HYPERTHYROIDISM Choosing the dose of radioactive iodine that cures hyperthyroidism without causing hypothyroidism Most Graves’ disease patients in the United States are eventually treated with radioactive iodine. Most of the time, this results in permanent hypothyroidism. The goal of this study was determine a method to choose a dose of radioactive iodine that would cure the hyperthyroidism without causing hypothyroidism. Chen DY et al Striving for euthyroidism in radioactive iodine therapy of Graves’ disease: a 12-year prospective, randomized, open-label blinded end point study. Thyroid 2011;21:647-54. Epub May 12, 2011. 

GRAVES’ DISEASE Selenium improves mild Graves’ eye disease Thyroid eye disease (TED) occurs in some form in up to 50% of patients with hyperthyroidism from Graves’ disease. In approximately 15% of patients, TED is progressive and can be very severe. The current study evaluated the effect of two medications in the treatment of mild TED. Marcocci C, et al. Selenium and the Course of Mild Graves’ Orbitopathy. N Engl J Med 2011;364:1920-31. 

HYPOTHYROIDISM AND PREGNANCY Treatment of subclinical hypothyroidism is beneficial in women undergoing in-vitro fertilization treatment Pregnant women with hypothyroidism, either subclinical or overt hypothyroidism, are at increased risk of miscarriages and premature deliveries. The goal of this study was to determine if levothyroxine treatment of infertile women with subclinical hypothyroidism before undergoing in vitro fertilization would decrease the risk of miscarriage. Kim C-H et al. Effect of levothyroxine treatment on in vitro fertilization and pregnancy outcome in infertile women with subclinical hypothyroidism undergoing in vitro fertilization/ intracytoplasmic sperm injection. Fertil Steril 2011; 95:1650-4. Epub December 30, 2010. 

HYPOTHYROIDISM Immune-promoting chemicals can be measured in blood which probably cause the early stages of thyroid damage and hypothyroidism in Hashimoto’s thyroiditis Hashimotos thyroiditis is caused by lymphocytes that produce antibodies that attack the thyroid and destroy the gland. Activated lymphocytes release “chemokines” which are chemicals which cause inflammation in the thyroid, leading to hypothyroidism. This study measured chemokine levels to determine if they could become additional tests which might improve the ability to predict the future course of Hashimoto’s thyroiditis in individual patients. Antonelli A et al Increase of circulating CXCL 9 and CXCL 11 associated with euthyroid or subclinically hypothyroid autoimmune thyroiditis. J Clin Endocrinology and Metab., 2011, 96:1859-63. 

HYPOTHYROIDISM Patients with chronic hepatitis C treated with interferon have a spectrum of different thyroid problems Interferon is a medication used to treat patients with chronic hepatitis C. Treatment with interferon can cause thyroid problems, most often hypothyroidism but also rarely hyperthyroidism. The goal of this study was to evaluate the type of thyroid problem and the immune response in patients with chronic hepatitis C who receive treatment with interferon. Soldevila B et al. A prospective study of T- and B-lymphocyte subpopulations, Th1/Th2 balance and regulatory CD4+CD25+ CD127low/-FoxP3+ T cells in patients with chronic hepatitis C virus infection developing interferon-induced thyroiditis. Clin Endocrinol (Oxf) 2011 May 19. doi: 10.1111/j.1365-2265.2011.04112.x. [Epub ahead of print]. 

THYROID NODULES RET/PTC rearrangement may determine rapid growth of benign thyroid nodules The factors that determine the growth of benign thyroid nodules are largely unknown. Mutations in certain cancer-associated genes, including the RET/PTC gene, can be seen in thyroid cancer. How- ever, mutations in the RET/PTC gene are also commonly found in benign nodules. The goal of this study was to compare the growth of benign nodules that carry the RET/PTC mutation to the growth of benign nodules that do not carry that mutation. Sapio MR et al High growth rate of benign thyroid nodules bearing RET/PTC rearrangements. J Clin Endocrinol Metab 2011;96:E916-9. Epub March 16, 2011. 

THYROID CANCER Increasing rate of BRAF gene mutation in patients with papillary thyroid cancer Mutations in the BRAF gene are seen in a large percentage of papillary cancers. This study looked at presence of mutations in the BRAF gene in papillary cancer over the last 15 years. Mathur et al. Higher rate of BRAF mutation in papillary thyroid cancer over time: A single-institution study Surgical results of thyroid nodules according to management guideline based on BRAF-V600E mutation status. Cancer. Mar 15, 2011[Epub ahead of print] doi:10.1200/jc.2010-1082. 

ATA ALLIANCE FOR THYROID PATIENT EDUCATION Calendar of Events ATA Graves’ Disease Brochure ATA Hyperthyroidism Brochure
EDITOR’S COMMENTS

Welcome to Clinical Thyroidology for Patients. This publication is a collection of summaries of the top articles from the recent medical literature that cover the broad spectrum of thyroid disorders. Clinical Thyroidology for Patients is published on a monthly basis and includes summaries of research studies that were discussed in the previous month’s issue of Clinical Thyroidology, a publication of the American Thyroid Association for physicians. This means that you, the patients, are getting the latest information on thyroid research and treatment almost as soon as your physicians. The Calendar of Events highlights educational forums and support groups that are organized around the country by members of the Alliance for Thyroid Patient Education. The Alliance member groups consist of: the American Thyroid Association, the Graves’ Disease Foundation, the Light of Life Foundation and ThyCa: Thyroid Cancer Survivors Association.

The American Thyroid Association recently came out with guidelines for the management of hyperthyroidism and Graves’ disease. Our patient education brochures have been updated with this latest information. We have included the updated Hyperthyroidism and Graves’ Disease brochures on pages 14 and 16.

In this issue, the studies ask the following questions:

- How do you choose the best dose of radioactive iodine for treatment of Graves’ disease?
- Can selenium help Graves’ eye disease?
- Should women with subclinical hypothyroidism start treatment before staring infertility treatment?
- Can we predict the course of Hashimotos thyroiditis?
- Can we identify which patients on interferon therapy will develop thyroid problems?
- Can we identify which benign thyroid nodules will grow?
- Is the recent increase in thyroid cancer due to increased frequency of gene mutation?

We welcome your feedback and suggestions. Let us know what you want to see in this publication. I hope you find these summaries interesting and informative.

— Alan P. Farwell, MD

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

Choosing the dose of radioactive iodine that cures hyperthyroidism without causing hypothyroidism

BACKGROUND
Graves’ disease is the most common type of hyperthyroidism in the United States. While hyperthyroidism may be treated with antithyroid meds, radioactive iodine or surgery, radioactive iodine is eventually used in ~85% of patients in the United States. Radioactive iodine works by being taken up into the overactive thyroid and destroying the gland. Most of the time, this results in permanent hypothyroidism. Indeed, this is often the goal of treatment. The goal of this study was determine a method to choose a dose of radioactive iodine that would cure the hyperthyroidism without causing hypothyroidism.

THE FULL ARTICLE TITLE:

SUMMARY OF THE STUDY
A total of 529 patients who had Graves’ disease participated in this study from China. The patients were randomly assigned to one of five groups that received different doses of radioactive iodine based on the size of the thyroid and the 24-hour radioactive iodine thyroid uptake. The dose was also adjusted based on a scoring system for six clinical factors, including gland texture, duration of disease, previous use of antithyroid drugs, severity of disease, complications and age. Gland weight was estimated by ultrasound.

The average age of the patients was ~35 years, three fourths were women, the average gland was 2–3-fold enlarged and the average 24-hour radioactive iodine thyroid uptake was about 65%. Using the clinical scoring system to determine the dose of radioactive iodine given, the hyperthyroidism was successfully treated initially in 94% of patients. Only 22% became hypothyroid, but 14% had recurrences of their hyperthyroidism during the 12-year follow-up.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This is an important study for patients with Graves’ disease, since it allows for an increased likelihood that life-long medical therapy will not be needed. The trade-off for less hypothyroidism after a radioactive treatment is an increase in either inadequate treatment or a relapse of the hyperthyroidism, both of which may require a second treatment with radioactive iodine. In this study, ~20% had either persistence or a relapse of the hyperthyroidism, about the same amount of patients that had permanent hypothyroidism. Further studies are needed in the United States before this method can be recommended to patients.

— Alan P. Farwell, MD

ATA THYROID BROCHURE LINKS
Hyperthyroidism: http://thyroid.org/patients/patient_brochures/hyperthyroidism.html
Graves’ disease: http://thyroid.org/patients/patient_brochures/graves.html

continued on next page
HYPERTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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.

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.

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

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).

Radioactive iodine uptake (RAIU): this is a measurement of activity of the thyroid gland and is reported as the percent of a dose of radioactive iodine that is retained in the thyroid gland 24 h after the dose is given. An increase in RAIU usually indicates hyperthyroidism.

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.
GRAVES’ DISEASE

Selenium improves mild Graves’ eye disease

BACKGROUND

Graves’ disease is the most common cause of hyperthyroidism in the United States. Thyroid eye disease (TED) also known as Graves’ ophthalmopathy, occurs in some form in up to 50% of patients with hyperthyroidism from Graves’ disease. TED is mild in the majority of patients and may improve on its own. In approximately 15% of patients, however, TED is progressive and can be very severe. Progressive TED is very difficult to treat. Two medications have been reported to have some effect on the course of TED: pentoxifylline, which causes dilation of blood vessels, and selenium, a mineral found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. The current study evaluated the effect of these two medications in the treatment of mild TED.

THE FULL ARTICLE TITLE:

SUMMARY OF THE STUDY

A total of 159 patients with mild TED were given selenium (100 mcg twice daily), pentoxifylline (600 mcg twice daily) or placebo (twice daily) orally for 6 months. They were then followed for an additional six months after treatment was withdrawn. Patients were evaluated at baseline, 3, 6 and 12 months by an ophthalmologist who determined a clinical activity score that evaluated seven items. They also completed a quality of life questionnaire. The overall outcome at 6 months was significantly better in the group receiving selenium compared to both the placebo group and those receiving pentoxifylline. TED improved in 61% of patients receiving selenium compared with an improvement in 35% of patients receiving pentoxifylline and 36% receiving placebo. TED worsened in 7% receiving selenium, 10% receiving pentoxifylline and 26% receiving placebo. The beneficial effect of selenium persisted for 6 months after treatment was withdrawn, and no adverse effects were noted in patients taking selenium.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The present study provides significant evidence that the use of selenium, an inexpensive and easy to administer medication, provides some degree of protection for those patients with mild TED. Its use should be strongly considered in this group of patients.

— Frank Cranz, MD

ATA THYROID BROCHURE LINKS

Graves’ disease: http://thyroid.org/patients/patient_brochures/graves.html

ABBREVIATIONS & DEFINITIONS

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.

Thyroid eye disease (TED): also known as Graves ophthalmopathy. TED is most often seen in patients with Graves’ disease, but also can be seen with Hashimoto’s thyroiditis. TED includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

Selenium: a mineral found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. It is needed in small amounts by the body.
HYPOTHYROIDISM AND PREGNANCY

Treatment of subclinical hypothyroidism is beneficial in women undergoing in-vitro fertilization treatment

BACKGROUND
Subclinical hypothyroidism, where there is an increase in serum TSH but normal thyroid hormone levels, is common. However, since many patients with subclinical hypothyroidism do not have any symptoms, it is controversial who should be offered treatment. Pregnant women with hypothyroidism, either subclinical or overt hypothyroidism, are at increased risk of miscarriages and premature deliveries. This is true whether the pregnancy occurs naturally or as a result of in-vitro fertilization. Some studies have shown that treatment of subclinical hypothyroidism during pregnancy helps decrease the risk of miscarriage. The goal of this study was to determine if levothyroxine treatment of infertile women with subclinical hypothyroidism before undergoing in-vitro fertilization would decrease the risk of miscarriage.

THE FULL ARTICLE TITLE:

SUMMARY OF THE STUDY
A total of 64 infertile patients with subclinical hypothyroidism participated in this study from Seoul, South Korea. Patients were randomly assigned to receive either levothyroxine or no treatment prior to starting the in-vitro fertilization process.

There was no significant difference in the clinical pregnancy rate between the two groups. However, the miscarriage rate was significantly lower in the levothyroxine treatment group than in the group that was not treated.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study confirms prior studies that found that levothyroxine treatment can decrease the miscarriage rate in women with subclinical hypothyroidism. This is true regardless of how the pregnancy was achieved. In general, all women with subclinical hypothyroidism who are considering pregnancy or who are found to be pregnant should be treated with levothyroxine for the duration of the pregnancy.

— Alan P. Farwell, MD

ABBREVIATIONS & DEFINITIONS

In-vitro fertilization: a procedure when an egg is fertilized outside of the body and then implanted in a woman to achieve a pregnancy.

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

Subclinical Hypothyroidism: a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

Overt Hypothyroidism: clear hypothyroidism and increased TSH and a decreased T4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

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

Levothyroxine: the major hormone produced by the thyroid gland and available in pill form as Levoxyl™, Synthroid™, Levothroid™ and generic preparations.

TSH: Thyroid Stimulating Hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.
HYPOTHYROIDISM

Immune-promoting chemicals can be measured in blood which probably cause the early stages of thyroid damage and hypothyroidism in Hashimoto’s thyroiditis

BACKGROUND
Hashimotos thyroiditis is the most common cause of hypothyroidism in the United States. It is caused by lymphocytes producing antibodies that attack the thyroid and destroy the gland. Some thyroid antibodies, such as TPO antibodies, can be measured in the blood and are useful in diagnosing Hashimoto’s thyroiditis. However, they can also be measured in the blood of individuals who may never develop thyroid problems. While it is unknown what makes antibodies attack the thyroid, the attack begins by the antibody-producing cells secreting chemicals which activate susceptible thyroid and lymphocyte blood cells. These activated thyroid cells and lymphocytes release “chemokines” which are chemicals which cause inflammation in the thyroid, leading to hypothyroidism. Three chemokines, CXCL9, CXCL10 and CXCL11, have been measured in blood, but only CXCL10 has been consistently high in Hashimoto’s patients. This study measured CXCL 9 and 11 to determine if blood levels were higher in Hashimoto’s patients. If so, they could become additional tests which might improve the ability to predict the future course of Hashimoto’s thyroiditis in individual patients.

SUMMARY OF THE STUDY
A total of 141 patients with Hashimoto’s thyroiditis were studied. Most had positive TPO antibodies, hypothyroidism or typical ultrasound features of Hashimotos's thyroiditis. They were compared to patients with negative TPO antibodies, both with and without thyroid problems.

The results were that blood levels of the chemokines CXCL9 and CXCL11 were higher in the Hashimoto’s patients than the two other groups, especially when patients were hypothyroid, had characteristic ultrasound features or were older than 50.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study suggests that blood levels of the chemokines CXCL 9 and 11 may become newer tests to predict which patients with positive TPO antibodies will develop hypothyroidism. This may allow earlier detection and treatment of patients with Hashimoto’s thyroiditis.

— Jerrold Stock, MD

ATA THYROID BROCHURE LINKS
Hypothyroidism: http://thyroid.org/patients/patient_brochures/hypothyroidism.html
Thyroiditis: http://thyroid.org/patients/patient_brochures/thyroiditis.html

ABBREVIATIONS & DEFINITIONS

Hashimotos thyroiditis: the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy the gland.

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.

TPO antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

Lymphocytes: cells of the immune system that produce antibodies to fight infection.

Chemokines: chemicals produced by lymphocytes that cause inflammation in affected tissues. One chemokine, CXCL10, has been reported to be elevated in the blood of patients with Hashimotos’s thyroiditis.
HYPOTHYROIDISM

Patients with chronic hepatitis C treated with interferon have a spectrum of different thyroid problems

BACKGROUND:
Interferon and ribavirin are medications used to treat patients with chronic hepatitis C. It has been known for a while that treatment with interferon can cause thyroid problems, most often hypothyroidism but also rarely hyperthyroidism. This medication is thought to affect the thyroid function through changes in the immune system and also through direct effects on thyroid cells in certain patients. However, the exact mechanisms of how this happens are not known. The goal of this study was to evaluate the type of thyroid problem and the immune response in patients with chronic hepatitis C who receive treatment with interferon and ribavirin.

THE FULL ARTICLE TITLE:

SUMMARY OF THE STUDY:
The study included 120 patients with chronic hepatitis C treated with interferon and ribavirin 11 of whom developed thyroid problems. All patients had normal thyroid function tests and negative antithyroid antibodies before receiving this treatment. The 11 patients who developed thyroid problems were compared to similar patients in the group that did not develop thyroid problems. Among the 11 patients who developed thyroid disease, 9 developed hypothyroidism, 1 developed hyperthyroidism and 1 developed thyroid antibodies but the thyroid function remained normal. The thyroid problems developed in the first 6 months of treatment in the majority of these patients.

Blood immune cells were collected when thyroid disease was detected and analyzed to evaluate changes in the immune system on interferon treatment. The patients who developed thyroid problems had a greater increase in type 1 helper T cells that stimulate and coordinate the immune response in the body. The same immune response was noted in all of the 11 patients who developed thyroid problems.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study shows that patients who develop thyroid problems during treatment with interferon develop a specific immune response that is different than those patients that remain with normal thyroid function. The same immune response occurred whether the patients developed hypothyroidism or hyperthyroidism. Further studies are required to evaluate why how this immune response causes the thyroid problems.

— Alina Gavrila, MD

ATA THYROID BROCHURE LINKS
Hypothyroidism: http://thyroid.org/patients/patient_brochures/hypothyroidism.html
Hyperthyroidism: http://thyroid.org/patients/patient_brochures/hyperthyroidism.html

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**ABBREVIATIONS & DEFINITIONS**

**Immune system:** a system of organs, tissues, and cells in our body that has the role to recognize potentially harmful foreign substances and organisms as well as abnormal body cells and produce antibodies to destroy these factors.

**Thyroid antibodies:** these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

**Type 1 helper T cells:** these are cells of the immune system that that stimulate and coordinate the immune response in the body.

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

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

RET/PTC rearrangement may determine rapid growth of benign thyroid nodules

BACKGROUND

Thyroid nodules are very common in the general population. Up to 10% of these nodules are cancerous and are expected to grow over time. Benign (non-cancerous) nodules can also grow over time. Ultrasound guided fine needle aspiration biopsy of growing nodules help identify the cancerous ones that require surgery. The factors that determine the growth of benign nodules are largely unknown. Mutations in certain cancer-associated genes, including the RET/PTC gene, can be seen in thyroid cancer. However, mutations in the RET/PTC gene are also commonly found in benign nodules. The goal of this study was to compare the growth of benign nodules that carry the RET/PTC mutation to the growth of benign nodules that do not carry that mutation.

THE FULL ARTICLE TITLE:


SUMMARY OF THE STUDY

A total of 125 Italian patients with biopsy-proven benign thyroid nodules were studied. The presence of the RET/PTC mutation in cytology specimens from those nodules was measured. Patients were followed with repeat neck ultrasound studies at 6 months intervals for up to 3 years. Change of thyroid nodule volume was measured at each follow-up visit.

A total of 19 nodules carried the RET/PTC mutation. While all nodules significantly grew at the end of the follow-up period, those with the RET/PTC mutation grew at a faster rate.

WHAT ARE THE IMPLICATIONS OF THIS STUDY

The presence of mutations in the RET/PTC gene increases the growth rate of benign thyroid nodules. Identification of this mutation may help identify which nodules are likely to require surgery even if they are benign. Further studies are needed to identify other factors influencing thyroid nodules growth.

— Mona Sabra, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html

ABBREVIATIONS & DEFINITIONS

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

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.

RET/PTC gene — this is gene that codes for a protein that is involved in a signalling pathway and is important for cell growth. Mutations in the RET/PTC gene are seen in both thyroid cancer and benign thyroid nodules.
THYROID CANCER

Increasing rate of BRAF gene mutation in patients with papillary thyroid cancer

BACKGROUND
The number of patients with thyroid cancer has been rapidly increasing over the past 10 years. The reason for this increase in thyroid cancer is still unclear. Mutations in certain cancer-associated genes can be seen in thyroid cancer. In particular, mutations in the BRAF gene are seen in a large percentage of papillary cancers. This study looked at presence of mutations in the BRAF gene in papillary cancer over the last 15 years.

THE FULL ARTICLE TITLE:

SUMMARY OF THE STUDY
The authors studied 628 patients with papillary cancer seen between 1991–2005. The presence of BRAF mutations were examined in the pathology specimens from these patients and the results separated into the following 5-year periods: 1991–1995, 1996–2000 and 2001–2005. Age at diagnosis, sex, ethnicity and cancer stage were not different between these 3 groups. The frequency of BRAF mutation was higher (88%) in patients diagnosed between 2001–05 as compared to those diagnosed between 1991–1995 (51%) or 96–2000 (43%).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study shows that the frequency of mutations in the BRAF gene in patients with papillary thyroid cancer increased during the last 15 years. This suggests that an increase in BRAF gene mutation may be a cause for the increasing number of patients with papillary thyroid cancer. It is not known what is the cause for this increase in BRAF gene mutation. In general, radiation exposure does not appear to increase the frequency of BRAF gene mutation. Current research is looking at toxic chemicals in our environment as potential causes.

— Jamshid Farahati, MD

ATA THYROID BROCHURE LINKS
Thyroid cancer: http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html

ABBREVIATIONS & DEFINITIONS

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

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 signalling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.
GOAL
The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases.

WHO WE ARE

AMERICAN THYROID ASSOCIATION

www.thyroid.org
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 Patients. We welcome your support.

GRAVES’ DISEASE FOUNDATION

www.ngdf.org
Phone (toll-free): 1-877-NGDF-123 or 643-3123
e-mail: Gravessdiseasefd@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
e-mail: info@checkyourneck.com

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

THYCA: THYROID CANCER SURVIVORS’ ASSOCIATION, INC.

www.thyca.org
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.
# ATA Alliance for Thyroid Patient Education

## CALENDAR OF EVENTS

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

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

- **Saturday, October 29, 2011**
- **1:00 pm – 3:00 pm** — Indian Wells, CA
- **FREE Public Health Forum — Thyroid Disease and You**

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

- **Fall, 2011** — Boston, MA
- **Annual Patient & Family Conference**

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

- **Ongoing** — [www.checkyourneck.com](http://www.checkyourneck.com)
- **Thyroid Cancer Awareness campaign with Cindy Crawford and Brooke Shields**

  - **June 12, 2010** — a previous symposium available online at: [http://www.checkyourneck.com/About-Thyroid-Cancer/Thyroid-Cancer-Symposium-Presentations](http://www.checkyourneck.com/About-Thyroid-Cancer/Thyroid-Cancer-Symposium-Presentations)

  - **Thyroid Cancer Symposium Presentations: What’s New in Thyroid Cancer? A Day for Patients and Their Families**

    Please visit the Light of Life Foundation website to view the Patient Educational Symposium which took place in NYC in 2010. As part of the Patient Educational Program these online presentations provide valuable information in hopes that patients everywhere can gain further information and support about their disease.

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

- **October 14–16, 2011** — Los Angeles, California
- **14th International Thyroid Cancer Survivors’ Conference**
  
  (at the Hilton Los Angeles Airport Hotel, 5711 West Century Boulevard, Los Angeles, California)

- **September, 2011** — Worldwide
- **Thyroid Cancer Awareness Month**
Hyperthyroidism

WHAT IS HYPERTHYROIDISM?
The term hyperthyroidism refers to any condition in which there is too much thyroid hormone produced in the body. In other words, the thyroid gland is overactive. Another term that you might hear for this problem is thyrotoxicosis, which refers to high thyroid hormone levels in the blood stream, irrespective of their source.

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 and at the FDA website www.fda.gov (search for Potassium iodide).

SYMPTOMS
WHAT ARE THE SYMPTOMS OF HYPERTHYROIDISM?
Thyroid hormone plays a significant role in the pace of many processes in the body. These processes are called your metabolism. If there is too much thyroid hormone, every function of the body tends to speed up. It is not surprising then that some of the symptoms of hyperthyroidism are nervousness, irritability, increased perspiration, heart racing, hand tremors, anxiety, difficulty sleeping, thinning of your skin, fine brittle hair and weakness in your muscles—especially in the upper arms and thighs. You may have more frequent bowel movements, but diarrhea is uncommon. You may lose weight despite a good appetite and, for women, menstrual flow may lighten and menstrual periods may occur less often. Since hyperthyroidism increases your metabolism, many individuals initially have a lot of energy. However, as the hyperthyroidism continues, the body tends to break down, so being tired is very common.

Hyperthyroidism usually begins slowly but in some young patients these changes can be very abrupt. At first, the symptoms may be mistaken for simple nervousness due to stress. If you have been trying to lose weight by dieting, you may be pleased with your success until the hyperthyroidism, which has quickened the weight loss, causes other problems.

In Graves’ disease, which is the most common form of hyperthyroidism, the eyes may look enlarged because the upper lids are elevated. Sometimes, one or both eyes may bulge. Some patients have swelling of the front of the neck from an enlarged thyroid gland (a goiter).

CAUSES
WHAT CAUSES HYPERTHYROIDISM?
The most common cause (in more than 70% of people) is overproduction of thyroid hormone by the entire thyroid gland. This condition is also known as Graves’ disease (see the Graves’ Disease brochure for details). Graves’ disease is caused by antibodies in the blood that turn on the thyroid and cause it to grow and secrete too much thyroid hormone. This type of hyperthyroidism tends to run in families and it occurs more often in young women. Little is known about why specific individuals get this disease. Another type of hyperthyroidism is characterized by one or more nodules or lumps in the thyroid that may gradually grow and increase their activity so that the total output of thyroid hormone into the blood is greater than normal. This condition is known as toxic nodular or multinodular goiter. Also, people may temporarily have symptoms of
hyperthyroidism if they have a condition called thyroiditis. This condition is caused by a problem with the immune system or a viral infection that causes the gland to leak stored thyroid hormone. The same symptoms can also be caused by taking too much thyroid hormone in tablet form. These last two forms of excess thyroid hormone are only called thyrotoxicosis, since the thyroid is not overactive.

DIAGNOSIS

HOW IS HYPERTHYROIDISM DIAGNOSED?

If your physician suspects that you have hyperthyroidism, diagnosis is usually a simple matter. A physical examination usually detects an enlarged thyroid gland and a rapid pulse. The physician will also look for moist, smooth skin and a tremor of your fingertips. Your reflexes are likely to be fast, and your eyes may have some abnormalities if you have Graves’ disease.

The diagnosis of hyperthyroidism will be confirmed by laboratory tests that measure the amount of thyroid hormones—thyroxine (T4) and triiodothyronine (T3)—and thyroid-stimulating hormone (TSH) in your blood. A high level of thyroid hormone in the blood plus a low level of TSH is common with an overactive thyroid gland. If blood tests show that your thyroid is overactive, your doctor may want to obtain a picture of your thyroid (a thyroid scan). The scan will find out if your entire thyroid gland is overactive or whether you have a toxic nodular goiter or thyroiditis (thyroid inflammation). A test that measures the ability of the gland to collect iodine (a thyroid uptake) may be done at the same time.

TREATMENT

HOW IS HYPERTHYROIDISM TREATED?

No single treatment is best for all patients with hyperthyroidism. The appropriate choice of treatment will be influenced by your age, the type of hyperthyroidism that you have, the severity of your hyperthyroidism, other medical conditions that may be affecting your health, and your own preference. It may be a good idea to consult with an endocrinologist who is experienced in the treatment of hyperthyroid patients. If you are unconvincing or unclear about any thyroid treatment plan, a second opinion is a good idea.

ANTITHYROID DRUGS

Drugs known as antithyroid agents—methimazole (Tapazole®) or in rare instances propylthiouracil (PTU)—may be prescribed if your doctor chooses to treat the hyperthyroidism by blocking the thyroid gland’s ability to make new thyroid hormone. Methimazole is presently the preferred one due to less severe side-effects. These drugs work well to control the overactive thyroid, bring quick control of hyperthyroidism and do not cause permanent damage to the thyroid gland. In about 20% to 30% of patients with Graves’ disease, treatment with antithyroid drugs for a period of 12 to 18 months will result in prolonged remission of the disease. For patients with toxic nodular or multinodular goiter, antithyroid drugs are sometimes used in preparation for either radiiodine treatment or surgery.

Antithyroid drugs cause allergic reactions in about 5% of patients who take them. Common minor reactions are red skin rashes, hives, and occasionally fever and joint pains. A rarer (occurring in 1 of 500 patients), but more serious side effect is a decrease in the number of white blood cells. Such a decrease can lower your resistance to infection. Very rarely, these white blood cells disappear completely, producing a condition known as agranulocytosis, a potentially fatal problem if a serious infection occurs. If you are taking one of these drugs and get an infection such as a fever or sore throat, you should stop the drug immediately and have a white blood cell count that day. Even if the drug has lowered your white blood cell count, the count will return to normal if the drug is stopped immediately. But if you continue to take one of these drugs in spite of a low white blood cell count, there is a risk of a more serious, even life-threatening infection. Liver damage is another very rare side effect. A very serious liver problem can occur with PTU use which is why this medication should not generally be prescribed. You should stop either methimazole or PTU and call your doctor if you develop yellow eyes, dark urine, severe fatigue, or abdominal pain.

RADIOACTIVE IODINE

Another way to treat hyperthyroidism is to damage or destroy the thyroid cells that make thyroid hormone. Because these cells need iodine to make thyroid hormone, they will take up any form of iodine in your blood stream, whether it is radioactive or not. The radioactive iodine used in this treatment is administered by mouth, usually in a small capsule that is taken just once. Once swallowed, the radioactive iodine gets into your blood stream and quickly is taken up by the overactive thyroid cells. The radioactive iodine that is not taken up by the thyroid cells disappears from the body within days. Over a period of several weeks to several months (during which time drug treatment may be used to control hyperthyroid symptoms), radioactive iodine destroys the cells that have taken it up. The result is that the thyroid or thyroid nodules shrink in size, and the level of thyroid hormone in the blood returns to normal. Sometimes patients will remain hyperthyroid, but usually to a lesser degree than before. For them, a second radiiodine treatment can be given if needed. More often, hypothyroidism (an underactive thyroid) occurs after a few months and lasts lifelong, requiring treatment. In fact, when patients have Graves’ disease, a dose of radioactive iodine is chosen with the goal of making the patient hypothyroid so that the hyperthyroidism does not return in the future. Hypothyroidism can easily be treated with a thyroid hormone supplement taken once a day (see Hypothyroidism brochure).

Radioactive iodine has been used to treat patients for hyperthyroidism for over 60 years and has been shown to be generally safe. Importantly, there has been no clear increase in cancer in hyperthyroid patients that have been treated with radioactive iodine. As a result, in the United States more than 70% of adults who develop hyperthyroidism are treated with radioactive iodine. More and more children over the age of 5 are also being safely treated with radioidine.

SURGERY

Your hyperthyroidism can be permanently cured by surgical removal of most of your thyroid gland. This procedure is best performed by a surgeon who has much experience in thyroid surgery. An operation could be risky unless your hyperthyroidism is first controlled by an antithyroid drug (see above) or a beta-blocking drug (see below). Usually for some days before surgery, your surgeon may want you to take drops of nonradioactive iodine—either Lugol’s iodine or supersaturated potassium iodide (SSKI). This extra iodine reduces the blood supply to the thyroid gland and thus makes the surgery easier and safer. Although any surgery is risky, major complications of thyroid surgery occur in less than 1% of patients operated on by an experienced thyroid surgeon. These complications include damage to the parathyroid glands that surround the thyroid and control your body’s calcium levels (causing problems with low calcium levels) and damage to the nerves that control your vocal cords (causing you to have a hoarse voice).

After your thyroid gland is removed, the source of your hyperthyroidism is gone and you will likely become hypothyroid. As with hypothyroidism that develops after radiiodine treatment, your thyroid hormone levels can be restored to normal by treatment once a day with a thyroid hormone supplement.

BETA-BLOCKERS

No matter which of these three methods of treatment are used for your hyperthyroidism, your physician may prescribe a class of drugs known as the beta adrenergic blocking agents that block the action of thyroid hormone on your body. They usually make you feel better within hours to days, even though they do not change the high levels of thyroid hormone in your blood. These drugs may be extremely helpful in slowing down your heart rate and reducing the symptoms of palpitations, shakes, and nervousness until one of the other forms of treatment has a chance to take effect. Propranolol (Inderal®) was the first of these drugs to be developed. Some physicians now prefer related, but longer-acting beta-blocking drugs such as atenolol (Tenormin®), metoprolol (Lopressor®), nadolol (Corgard®), and Inderal-LA® because of their more convenient once- or twice-a-day dosage.

OTHER FAMILY MEMBERS AT RISK

Because hyperthyroidism, especially Graves’ disease, may run in families, examinations of the members of your family may reveal other individuals with thyroid problems.
Graves’ Disease

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.

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 and at the FDA website www.fda.gov (search for Potassium iodide).
What Causes Graves' 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.

Diagnosis

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.

Treatment

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.
FREE Public Health Forum

Thyroid Experts from the American Thyroid Association and thyroid patients join together to inform the general public, other thyroid patients, and their friends and families about:

**Thyroid Disease and You**

Have you experienced a significant change in:

- Energy?
- Memory?
- Fatigue level after a good night’s sleep?
- Depression?
- Rapid heart beat?
- Restlessness?
- Infertility?
- Weight?
- Hair?
- A lump on your neck?

**Could it be your thyroid?**

Public Forum will be held on Saturday, October 29, 2011

1:00 pm – 3:00 pm • Indian Wells, California

Renaissance Esmeralda Resort and Spa, 44-400 Indian Wells Lane, Indian Wells CA 92210-8708
Phone: 760-773-4444 or toll free at 800-446-9875

Physician experts will discuss thyroid disorders. This program is free and all are welcome, including walk-in-attendees. Reservations are encouraged to ensure we have enough seating. For more information and to register, please e-mail ThyCa at thyca@thyca.org.

Who should attend? Anyone who has had an overactive or underactive thyroid, thyroiditis, a thyroid nodule, thyroid cancer, or a family history of thyroid problems or related disorders, including rheumatoid arthritis, juvenile diabetes, pernicious anemia, or prematurely gray hair (starting before age 30) Please come if you have questions, symptoms, or concerns about a thyroid problem. Receive free educational materials.

Reservations requested. Walk-ins welcome. E-mail thyca@thyca.org to RSVP
(Please indicate in your message the thyroid condition you are most concerned about.)

Online educational information for patients is provided by all members of the ATA Alliance for Patient Education co-sponsoring this forum: ThyCA: Thyroid Cancer Survivors’ Association, Light of Life Foundation, and Graves’ Disease Foundation. Go online to www.thyroid.org and click on “Patients and Public” to access the resources you need.