hypothyroidism cause by failure of the thyroid grand.

Levothyroxine  $(T_4)$ : the major hormone produced by the thyroid gland and available in pill form as Synthroid<sup>TM</sup>, Levoxyl<sup>TM</sup>, Tyrosint<sup>TM</sup> and generic preparations.

Thyroid hormone therapy: patients with hypothyroid-ism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal. Replacement therapy means the goal is a TSH in the normal range and is the usual therapy. Suppressive therapy means that the goal is a TSH below the normal range and is used in thyroid cancer patients to prevent growth of any remaining cancer cells.

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.

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).

Bariatric surgery is an operation on the stomach and/or intestines that helps patients with extreme obesity to lose weight. This surgery is an option for people who cannot lose weight by other means or who suffer from serious health problems related to obesity.

Leptin: A hormone made in the fat cells, which goes to the blood and reaches the brain where it sends a message that there is enough energy around

Body Composition: The human body is composed of fat mass, muscle mass (lean body mass) and bone mass. Total body water is included in the measurements of muscle mass.

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#### **GRAVES' DISEASE**

#### Predicting Graves' Disease recurrence

#### **BACKGROUND**

Graves' disease, the most common type of hyperthyroidism in the United States, is an autoimmune disease where the body produces an antibody that attacks and turns on the thyroid. Graves' disease occasionally can go into remission if the antibody decreases or goes away. Patients with Graves' disease can choose between a two general treatment methods: destruction of the thyroid by either surgical removal or radioactive iodine therapy or management with anti-thyroid drugs (ATDs). Treatment with ATDs is used to either prepare the patient for either surgery or radioactive iodine or to treat until a remission occurs. Although many patients choose ATD treatment at initial diagnosis, recurrence rates can be high (~50-70%) following discontinuation of the medication. This study sought to develop a model for predicting recurrence/ remission of Graves' disease.

#### THE FULL ARTICLE TITLE

Vos XG et al. Predicting the Risk of Recurrence Before the Start of Antithyroid Drug Therapy in Patients with Graves' Hyperthyroidism. J. Clin. Endocrinol. Metab. 2016. 101 (4): 1381-1389.

#### **SUMMARY OF THE STUDY**

This study included patients with new onset Graves' disease in The Netherlands. Clinical assessment and genetic testing was performed on all patients before the start of therapy for Graves' disease. All patients were treated with a "block and replace" strategy which consisted of blocking thyroid function with the methimazole and correcting the ensuing hypothyroidism with thyroid hormone replacement to keep the free T4 in the normal range. The medications were discontinued after 1 year and the patients were followed for 2 years to evaluate for

recurrence of their Graves' disease. A total of 37% of the 178 patients had a recurrence. Graves' disease recurrence was associated with younger age, higher blood free T4 levels, larger thyroid gland and higher thyroid antibodies. Several gene types were also associated with higher recurrence rates. The investigators developed a scoring system using clinical factors that they termed "GREAT," which was short for the longer title "Graves' Recurrent Events After Therapy." This score combined with certain genetic factors was termed "GREAT+." They found that the patient's GREAT and GREAT+ scores could predict the likelihood of recurrent Graves' disease after treatment discontinuation. The higher the scores, the higher the rate of recurrence and the addition of genetic testing seemed to be most helpful in patients whose scores put them at medium risk.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Due to the high recurrence rates of Graves' disease following discontinuation of ATD therapy, it would be helpful to know which patients are at greatest risk of recurrence so they may perhaps be able to consider other more permanent treatment options initially, such as surgery or radioiodine. The use of a scoring system may be helpful in predicting this risk so as to provide additional information to the patient to aid in treatment decisions. Genetic testing may improve this prediction to allow more individualized treatments for patients with Graves' disease.

-Whitney Woodmansee, MD

#### **ATA THYROID BROCHURE LINKS**

Hyperthyroidism: <a href="http://www.thyroid.org/">http://www.thyroid.org/</a>

hyperthyroidism/

Graves' disease: <a href="http://www.thyroid.org/graves-disease/">http://www.thyroid.org/graves-disease/</a>

#### **ABBREVIATIONS & DEFINITIONS**

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).

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.

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Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Antibodies: proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses that cause infections. Occasionally the

antibodies get confused and attack the body's own tissues, causing autoimmune disease.

Methimazole: an antithyroid medication that blocks the thyroid from making thyroid hormone. Methimazole is used to treat hyperthyroidism, especially when it is caused by Graves' disease.

September 21-25, 2016

# 86<sup>th</sup> Annual Meeting of the American Thyroid Association

DENVER, COLORADO www.thyroid.org



#### A publication of the American Thyroid Association

# AMERICAN THYROID ASSOCIATION FOUNDED 1923

www.thyroid.org

#### **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.

We look forward to future collaborations and continuing to work together towards the improvement of thyroid education and resources for patients.

#### WHO WE ARE (in alphabetical order)

- American Thyroid Association
- Bite Me Cancer
- Graves' Disease and Thyroid Foundation
- Light of Life Foundation
- ThyCa: Thyroid Cancer Survivors' Association, Inc.
- Thyroid Cancer Canada
- Thyroid Federation International

#### **AMERICAN THYROID ASSOCIATION**

#### www.thyroid.org

ATA Patient Resources: http://www.thyroid.org/patients-portal/

Find a Thyroid Specialist: www.thyroid.org Phone (toll-free): I-800-THYROID e-mail: 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 the Public*. We welcome your support.

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ThyCa: Thyroid Cancer Survivors' Association, Inc.sw www.thyca.org







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# ASSOCIATION www.thyroid.org

#### **ATA Alliance for Thyroid Patient Education**

#### Continued...

#### **BITE ME CANCER**

#### http://www.bitemecancer.org

Bite Me Cancer was formed as a nonprofit foundation in September, 2010, by Nikki Ferraro, who was 17-years old at the time. Nikki was diagnosed with a rare form of thyroid cancer in April 2010 when she was a junior at Chantilly HS in Virginia. Nikki was determined to lead a Relay for Life team just two weeks after her diagnosis. She named the team Bite Me Cancer and experienced immediate success. When Nikki decided to create a foundation a few months later, she wanted to continue the legacy of her team name and thus her foundation became the Bite Me Cancer Foundation.

#### **GRAVES' DISEASE AND THYROID FOUNDATION**

#### www.gdatf.org

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

e-mail: Gravesdiseasefd@gmail.com

e-mail: info@bitemecancer.org

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

email: 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.

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ThyCa: Thyroid Cancer Survivors' Association, Inc.sm

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#### **ATA Alliance for Thyroid Patient Education**

#### Continued...

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

www.thyca.org

Phone (toll-free): 877 588-7904 e-mail: 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.

#### **THYROID CANCER CANADA**

www.thyroidcancercanada.org

Phone: 416-487-8267 Fax: 416-487-0601

e-mail: info@thyroidcancercanada.org

Thyroid Cancer Canada is a non-profit organization founded in 2000. The organization works towards creating an environment in which people who are dealing with thyroid cancer, especially the newly diagnosed, are met with support and information. Their goals & objectives include facilitating communication among thyroid cancer patients, providing credible information about the disease, providing emotional support, and assisting thyroid cancer patients with voicing their needs to health care professionals and those who are responsible for health care policy.

#### THYROID FEDERATION INTERNATIONAL

www.thyroid-fed.org

e-mail: tfi@thyroid-fed.org

Thyroid Federation International (TFI) was established in Toronto in 1995. Thyroid Federation International aims to work for the benefit of those affected by thyroid disorders throughout the world by providing a network of patient support organizations.









ThyCa: Thyroid Cancer Survivors' Association, Inc.sm

www.thyca.org







# Join us for the

September 21-25, 2016

# 86<sup>th</sup> Annual Meeting of the American Thyroid Association

DENVER, COLORADO www.thyroid.org

JOIN EXPERTS AND THOUGHT LEADERS IN FIELD OF THYROIDOLOGY TO HEAR INNOVATIVE TALKS, participate in interactive sessions, and network with friends and colleagues at the ATA Annual Meeting. Held at the Sheraton Denver Downtown Hotel in Denver, Colorado, the ATA meeting is open to all health care professionals interested in broadening their knowledge of the thyroid gland and its disorders. The ATA Program Committee led, by Co-Chairs Peter Arvan and Stephanie Fish, have developed a scientific program to satisfy the interests of all audiences. The Ridgway Trainee Conference, the full-day satellite ultrasound course and focused discussion debate, will be available to accent the robust meeting agenda. Don't miss your opportunity to earn CME credits, develop professionally and foster long lasting connections.

#### ATA 2016 CALL FOR ABSTRACT SUBMISSIONS

**Regular Call:** 

Site Closed – Wednesday, May 25, 2016

**Short Call:** 

Site Opens – Wednesday, July 27, 2016 Site Closes – Wednesday, August 10, 2016

#### REGISTRATION and HOUSING OPEN NOW AT WWW.THYROID.ORG

Agenda, meeting updates, exhibitor and sponsor opportunities available online.

#### SAVE THE DATE FOR THESE UPCOMING ATA MEETINGS:

**87**<sup>th</sup> **Annual Meeting of the American Thyroid Association** – October 18-22, 2017 The Fairmont Empress and Victoria Conference Center, Victoria, BC, Canada

88<sup>th</sup> Annual Meeting of the American Thyroid Association - October 3-7, 2018

Marriott Marquis, Washington, DC

89<sup>th</sup> Annual Meeting of the American Thyroid Association – October 30-November 3, 2019 Sheraton Grand Chicago, Chicago, IL

> Spring Meeting of the American Thyroid Association – May 28-30, 2020 Westin New York at Times Square, New York, NY

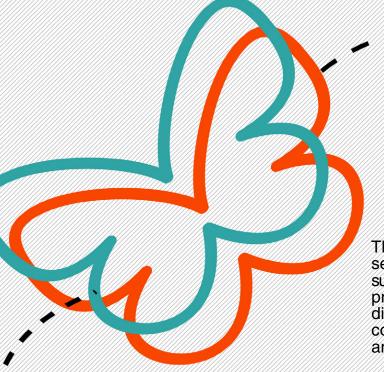


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#### **American Thyroid Association**

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Public & Thyroid Patients
The American Thyroid Association® is dedicated to serving as an educational resource for the public by supporting thyroid research and promoting the prevention, treatment and cure of thyroid-related diseases and thyroid cancer. Help support the continuation of our patient/public education programs and resources including:

Reason

- \*thyroid brochures
- +summarized medical literature
- +endocrinologist referral
- \*monthly newsletters
- +support links
- +patient alliance community
- +health and education forums

# Thyroid Physicians, Scientists & Professionals

The American Thyroid Association® provides outstanding leadership in thyroidology by promoting excellence and innovation in clinical management, research, education, and patient care. Help support thyroid specialists and the development of resources that advance our understanding of thyroid disorders and cancer including:

+clinical practice guidelines

- +position statements
- +early career training
- +research and education grants
- +leadership & service awards
- +community for collaboration
- +continuing education programs
- +peer-review biomedical journals
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- +up to date thyroid news & publications
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**American Thyroid Association** 

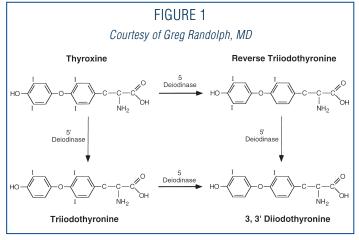
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# **Thyroid Surgery**

#### WHAT IS THE THYROID GLAND?

The thyroid gland is a butterfly-shaped endocrine gland that is normally located in the lower front of the neck. The thyroid's job is to make thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormone helps the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should (Figure 1).

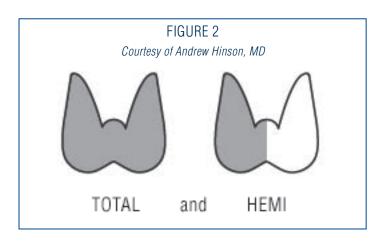


#### GENERAL INFORMATION

Thyroid operations are advised for patients who have a variety of thyroid conditions, including both cancerous and benign (non-cancerous) thyroid nodules, large thyroid glands (goiters), and overactive thyroid glands. There are several thyroid operations that a surgeon may perform, including:

- excisional biopsy removing a small part of the thyroid gland (rarely in use today);
- 2. lobectomy removing half of the thyroid gland (the most frequent way to remove a nodule); (Figure 2)
- 3. total thyroidectomy, which removes all identifiable thyroid tissue. (Figure 2)

There are specific indications for each of these operations. The main risks of a thyroid operation involve possible damage to important structures near the thyroid, primarily the parathyroid glands (which regulate calcium levels) and the recurrent and external laryngeal nerves (which control the vocal cords).



#### **QUESTIONS AND CONSIDERATIONS**

When thyroid surgery is recommended, patients should ask several questions regarding the surgery including:

- 1. Why do I need an operation?
- 2. Are there other means of treatment?
- 3. How should I be evaluated prior to the operation?
- 4. How do I select a surgeon?
- 5. What are the risks of the operation?
- 6. How much of my thyroid gland needs to be removed?
- 7. Will I need to take a thyroid pill after my operation?
- 8. What can I expect once I decide to proceed with surgery?
- 9. What will be my physical restrictions following surgery?
- 10. Will I lead a normal life after surgery?

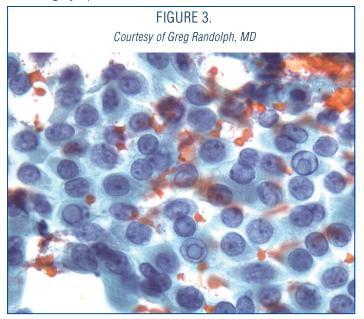
#### WHY DO I NEED AN OPERATION?

The most common reason for thyroid surgery is to remove a thyroid nodule, which has been found to be suspicious through a fine needle aspiration biopsy (see *Thyroid Nodule brochure*). Surgery may be recommended for the following biopsy results:

- 1. cancer (papillary cancer); (Figure 3)
- 2. possible cancer (follicular neoplasm or atypical findings); or
- 3. inconclusive biopsy;
- 4. molecular marker testing of biopsy specimen which indicates a risk for malignancy.

# Thyroid Surgery

Surgery may be also recommended for nodules with benign biopsy results if the nodule is large, if it continues to increase in size or if it is causing symptoms (pain, difficulty swallowing, etc.). Surgery is also an option for the treatment of hyperthyroidism (Grave's disease or a "toxic nodule" (see Hyperthyroidism brochure)), for large and multinodular goiters and for any goiter that may be causing symptoms.



#### ARE THERE OTHER MEANS OF TREATMENT?

Surgery is definitely indicated to remove nodules suspicious for thyroid cancer. In the absence of a possibility of thyroid cancer, there may be nonsurgical options of therapy depending on the diagnosis. You should discuss other options for therapy with your physician who has expertise in thyroid diseases.

### HOW SHOULD I BE EVALUATED PRIOR TO THE OPERATION?

As for other operations, all patients considering thyroid surgery should be evaluated preoperatively with a thorough and comprehensive medical history and physical exam including cardiopulmonary (heart) evaluation. An electrocardiogram and a chest x-ray prior to surgery are often recommended for patients who are over 45 years of age or who are symptomatic from cardiac disease. Blood tests may be performed to determine if a bleeding disorder is present.

Any patients who have had a change in voice or who have had a previous neck operation (thyroid surgery, parathyroid surgery, spine surgery, carotid artery surgery, etc.) and/or who have suspected invasive

thyroid disease should have their vocal cord function evaluated preoperatively. This is necessary to determine whether the recurrent laryngeal nerve that controls the vocal cord muscles is functioning normally and is becoming a norm of practice. Finally, if medullary thyroid cancer is suspected, patients should be evaluated for coexisting adrenal tumors (pheochromocytomas) and for hypercalcemia and hyperparathyroidism.

#### HOW DO I SELECT A SURGEON?

In general, thyroid surgery is best performed by a surgeon who has received special training and who performs thyroid surgery on a regular basis. The complication rate of thyroid operations is lower when the operation is done by a surgeon who does a considerable number of thyroid operations each year. Patients should ask their referring physician where he or she would go to have a thyroid operation or where he or she would send a family member.

#### WHAT ARE THE RISKS OF THE OPERATION?

The most serious possible risks of thyroid surgery include:

- 1. bleeding that can cause acute respiratory distress,
- injury to the recurrent laryngeal nerve that can cause permanent hoarseness, and breathing problems with possible tracheotomy in rare cases if injury is sustained on both sides and
- 3. damage to the parathyroid glands that control calcium levels in the body, causing hypoparathyroidism and hypocalcemia.

These complications occur more frequently in patients with invasive tumors or extensive lymph node involvement, in patients requiring a second thyroid surgery, and in patients with large goiters that go below the collarbone. Overall the risk of any serious complication should be less than 2%. However, the risk of complications discussed with the patient should be the particular surgeon's risks rather than that quoted in the literature. Prior to surgery, patients should understand the reasons for the operation, the alternative methods of treatment, and the potential risks and benefits of the operation (informed consent).

### HOW MUCH OF MY THYROID GLAND NEEDS TO BE REMOVED?

Your surgeon should explain the planned thyroid operation, such as lobectomy (hemi) or total thyroidectomy, and the reasons why such a procedure is recommended.

#### **FURTHER INFORMATION**



# Thyroid Surgery

For patients with papillary or follicular thyroid cancer many, but not all, surgeons recommend total or neartotal thyroidectomy when they believe that subsequent treatment with radioactive iodine might be beneficial. For patients with large (>1.5 cm) or more aggressive cancers and for patients with medullary thyroid cancer, more extensive lymph node dissection is necessary to remove possibly involved lymph node metastases.

Thyroid lobectomy may be recommended for overactive one-sided nodules or for benign one-sided nodules that are causing symptoms such as compression, hoarseness, shortness of breath or difficulty swallowing. A total or near – total thyroidectomy may be recommended for patients with Graves' Disease (see *Hyperthyroidism brochure*) or for patients with enlarged multinodular goiters

### WILL I NEED TO TAKE A THYROID PILL AFTER MY OPERATION?

The answer to this depends on how much of the thyroid gland is removed. If half (hemi) thyroidectomy is performed, there is an 80% chance you will not require a thyroid pill UNLESS you are already on thyroid medication for low thyroid (Hashimoto's thyroiditis). If you have your entire (total) or remaining (completion) thyroidectomy, then you have no internal source of thyroid hormone remaining and you will need lifelong thyroid hormone replacement.

### WHAT CAN I EXPECT ONCE I DECIDE TO PROCEED WITH SURGERY?

Once you have met with the surgeon and decided to proceed with surgery, you will be scheduled for your pre-op evaluation (see above) and will meet with the anesthesiologist (the person who will put you to sleep during the surgery). You should have nothing to eat or drink after midnight on the day before surgery and should leave valuables and jewelry at home. The surgery usually takes 2-21/2 hours, after which time you will slowly wake up in the recovery room. Surgery may be performed through a standard incision in the neck or may be done through a smaller incision with the aid of a video camera (Minimally invasive video assisted thyroidectomy). Under special circumstances, thyroid surgery can be performed with the assistance of a robot through a distant incision in either the axilla or the back of the neck. There may be a surgical drain in the incision in your neck (which will be removed after the surgery) and your throat may be sore because of the breathing tube placed during the operation. Once you are fully awake, you will be moved to a bed in a hospital room where you will be able to eat and drink as you wish. Many patients having thyroid operations are hospitalized

for about 24 hours and can be discharged on the morning following the operation.

## WHAT WILL BE MY PHYSICAL RESTRICTIONS FOLLOWING SURGERY?

Most surgeons prefer a brief limitation is extreme physical activities following surgery. This is primarily to reduce the risk of a post operative neck hematoma (blood clot) and breaking of stitches in the wound closure. These limitations are brief, usually followed by a quick transition back to unrestricted activity. Normal activity can begin on the first postoperative day. Vigorous sports, such as swimming, and activities that include heavy lifting should be delayed for at least ten days to 2 weeks.

### WILL I BE ABLE TO LEAD A NORMAL LIFE AFTER SURGERY?

Yes. Once you have recovered from the effects of thyroid surgery, you will usually be able to doing anything that you could do prior to surgery. Some patients become hypothyroid following thyroid surgery, requiring treatment with thyroid hormone (see Hypothyroidism brochure). This is especially true if you had your whole thyroid gland removed. Thyroid hormone replacement therapy might be delayed for several weeks if you are to receive radioactive iodine (RAI) therapy unless there is a plan for you to receive TSH injection prior to RAI.

#### REFERENCES

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer (2009)

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American Thyroid Association Statement on Surgical Application of Molecular Profiling for Thyroid Nodules: Current Impact on Perioperative Decision Making (2015)

American Thyroid Association Statement on Optimal Surgical Management of Goiter (2014)

American Thyroid Association Statement on Outpatient Thyroidectomy (2013)

American Thyroid Association Consensus Review and Statement Regarding the Anatomy, Terminology, and Rationale for Lateral Neck Dissection in Differentiated Thyroid Cancer (2012)



#### **FURTHER INFORMATION**

Further details on this and other thyroid-related topics are available in the patient information section on the American Thyroid Association® website at www.thyroid.org.