

Clinical THYROIDOLOGY FOR THE PUBLIC



AMERICAN
THYROID
ASSOCIATION
FOUNDED 1923

VOLUME 8 • ISSUE 7 • JULY 2015

www.thyroid.org



EDITOR'S COMMENTS2

THYROID AND WEIGHT3

Fat accumulation within the thyroid may affect the thyroid function

Recent data has clearly shown a role for fat cells in regulating a variety of functions of other cells. The normal thyroid gland contains a small amount of fat cells but their role in regulating thyroid function is unclear. The goal of this study is to evaluate whether there is fat accumulation in the thyroid gland in obese humans and mouse models and whether the changes in the thyroid fat content associated with obesity have an effect on the thyroid function.

Lee MH et al. Thyroid dysfunction associated with follicular cell steatosis in obese male mice and humans. *Endocrinology* 2015;156:1181-93. Epub January 2, 2015.

HYPOTHYROIDISM5

Serum TSH concentrations are associated with cholesterol levels in children and adolescents

In adults, thyroid hormone has a direct effect on cholesterol levels, which increase as the TSH increases and hypothyroidism develops. The few studies testing an association between thyroid function and cholesterol levels among children and adolescents are limited by their small sample sizes. The objective of this study was to test this association between hypothyroidism and cholesterol levels in children and adolescents using a large study sample.

Witte T et al Association between serum thyroid-stimulating hormone levels and serum lipids in children and adolescents: a population-based study of German youth. *J Clin Endocrinol Metab.* March 17, 2015 [ePub ahead of print].

THYROID AND PREGNANCY6

Graves' disease and pregnancy

Hyperthyroidism in young women of reproductive age is most commonly caused by Graves' disease, which is an autoimmune disorder. Autoimmune disorders can improve during pregnancy and get worse in the post-partum period due to changes in the immune system. This study was done to examine the incidence of Graves' disease before, during and after pregnancy in a population.

Andersen SL et al. Hyperthyroidism incidence fluctuates widely in and around pregnancy and is at variance with some other autoimmune diseases: A Danish population based study. *J. Clin. Endocrinol Metab.* 100: 1164-1171. 2015.

THYROID NODULES8

Benign thyroid nodules remain benign during follow-up

Thyroid nodules are very common and increase in frequency with age. The vast majority of nodules are benign. The goals of this study were to determine how often and how quickly benign nodules grow and to determine whether cancer was diagnosed in nodules that grew during a 5-year period of observation.

Durante C et al The natural history of benign thyroid nodules. *JAMA* 2015;313:926-35.

THYROID CANCER.....10

Lenvatinib increases survival in patients with metastatic radioiodine-resistant thyroid cancer

Occasionally, progressive thyroid cancer no longer takes up iodine and becomes "refractory to radioactive iodine." Treatment options are limited for these patients. This study was done to see whether Lenvatinib works to delay the growth of thyroid cancer in these patients. They also looked at overall survival of patients and the side effects.

Schlumberger M et al. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. *N Engl J Med* 2015;372:621-30.

ATA ALLIANCE FOR THYROID PATIENT EDUCATION12

AMERICAN THYROID ASSOCIATION ...15 Graves' Disease



AMERICAN
THYROID
ASSOCIATION

FOUNDED 1923

www.thyroid.org

Editor

Alan P. Farwell, MD
Boston Medical Center
Boston University School of Medicine
88 East Newton St., Boston, MA 02115
Director of Patient Education
American Thyroid Association
e-mail: thyroid@thyroid.org
www.thyroid.org/patients/ct/index.html

Editorial Board

Jessie Block-Galaraza, MD, Albany, NY
Gary Bloom, New York, NY
Jamshid Farahati, MD, Bottrop, Germany
Alina Gavriile-Filip, MD, Boston, MA
Julie E. Hallanger Johnson, MD, Fargo, ND
Ronald Kuppersmith, MD, College Station, TX
Maria Papaleontiou, MD, Ann Arbor, MI
Angela Leung, MD, Los Angeles, CA
Jennifer Rosen, MD, Washington, DC
Wendy Sacks, MD, Los Angeles, CA
Anna M. Sawka, MD, Toronto, ON, Canada
Phillip Segal, MD, Toronto, ON, Canada
Whitney Woodmansee, MD, Boston, MA

American Thyroid Association

President

Robert C. Smallridge, MD

Secretary/Chief Operating Officer

John C. Morris, III, MD

Treasurer

Gregory W. Randolph, MD.

President-Elect

Antonio Bianco, MD, PhD

Past-President

Hossein Gharib, MD

Secretary-Elect

Victor J. Bernet, MD

Executive Director

Barbara R. Smith, CAE
American Thyroid Association
6066 Leesburg Pike, Suite 550
Falls Church, VA 22041
Telephone: 703-998-8890
Fax: 703-998-8893
Email: thyroid@thyroid.org

Designed by

Karen Durland, kdurland@gmail.com

Clinical Thyroidology for the Public

Copyright © 2015 by the American Thyroid Association, Inc. All rights reserved.



CLINICAL THYROIDOLOGY **FOR THE PUBLIC**

A publication of the American Thyroid Association

VOLUME 8 • ISSUE 7 • JULY 2015

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 presented 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 [@thyroidfriends](https://twitter.com/@thyroidfriends) 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*.

July is **Graves' Disease Awareness Month**.

In this issue, the studies ask the following questions:

1. Does fat accumulation in the thyroid in obese individuals affect thyroid function?
2. Does hypothyroidism cause high cholesterol levels in children and adolescents?
3. What is the association between Graves' disease and pregnancy?
4. What is the natural history of benign thyroid nodules?
5. How effective is Levetinib in treating patients with thyroid cancer that doesn't respond to radioactive iodine?

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



Follow us on Facebook



Follow us on Twitter



THYROID AND WEIGHT

Fat accumulation within the thyroid may affect the thyroid function

BACKGROUND

Recent data has clearly shown a role for fat cells in regulating a variety of functions of other cells. The normal thyroid gland contains a small amount of fat cells but their role in regulating thyroid function is unclear. It is known that obesity causes fat accumulation in different organs, such as the liver, which impairs their function. Prior studies have reported thyroid problems in obese patients, however it is not known whether this is due to fat deposition in the thyroid gland. Studies have used obese mouse models to study fat accumulation in the thyroid. The goal of this study is to evaluate whether there is fat accumulation in the thyroid gland in obese humans and mouse models and whether the changes in the thyroid fat content associated with obesity have an effect on the thyroid function.

THE FULL ARTICLE TITLE

Lee MH et al. Thyroid dysfunction associated with follicular cell steatosis in obese male mice and humans. *Endocrinology* 2015;156:1181-93. Epub January 2, 2015.

SUMMARY OF THE STUDY

The study included 35 Korean patients who underwent total thyroidectomy for thyroid cancer; 9 patients had normal weight and 26 patients were obese. The normal thyroid lobe without thyroid cancer was examined for presence of fat deposits between the thyroid follicles and inside the thyroid cells. The study also evaluated the amount and localization of fat in the thyroid gland and the thyroid function of obese mice on a high fat diet compared to lean mice fed a normal diet as well as genetically obese mice with a more severe form of fat accumulation.

The frequency and amount of fat in the thyroid gland was higher in obese patients compared to non-obese patients. Most obese patients showed fat accumulation both inside and outside the thyroid cells. Most non-obese patients did not have a significant amount of fat in their thyroid, only a few patients showing fat accumulation outside the thyroid follicles with or without fat accumulation inside the thyroid cells; fat accumulation only inside the thyroid cells was not noted in non-obese patients. Blood TSH and T₄ levels were not different between obese and non-obese

patients. However, when evaluating the entire group, the blood TSH levels were higher in patients with fat accumulation compared to patients without fat accumulation in their thyroid, suggesting that fat accumulation may impair the thyroid function.

Obese mice fed a high fat diet showed a higher amount of fat outside the thyroid follicles compared to normal mice fed a regular diet, and the amount of fat correlated positively with the blood TSH level. Obese but not normal mice also showed fat accumulation inside the thyroid cells. Obese mice had higher triglyceride and cholesterol levels in their thyroid. Obese mice had higher blood TSH levels and lower blood T₃ and T₄ levels and showed decreased thyroid hormone production compared to normal mice. Similar findings were noted in genetically obese mice. These findings suggest that mice with diet induced and genetically induced obesity have primary thyroid dysfunction.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Obesity results in fat accumulation in the thyroid gland in humans and a mouse model. This may affect the thyroid hormone production and result in hypothyroidism, as suggested by studies in obese mice. Further studies in humans are needed to confirm these findings and evaluate whether weight loss can reverse the thyroid malfunction. Weight loss may be a better treatment option for obese patients with hypothyroidism compared to thyroid hormone replacement treatment.

— Alina Gavriila, MD, MMSC

ATA THYROID BROCHURE LINKS

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

Thyroid Function Tests: <http://www.thyroid.org/blood-test-for-thyroid>

Hypothyroidism: <http://www.thyroid.org/what-is-hypothyroidism>

Thyroid Hormone Treatment: <http://www.thyroid.org/thyroid-hormone-treatment>



THYROID AND WEIGHT, continued

ABBREVIATIONS & DEFINITIONS

Total thyroidectomy: surgery to remove the entire thyroid gland.

Thyroid follicle: small spherical vesicles located in the thyroid gland that are lined with thyroid cells and contain a fluid called colloid; thyroid hormones are produced by the thyroid cells and stored as a precursor named thyroglobulin inside the colloid.

Genetically obese mice: mice with certain changes in their genes (mutations) that predispose them to become obese.

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.

Thyroxine (T₄): the major hormone produced by the thyroid gland. T₄ gets converted to the active hormone T₃ in various tissues in the body.

Triiodothyronine (T₃): the active thyroid hormone, usually produced from thyroxine.

Triglycerides: a major form of body fat.

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





HYPOTHYROIDISM

Serum TSH concentrations are associated with cholesterol levels in children and adolescents

BACKGROUND

Thyroid hormone has a direct effect on cholesterol levels, which increase as the TSH increases and hypothyroidism develops. This association between hypothyroidism and high cholesterol levels has been demonstrated in several large studies, most of which involved adult patients. The few studies testing an association between thyroid function and cholesterol levels among children and adolescents are limited by their small sample sizes. The objective of this study was to test this association between hypothyroidism and cholesterol levels in children and adolescents using a large German population-based study sample.

THE FULL ARTICLE TITLE

Witte T et al Association between serum thyroid-stimulating hormone levels and serum lipids in children and adolescents: a population-based study of German youth. *J Clin Endocrinol Metab.* March 17, 2015 [ePub ahead of print].

SUMMARY OF THE STUDY

This study measured serum TSH and lipid levels, including total cholesterol, LDL cholesterol (bad cholesterol), HDL cholesterol (good cholesterol) and triglycerides in patients identified from the German Health Interview and Examination Survey for Children and Adolescents between 2003 to 2006. A total 6622

children (age range, 3 to 10 years) and 6134 adolescents (age range, 11 to 17 years) were studied. The average age was 7.4 years in children and ~14.4 years in adolescents. Over 95% of the total sample had serum TSH levels in the reference range. Cholesterol levels were not significantly different between boys and girls, nor between children and adolescents. The primary finding was a significant positive association between serum TSH and total and LDL cholesterol and triglycerides. This relationship was sustained when compared between normal, overweight, and obese children.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this large study, there was a significant, positive association between serum TSH and total cholesterol, LDL, and triglyceride concentrations in both children and adolescents. Thus, similar to what is seen in adults, the higher the TSH (and the worse the hypothyroidism), the higher the cholesterol levels. Because the bad long-term health effects of high cholesterol levels, this study suggests that there may be benefits to treating even mild hypothyroidism in children.

— Alan P. Farwell, MD

ATA THYROID BROCHURE LINKS

Hypothyroidism: <http://www.thyroid.org/what-is-hypothyroidism>

ABBREVIATIONS & DEFINITIONS

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

Lipids: the general term used to describe fat molecules in the blood. Examples of blood lipids include

cholesterol, HDL ("good") cholesterol, LDL ("bad") cholesterol and triglycerides.

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.



THYROID AND PREGNANCY

Graves' disease and pregnancy

BACKGROUND

Hyperthyroidism in young women of reproductive age is most commonly caused by Graves' disease. Graves' disease is an autoimmune disorder wherein the individual's immune system makes antibodies that get confused and attack the thyroid and turn it on. These antibodies stimulate the thyroid gland to produce excess thyroid hormone causing hyperthyroidism. It is known that immune function varies during and after pregnancy. Studies have shown that immune function is suppressed during pregnancy, presumably to allow the mother's immune system to "tolerate" the developing baby, and rebounds after delivery during the post-partum period. Autoimmune disorders can improve during pregnancy and get worse in the post-partum period due to changes in the immune system. This study was done to examine the incidence of hyperthyroidism, presumed to be due to Graves' disease, during and around pregnancy in a population and compare to the incidence patterns of other autoimmune disorders.

THE FULL ARTICLE TITLE

Andersen SL et al. Hyperthyroidism incidence fluctuates widely in and around pregnancy and is at variance with some other autoimmune diseases: A Danish population based study. *J. Clin. Endocrinol Metab.* 100: 1164-1171. 2015.

SUMMARY OF THE STUDY

This study was a population based study of Danish women in a national registry. These investigators included all women (403,958) who gave birth to a child in Denmark between 1999 and 2008. They examined the incidence of hyperthyroidism in women 2 years before and 2 years after their first pregnancy. Hyperthyroidism was determined by review of prescriptions for anti-thyroid medications using the National Danish Prescription Register. The authors presumed the prescription for anti-thyroid medications in these women were indicative of Graves disease in this population since the most common cause of hyperthyroidism in women in this age group is Graves' disease and the first choice for treatment of Graves' disease in Denmark is anti-thyroid medications.

Thus, these investigators used prescriptions filled for anti-thyroid medications as a surrogate indicator of Graves' disease. They also examined the incidence of two other autoimmune disorders: rheumatoid arthritis and inflammatory bowel disease. Hyperthyroidism was found around pregnancy in 3673 women (0.9%) with a calculated incidence rate of 65 women per 100,000 per year. They noted a peak in incidence within the first trimester of pregnancy and 7-9 months following delivery. The lowest incidence of hyperthyroidism was in the 3rd trimester and highest incidence (3.8 times the rest of the study time), was in the post partum period. This pattern was not seen in the incidence of rheumatoid arthritis or inflammatory bowel disease.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that the incidence of Graves' disease varies before, during and after pregnancy. Two peaks of increased incidence were observed, one in the first trimester and the second, larger peak post-partum. The higher rates of post-partum hyperthyroidism seen, presumably due to Graves' disease, are consistent with studies demonstrating exacerbation of autoimmune disorders in this time frame.

This study is important for patients in that it provides information to increase awareness of both patients and health care providers of the higher incidence of hyperthyroidism in early pregnancy and post-partum. Patients with Graves' disease or those at risk for autoimmune thyroid disease should be aware of the potential exacerbations during these times and consequently be watchful for signs and symptoms of hyperthyroidism.

—Whitney Woodmansee MD

ATA THYROID BROCHURE LINKS

Thyroid and Pregnancy: <http://www.thyroid.org/thyroid-disease-and-pregnancy>

Graves' disease: <http://www.thyroid.org/what-is-graves-disease>



THYROID AND PREGNANCY, continued

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).

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.

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.

Autoimmune disorders: A diverse group of disorders that are caused by antibodies that get confused

and attack the body's own tissues. The disorder depends on what tissue the antibodies attack. Graves' disease and Hashimoto's thyroiditis are examples of autoimmune thyroid disease. Other Autoimmune disorders include: type I diabetes mellitus, Addison's disease (adrenal insufficiency), vitiligo (loss of pigment of some areas of the skin), systemic lupus erythematosus, pernicious anemia (B12 deficiency), celiac disease, inflammatory bowel disease, myasthenia gravis, multiple sclerosis, and rheumatoid arthritis.

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.



THYROID NODULES

Benign thyroid nodules remain benign during follow-up

BACKGROUND

Thyroid nodules are very common and increase in frequency with age. Most nodules are found during examination for other conditions. Ultrasound imaging is used to identify and characterize the size of thyroid nodules. Larger nodules (over 1–1.5 cm) usually undergo fine-needle aspiration biopsy to determine if cancer is present. Only ~8% of thyroid nodules are cancerous, so the vast majority are non-cancerous (benign). When the nodule is benign, guidelines recommend repeat ultrasound evaluation and repeat biopsy if there is significant growth of the nodule.

The goals of this multicenter Italian study were to determine how often and how quickly benign nodules grow and to determine whether cancer was diagnosed in nodules that grew during a 5-year period of observation.

THE FULL ARTICLE TITLE:

Durante C et al The natural history of benign thyroid nodules. *JAMA* 2015;313:926-35.

SUMMARY OF THE STUDY

The study was performed in four academic centers in Italy. Patients were enrolled between January 2006 and January 2008. Patients underwent complete evaluation, including tests of thyroid function and anti-thyroid antibodies and ultrasound examination for thyroid nodules.

All nodules that had ultrasound features suspicious for malignancy or were solid and larger than 10 mm were biopsied. Suspicious features included hypoechogenicity, microcalcifications, irregular margins, taller-than-wide shape, and intranodular vascularity. When a patient had multiple suspicious nodules, only the largest nodule was biopsied. The size of each nodule was measured in three dimensions. Each patient had annual ultrasound examination and thyroid function tests. When a nodule was found to be suspicious during the follow-up, a repeat biopsy was performed. At the 5-year follow-up, most nodules >1 cm underwent repeat biopsy.

A total of 992 patients were studied, with a total of 1567 nodules. The average age was 52 years, 82% were women, and about half had a family history of thyroid

nodules. In 579 patients, 630 nodules (40% of the total) were classified as benign based on biopsy. Data representing 5 years of follow-up were available for 875 patients. Shorter follow-up occurred in 117 patients; 71 were lost to follow-up, 4 died of unrelated causes, and 42 had thyroidectomy for nodule growth or suspected thyroid cancer.

In 69% of the patients, the nodule size remained stable during follow-up. In 18.5%, one or more nodules shrank. Significant growth of the nodule occurred in 15.4% of patients. Overall, 174 of the 1567 original nodules increased in size, with an average change in the largest diameter of more than 4.9 mm. New nodules were found in 93 patients (9.4%). Multiple nodules, nodule volume, younger age, and male sex were associated with nodule growth, whereas age >60 years was associated with a lower growth rate. Repeat biopsy was performed in 365 cases, with confirmation of the original diagnosis in 99%.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that benign thyroid nodules usually remain stable, as 85% of asymptomatic benign thyroid nodules did not change in size during 5 years of follow-up. Only 15% of nodules grew significantly during a 5-year follow up and a new finding of thyroid cancer was rare. Less than 1% of patients had features of a thyroid cancer during careful follow-up. Of the 7 cancers identified, 2 were in nodules that were not present in the initial evaluation. The data show that benign nodules may grow, but only a small proportion are diagnosed as cancers during follow-up.

— Ronald B. Kuppersmith, MD, FACS

ATA THYROID BROCHURE LINKS

Thyroid Nodules: <http://www.thyroid.org/what-are-thyroid-nodules>

Thyroid Function Tests: <http://www.thyroid.org/blood-test-for-thyroid>

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid-gland>



THYROID NODULES, continued

ABBREVIATIONS & DEFINITIONS

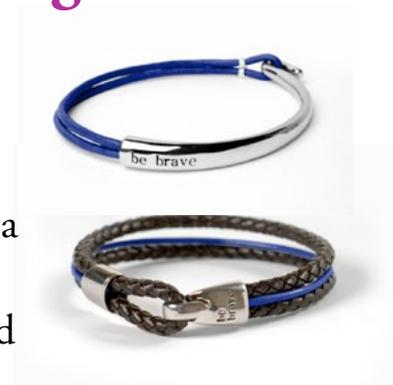
Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

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 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.

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 July is **Graves' Disease Awareness Month** and a bracelet is available through the [ATA Marketplace](#) to support thyroid cancer awareness and education related to thyroid disease.





THYROID CANCER

Lenvatinib increases survival in patients with metastatic radioiodine-resistant thyroid cancer

BACKGROUND

Treatment of thyroid cancer involves surgery to remove the thyroid and any lymph nodes that may contain cancer. This is followed by radioactive iodine therapy in some patients. In addition, patients take thyroid hormone pills for suppression to prevent cancer recurrences. Most people have excellent outcomes; however about 5-10% of patients have worsening thyroid cancer even though they have been treated with surgery, radioactive iodine and thyroid hormone suppression. Often times, the cancer cells do not take up iodine anymore and become “refractory to radioactive iodine”. Treatment options are limited for these patients. Newer chemotherapeutic drugs target the proteins (tyrosine kinases) that cause cells to become cancer cells. These drugs are called tyrosine kinase inhibitors (TKI) and some of them help kill thyroid cancer cells. This study was done to see whether Lenvatinib, a TKI drug, works to delay the growth of thyroid cancer that cannot be removed surgically or is refractory to radioactive iodine. They also looked at overall survival of patients and the side effects.

THE FULL ARTICLE TITLE

Schlumberger M et al. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. *N Engl J Med* 2015;372:621-30.

SUMMARY OF THE STUDY

This is a Phase III clinical study of 392 patients with thyroid cancer refractory to radioactive iodine that demonstrated cancer growth within 12 months of entering the study. Patients were from multiple centers throughout the world and then divided in 2 groups: those that received Lenvatinib and those that received a placebo. Neither the treating doctor, nor the patient knew which pill they were taking. A total of 261 patients received

Lenvatinib and 131 patients got the placebo. Of these patients, 51% had papillary thyroid cancer, 13% poorly differentiated cancer, 18% follicular thyroid cancer, and 18% Hurthle cell carcinoma.

The results showed that fewer patients taking the Lenvatinib showed progression of the thyroid cancer (35%) compared to those on placebo (83.2%). Patients in the Lenvatinib group showed progression of their cancer at 18.3 months compared to 3.6 months in the placebo group. Side effects occurred in 97% of the patients taking Lenvatinib and significant side effects occurred in 30% of the Lenvatinib group compared to 10% in the placebo group. The main side effects of the drug noted in the study include: high blood pressure, diarrhea, fatigue, decreased appetite, skin rash, kidney problems and blood clots. There were 6 deaths in the Lenvatinib group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Because of the excellent results shown in this study, Lenvatinib was approved by the FDA earlier this year for the treatment of progressive thyroid cancer refractory to radioactive iodine. There are now 2 approved targeted chemotherapeutic agents for treating metastatic thyroid cancer refractory to iodine: Sorafenib and Lenvatinib. These drugs can delay progression of thyroid cancer, but also have significant side effects. Therefore, the risks and benefits of TKI treatments such as these drugs must be carefully reviewed with patients before starting them.

—Wendy Sacks, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid-gland>

ABBREVIATIONS & DEFINITIONS

Cancer metastasis: spread of the cancer from the initial organ where it developed to other organs, such as the lungs and bone.

Thyroid hormone 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.



THYROID CANCER, continued

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).

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

Clinical trials: when a new drug is developed, it must undergo an extensive series of steps, called phases, to prove that it is more effective in patients than the drugs

that are currently available to treat the condition. A Phase I trial tests a new drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range and identify side effects. A Phase II trial gives the drug to a larger group of people to see if it is effective and to further evaluate its safety. A Phase III trial gives the drug to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments and collect information that will allow the drug or treatment to be used safely.

Placebo: A placebo is a pill that has no effect on any disease process. In a clinical trial, a placebo is used as a way to determine whether a drug being studied can cause an improvement in a disease.



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/>

Find a Thyroid Specialist: www.thyroid.org

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

continued on next page



AMERICAN
THYROID
ASSOCIATION
FOUNDED 1923



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

e-mail: info@bitemecancer.org

GRAVES' DISEASE AND THYROID FOUNDATION

www.gdatf.org

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

e-mail: 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

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.

continued on next page



AMERICAN
THYROID
ASSOCIATION
FOUNDED 1923



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





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

<http://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.



AMERICAN
THYROID
ASSOCIATION
FOUNDED 1923



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



Graves' Disease

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.

WHAT IS GRAVES' DISEASE?

Graves' disease is caused by a generalized overactivity of the entire thyroid gland (*hyperthyroidism*). It is named for Robert Graves, an Irish physician, who described this form of hyperthyroidism about 150 years ago.

WHAT ARE THE SYMPTOMS OF GRAVES' DISEASE?

• HYPERTHYROIDISM

The majority of symptoms of Graves' disease are caused by the excessive production of thyroid hormones by the thyroid (*see Hyperthyroidism brochure*).

• EYE DISEASE

Graves' disease is the only kind of hyperthyroidism that can be associated with inflammation of the eyes, swelling of the tissues around the eyes and bulging of the eyes (*called Graves' ophthalmopathy*). Although many patients with Graves' disease have redness and irritation of the eyes at some time, less than five percent ever develop enough inflammation of the eye tissues to cause serious or permanent trouble. Patients who have more than very mild eye symptoms do require an evaluation with an eye doctor (*an ophthalmologist*) as well as their endocrinologist.

Eye symptoms most often begin about six months before or after the diagnosis of Graves' disease has been made. Seldom do eye problems occur long after the disease has been treated. In some patients with eye symptoms, hyperthyroidism never develops and, rarely, patients may be hypothyroid. The severity of the eye symptoms is not related to the

severity of the hyperthyroidism. Early signs of trouble might be red or inflamed eyes, a bulging of the eyes due to inflammation of the tissues behind the eyeball or double vision. Diminished vision or double vision are rare problems that usually occur later if at all. We do not know why, but problems with the eyes occur much more often and are more severe in people with Graves' disease who smoke cigarettes.

• SKIN DISEASE

Rarely, patients with Graves' disease develop a lumpy reddish thickening of the skin in front of the shins known as pretibial myxedema. This skin condition is usually painless and relatively mild, but can be painful. Like the eye trouble of Graves' disease, the skin problem does not necessarily begin precisely when the hyperthyroidism starts. Its severity is not related to the level of thyroid hormone.

WHAT CAUSES GRAVES' DISEASE?

• IMMUNE SYSTEM

Graves' disease is triggered by some process in the body's immune system, which normally protects us from foreign invaders such as bacteria and viruses. The immune system destroys foreign invaders with substances called antibodies produced by blood cells known as lymphocytes. Some people inherit an immune system that can cause problems. Their lymphocytes make antibodies against their own tissues that stimulate or damage them. In Graves' disease, antibodies bind to the surface of thyroid cells and stimulate those cells to overproduce thyroid hormones. This results in an overactive thyroid.

• EYE CHANGES

These same antibodies may also be involved in the eye changes seen in Graves' ophthalmopathy, since the receptors on the thyroid may also be found on the surface of cells behind the eye. Physicians have long suspected that severe emotional stress, such as the death of a loved one, can set off Graves' disease in some patients. Dr. Graves himself commented on stressful events in his patients' lives that came several months before the development of hyperthyroidism. However, most patients who develop Graves' disease report no particular recent stress in their lives.

Graves' Disease

HOW IS THE DIAGNOSIS OF GRAVES' DISEASE MADE?

The diagnosis of hyperthyroidism is made on the basis of your symptoms and findings during a physical exam and it is confirmed by laboratory tests that measure the amount of thyroid hormone (*thyroxine, or T4, and triiodothyronine, or T3*) and thyroid-stimulating hormone (*TSH*) in your blood (*see the Hyperthyroidism brochure*). Sometimes your doctor may want you to have a radioactive image, or scan, of the thyroid to see whether the entire thyroid gland is overactive. Your doctor may also wish to do a blood test to confirm the presence of thyroid-stimulating antibodies (*TSI or TRAb*) that cause Graves' disease, but this test is not usually necessary.

Clues that your hyperthyroidism is caused by Graves' disease are the presence of Graves' eye disease (see above), an enlarged thyroid and a history of other family members with thyroid or autoimmune problems. Some relatives may have had hyperthyroidism or an underactive thyroid; others may have other autoimmune diseases including premature graying of the hair (*beginning in their 20's*). Similarly, there may be a history of related immune problems in the family, including juvenile diabetes, pernicious anemia (*due to lack of vitamin B12*) or painless white patches on the skin known as vitiligo.

HOW IS GRAVES' DISEASE TREATED?

The treatment of hyperthyroidism is described in detail in the Hyperthyroidism brochure. Treatment includes antithyroid drugs (*generally methimazole [Tapazole®], although propylthiouracil [PTU]* may be used in rare instances), radioactive iodine and surgery. Although each treatment has its advantages and disadvantages, most patients will find one that is just right for them. Hyperthyroidism due to Graves' disease is, in general, easily controlled and safely treated and treatment is almost always successful.

WHAT WILL BE THE OUTCOME OF TREATMENT?

No matter how your hyperthyroidism is controlled, you will probably eventually develop hypothyroidism (*underactive thyroid*). Hypothyroidism will occur sooner if your thyroid has been treated by radioactive iodine or removed in an operation. Even if you are treated with antithyroid drugs alone, hypothyroidism still can occur.

Because of this natural tendency to progress toward hypothyroidism sometime after you have been hyperthyroid, every patient who has ever had hyperthyroidism due to Graves' disease should have blood tests at least once a year to measure thyroid function. When hypothyroidism occurs, a thyroid hormone tablet taken once a day can treat it simply and safely (*see the Hypothyroidism brochure*).

OTHER FAMILY MEMBERS AT RISK

Because Graves' disease is related to a genetic predisposition, examinations of the members of your family may reveal other individuals with thyroid problems.



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.