Clinical THYROIDOLOGY FOR THE PUBLIC

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

VOLUME 8 • ISSUE 8 • AUGUST 2015

www.thyroid.org

HYPOTHYROIDISM

The presence of hypothyroid symptoms is more reliable in diagnosing hypothyroidism in men than in women

Hypothyroidism is a very common condition and affects more women than men. No study has been done to investigate whether symptoms of hypothyroidism are present at the same level in both men and women. This study was done to understand the differences in type and intensity of symptoms that are present in men and women when they are just diagnosed with Hashimoto's thyroiditis.

Carlé A et al. Gender differences in symptoms of hypothyroidism: a population-based DanThyr study. Clin Endocrinol (Oxf). April 2, 2015 [Epub ahead of print].

THYROID CANCER

Increasing trend of thyroid cancer

Thyroid cancer has been rising in recent decades and the cause of this increase is not clear. This study was done to analyze the trends and ways in how thyroid cancer is detected using nearly 80 years of patient data from residents living in Olmsted County, Minnesota in the U.S.

Brito JP et al. The impact of subclinical disease and mechanism of detection on the rise in thyroid cancer incidence: a population-based study in Olmsted County, Minnesota during 1935 through 2012. Thyroid (ePub)

HYPERTHYROIDISM

Could pretreatment with MMI be as effective as rhTSH in treating subclinical toxic multinodular goiter with ^{131}I?

Treatment of a toxic multinodular goiter with radioactive iodine is often difficult the radioactive iodine uptake in these patients is often low. Several approaches have been tried in order to increase the radioactive iodine uptake and make the radioactive iodine more effective in shrinking the goiter. This study compares the effect of 6 weeks of a low-iodine diet with 6 weeks of treatment with methimazole.

Kyrilli A et al Thiamazole pretreatment lowers the ^{131}I activity needed to cure hyperthyroidism in patients with nodular goiter. J Clin Endocrinol Metab. April 13, 2015 [E-pub ahead of print].

HYPERTHYROIDISM

Radioactive iodine increases the risk of strokes in patients with hyperthyroidism or nodular goiter

Radioactive iodine is an effective treatment for hyperthyroidism and nodular goiter. However, studies have suggested that hyperthyroid patients treated with radioactive iodine have an increased risk of having strokes. This study was done to examine whether radioactive iodine itself might contribute to strokes.

la Cour JL et al. Radioiodine therapy increases the risk of cerebrovascular events in hyperthyroid and euthyroid patients. Eur J Endocrinol 2015; 172:771-8.

THYROID CANCER

Radioactive iodine treatment improves survival in adults with intermediate risk papillary thyroid cancer

Radioactive iodine therapy after surgery is being used less frequently and is now generally reserved for patients with more advanced or aggressive cancers. The decision to use radioactive iodine depends on a risk assessment done after surgery. This study aims to evaluate overall survival in patients with intermediate risk papillary cancer treated with radioactive iodine or without radioactive iodine.

Ruel E. Adjuvant Radioactive Iodine Therapy Is Associated With Improved Survival for Patients with Intermediate-Risk Papillary Thyroid Cancer. J Clin Endocrine Metab April, 2015;100:1529-36.

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CLINICAL THYROIDOLOGY **FOR THE PUBLIC**
A publication of the American Thyroid Association
VOLUME 8 • ISSUE 8 • AUGUST 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 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*.

August is Thyroid and Pregnancy Awareness Month.

In this issue, the studies ask the following questions:

1. Do men and women have different symptoms of hypothyroidism?
2. Why is thyroid cancer increasing in frequency?
3. What are the options to improve the effectiveness of radioactive iodine therapy in toxic nodular goiters?
4. Does radioactive iodine therapy cause strokes?
5. Does radioactive iodine therapy have a role in the treatment of intermediate risk thyroid cancer patients?

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

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HYPOTHYROIDISM

The presence of hypothyroid symptoms is more reliable in diagnosing hypothyroidism in men than in women

BACKGROUND

Hypothyroidism is a very common condition and affects more women than men. The most common cause of hypothyroidism is Hashimotos thyroiditis, an autoimmune condition. The symptoms of hypothyroidism are many and can have a significant impact in quality of life. Most symptoms are non-specific and the is no one diagnostic symptom for hypothyroidism. Many studies show that a proportion of hypothyroid patients who take thyroid hormone and are considered to have normal thyroid hormone levels still continue to report symptoms that are consistent with hypothyroidism. As a result of this, many patients request to be treated with nonstandard therapies, with the hope of finding complete relief of such symptoms.

No study has been done to investigate whether symptoms of hypothyroidism may be different in men and women when they are first diagnosed, or whether these symptoms present at the same level in both sexes. This study was done to understand the differences in type and intensity of symptoms that are present in men and women when they are just diagnosed with Hashimoto's thyroiditis.

THE FULL ARTICLE TITLE

Carlé A et al. Gender differences in symptoms of hypothyroidism: a population-based DanThyr study. Clin Endocrinol (Oxf). April 2, 2015 [Epub ahead of print].

SUMMARY OF THE STUDY

This study was done in Denmark and included patients who had just been diagnosed with hypothyroidism while they were participating in a DanThyr study which was designed to study iodine intake and thyroid disease in that country. Once a patient was identified as having hypothyroidism through their blood work with an elevated TSH and a low free thyroxine level, their medical records were reviewed to confirm the new diagnosis of Hashimoto's thyroiditis. A total of 147 patients participated in this study. The investigators also recruited volunteers that were very similar in age, area of origin and gender, but that had normal thyroid hormone levels, so that they could be compared to the patients in the study.

All participants (patients and normal volunteers) completed a questionnaire regarding hypothyroid symptoms present in the last 12 months. These survey also included questions about neck symptoms such as trouble swallowing due to an enlarged thyroid (goiter). In total, 140 patients and 560 normal volunteers were included and 16% of them were men.

In the group of the hypothyroid patients, 94.9% of women and 91.3% of men reported at least one symptom. The most common symptoms were fatigue (80.6%), dry skin (62.1%) and difficulty breathing (51.4%). In the normal volunteers, 73.7% of women and 51.1% of men also reported at least one hypothyroid symptom. In this group, the following symptoms were much more significantly present in women than men: fatigue, difficulty breathing, dry skin, mood changes, palpitations, constipation and the sensation of "something in the throat".

When the data from all participants was analyzed together (males and females, patients and controls), it was seen that the presence of symptoms was indicative of hypothyroidism. However, the data also showed that men with two to three hypothyroid symptoms were likely to have hypothyroidism, but women reporting two to three symptoms were likely to have normal thyroid levels.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this study, the presence of hypothyroid symptoms did not differ significantly between men and women with hypothyroidism. However, it was also shown that normal women were significantly more likely than normal men to report hypothyroid symptoms. Therefore, the presence or absence of symptoms is more reliable in diagnosing hypothyroidism in men than in women. Another implication of this study is that since so many patients who do not have hypothyroidism report symptoms consistent with such, complaints of persistent symptoms even after the treatment of hypothyroidism would be very common especially in female patients.

— Jessie Block-Galarza, MD.

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HYPOTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

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

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

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

ABBREVIATIONS & DEFINITIONS

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

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).

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

Thyroxine (T_4): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

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THYROID CANCER

Increasing trend of thyroid cancer

BACKGROUND

Thyroid cancer has been rising in recent decades and the cause of this increase is not clear. Some have suggested that this may perhaps be related to the increased use of radiology studies (like CT scans) that detect very small cancers. These very small thyroid cancers may not significantly impact health outcomes, but managing them contributes to the rising costs of healthcare since most patients will require surgery and all patients will require ongoing monitoring and medical follow-up. This study was done to analyze the trends and ways in how thyroid cancer is detected using nearly 80 years of patient data from residents living in Olmsted County, Minnesota in the U.S.

THE FULL ARTICLE TITLE

Brito JP et al. The impact of subclinical disease and mechanism of detection on the rise in thyroid cancer incidence: a population-based study in Olmsted County, Minnesota during 1935 through 2012. Thyroid (ePub)

SUMMARY OF THE STUDY

This study used information from the Rochester Epidemiology Project, a database of medical records of patients between 1935-2012 living in Olmsted County, Minnesota. During the study period from 1935-2012, there were 476 cases of thyroid cancer. Only 64% had come to attention because of symptoms in the neck or if a physician felt a lump in the neck. The remaining 32% were discovered because of other tests done, including radiologic imaging studies, in patients who had no local neck symptoms. The frequency of new thyroid cancer cases increased steadily from 1935 until 1970, when the number of new thyroid cancer patients in each year remained stable until 1990. However, the frequency of new cases again increased between 1990-2012. While the frequency of new thyroid cancers found because of symptoms or a neck lump remained stable throughout the nearly 80 years, the thyroid cancers identified by imaging studies were the ones which steadily increased. Furthermore, those cancer which were less aggressive tended to be the ones which were becoming more common. Overall, despite the increased rate of diagnosing thyroid cancer, only 2.3% of patients died from their thyroid cancer. This figure has been stable when comparing between those with the disease during the 1930s vs. those in the 2000s.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The reasons for why thyroid cancer has been increasing in recent decades are controversial. The investigators suggest that the increasing common use of radiologic imaging studies done for other reasons, which detected thyroid cancers that were more likely to be without symptoms in this study, is one of the major reasons. Since the rate of death from thyroid cancer has remained completely stable despite this, one can question whether finding occult thyroid cancers necessarily impacts a person's health. Others have also suggested that thyroid autoimmunity, iodine nutrition, environmental exposures, genetic factors, variable access to medical care, treatment patterns, and obesity may also be important reasons that explain why thyroid cancer has become more common. More research is needed to better understand the complexities related to the rising trend of thyroid cancer observed in recent decades.

— Angela M. Leung, MD, MSc

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

Database: collection of patient information gathered over many years used to analyze certain trends in medical conditions

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HYPERTHYROIDISM

Could pretreatment with MMI be as effective as rhTSH in treating subclinical toxic multinodular goiter with ^{131}I?

BACKGROUND

A multinodular goiter is an enlarged thyroid gland containing several nodules that are overactive. In the United States, this is most commonly seen in older patients and in immigrant patients coming from areas of iodine deficiency. This can often lead to excess production of thyroid hormone (hyperthyroidism) by the nodules. Even though surgery is an option, in patients who refuse surgery or have increased risks for surgery, treatment with radioactive iodine is reasonable. Because the radioactive iodine uptake in these patients is often low, several approaches have been tried in order to increase the radioactive iodine uptake and make the radioactive iodine more effective in shrinking the goiter. Increasing TSH levels by treating with recombinant human TSH has been shown to be effective but is expensive. Alternatively, TSH levels can be increased by treating with antithyroid drugs or a low iodine diet for a period of time before the radioactive iodine. This study compares the effect of 6 weeks of a low-iodine diet with 6 weeks of treatment with an antithyroid medication called methimazole.

THE FULL ARTICLE TITLE

Kyrilli A et al Thiamazole pretreatment lowers the ^{131}I activity needed to cure hyperthyroidism in patients with nodular goiter. J Clin Endocrinol Metab. April 13, 2015 [E-pub ahead of print].

SUMMARY OF THE STUDY

The study included patients referred to the Nuclear Medicine department at Erasme Hospital in Belgium with mild hyperthyroidism due to a multinodular goiter. Patients were randomly assigned to receive either 6 weeks of a low-iodine diet or 6 weeks of methimazole. Urine iodine levels and thyroid volumes were measured before treatment and 6 weeks after pretreatment. The dose of radioactive iodine was calculated and the radioactive iodine uptake was measured for each patient.

The authors found that in patients who took methimazole treatment for 6 weeks the average radioactive iodine uptake doubled, reducing the calculated radioactive iodine dose by a third. Treatment with a low-iodine diet for 6 weeks did not affect the radioactive iodine uptake. Approximately 30% of the patients who took methimazole became hypothyroid after the radioactive iodine treatement.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study is important because it shows that methimazole can be used to increase radioactive iodine uptake in patients with mild hyperthyroidism due to a multinodular goiter. However, this study was short and one third of patients developed an underactive thyroid. Therefore, a longer, larger and more closely monitored trial would be beneficial in determining the safety and efficacy of this treatment method as compared to current treatment options.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

Goiter: http://www.thyroid.org/what-is-a-goiter

Hyperthyroidism: http://www.thyroid.org/what-is-hyperthyroidism

Radioactive Iodine Therapy: http://www.thyroid.org/radioactive-iodine

DEFINITIONS AND ABBREVIATIONS

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

Toxic nodular goiter: 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 in the blood is greater than normal.

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HYPERTHYROIDISM, continued

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

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.

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

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.

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.

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HYPERTHYROIDISM

Radioactive iodine increases the risk of strokes in patients with hyperthyroidism or nodular goiter

BACKGROUND

The thyroid is a unique organ because it absorbs iodine, which it uses to make the thyroid hormones. Since most other cells in the body do not concentrate iodine, doctors are able to use radioactive iodine to treat hyperthyroidism or a nodular goiter without affecting other organs in the body. Radioactive iodine is given in the form of a capsule, is rapidly incorporated into the thyroid cells and, over time, destroys the thyroid calls and decreases the thyroid hormone levels. However, studies have suggested that hyperthyroid patients treated with radioactive iodine have an increased risk of having strokes. Until now this was felt to be from the hyperthyroidism itself or from the hypothyroidism that results after radioactive iodine therapy. This study was done to examine whether radioactive iodine itself might contribute to strokes.

THE FULL ARTICLE TITLE

la Cour JL et al. Radioiodine therapy increases the risk of cerebrovascular events in hyperthyroid and euthyroid patients. Eur J Endocrinol 2015; 172:771-8.

SUMMARY OF THE STUDY

The authors studied 5022 subjects 18 years of age or older who had been treated with radioactive iodine for hyperthyroidism (4000 patients) or nodular goiter (1022 patients) between 1975 and 2008 at three university hospitals in Denmark. Each patient was compared to 4 randomly selected normal volunteers without thyroid problems (total 20,540) who did not receive radioactive iodine. Patients were followed from the date of radioactive iodine treatment as to the number strokes that occurred.

The average age of subjects was 61 years, 14.3% of them were men and the average length of follow-up was 11.5 years. Even when other preexisting medical conditions were considered, radioactive iodine-treated subjects still had a 1.18 times higher risk of having a stroke when compared to normal volunteers. The risk was higher in both hyperthyroid (1.17 times) and nodular goiter (1.21 times) patients.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These results suggest that patients treated with radioactive iodine for hyperthyroidism or nodular goiter may have an increased risk of strokes. While further study is needed, the authors suggest that the radiation from radioactive iodine therapy affect the large arteries in the neck that supply blood to the brain thus increasing the risk of a stroke.

— Philip Segal, MD

ATA THYROID BROCHURE LINKS

Hyperthyroidism: http://www.thyroid.org/what-is-hyperthyroidism

Radioactive Iodine Therapy: http://www.thyroid.org/radioactive-iodine

Goiter: http://www.thyroid.org/what-is-a-goiter

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.

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

HYPERTHYROIDISM, 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).

Stroke: a clinical syndrome caused by disruption of blood supply to the brain. A stroke may be caused by a clogged artery in the brain or the vessels in the neck that supply the brain (ischemic stroke) or from bleeding in the brain (hemorrhagic stroke).

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 August is **Thyroid and Pregnancy Awareness Month** and a bracelet is available through the ATA Marketplace to support thyroid cancer awareness and education related to thyroid disease.

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THYROID CANCER

Radioactive iodine treatment improves survival in adults with intermediate risk papillary thyroid cancer.

BACKGROUND

Papillary thyroid cancer the fastest rising cancer in women. Treatment is primarily surgery to remove the thyroid. Radioactive iodine therapy after surgery is being used less frequently and is now generally reserved for patients with more advanced or aggressive cancers. The decision to use radioactive iodine depends on a risk assessment done after surgery. Low risk patients have smaller cancers and no spread of the cancer to the lymph nodes in the neck. Radioactive iodine is not typically necessary in these patients as there is an excellent prognosis anyway. High risk patients have larger and/or multiple cancers in the thyroid and obvious spread of the cancer to the lymph nodes in the neck as well as outside of the neck and clearly benefit from radioactive iodine. Intermediate risk patients have in-between size and the spread to the lymph nodes can be seen only with a microscope. It is unclear what benefit radioactive iodine adds to these patients. This study aims to evaluate overall survival in patients with intermediate risk papillary cancer treated with radioactive iodine or without radioactive iodine.

THE FULL ARTICLE TITLE

Ruel E. Adjuvant Radioactive Iodine Therapy Is Associated With Improved Survival for Patients with Intermediate-Risk Papillary Thyroid Cancer. J Clin Endocrine Metab April, 2015;100:1529-36.

SUMMARY OF THE STUDY

A total of 21,870 patients with intermediate risk papillary thyroid cancer within the National Cancer Database from 1998-2006 were reviewed. Overall survival was calculated as time to death or last follow-up. A total of 15,418 patients (70.5%) received radioactive iodine and 6452 patients (29.5%) did not. The follow-up was 6 years on average, 14 years at longest. A total of 730 (5%) patients who received radioactive iodine died and 424 (7%) who did not receive radioactive iodine died. Most patients were alive in 2006, so an average survival time was not calculated.

A total of 12,612 patients were younger than age 45 and 71.4% of them received radioactive iodine. In this younger group, there were 109 deaths (1%) in the radioactive iodine group, and 66 deaths (2%) in the no radioactive iodine group.

A total of 2122 patients were above age 65 years. In this older group, 1414 (66.6%) received radioactive iodine with 379 deaths (27%) and there were 222 deaths (31%) in the no radioactive iodine group. The average overall survival was 140 months in the radioactive iodine group and 128 months in the no- radioactive iodine group. Radioactive iodine was associated with a 29% reduced risk of death, and in the subgroup under age 45, there was a 36% reduced risk of death.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that radioactive iodine use was associated with improved overall survival in both young (under age 45) and older patients (65 years and older) with intermediate risk papillary thyroid cancer. Young patients with intermediate risk papillary thyroid cancer had a low death rate, but with the large number of patients in this study, the difference between 1% death rate in the radioactive iodine treatment group and 2% in the no radioactive iodine group was significant.

— Julie Hallanger Johnson, MD

ATA THYROID BROCHURE LINKS

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

Radioactive Iodine Therapy: http://www.thyroid.org/radioactive-iodine

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid.

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

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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.

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checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

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

Thyroid Federation International

Thyroid Cancer Canada
Cancer de la thyroïde Canada

BITE ME cancer
attitude is everything

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

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Light of Life Foundation checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

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

Thyroid Federation International

Thyroid Cancer Canada
Cancer de la thyroïde Canada

BITE ME cancer® attitude is everything.

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.

Thyroid Disease and Pregnancy

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 ARE THE NORMAL CHANGES IN THYROID FUNCTION ASSOCIATED WITH PREGNANCY?

HORMONE CHANGES. A normal pregnancy results in a number of important physiological and hormonal changes that alter thyroid function. These changes mean that laboratory tests of thyroid function must be interpreted with caution during pregnancy. Thyroid function tests change during pregnancy due to the influence of two main hormones: human chorionic gonadotropin (hCG), the hormone that is measured in the pregnancy test and estrogen, the main female hormone. HCG can weakly turn on the thyroid and the high circulating hCG levels in the first trimester may result in a slightly low TSH (called subclinical hyperthyroidism). When this occurs, the TSH will be slightly decreased in the first trimester and then return to normal throughout the duration of pregnancy (see Table 1). Estrogen increases the amount of thyroid hormone binding proteins in the serum which increases the total thyroid hormone levels in the blood since >99% of the thyroid hormones in the blood are bound to these proteins. However, measurements of "Free" hormone (that not bound to protein, representing the active form of the hormone) usually remain normal. The thyroid is functioning normally if the TSH, Free T4 and Free T3 are all normal throughout pregnancy.

SIZE CHANGES. The thyroid gland can increase in size during pregnancy (enlarged thyroid = goiter). However, pregnancy-associated goiters occur much more frequently in iodine-deficient areas of the world. It is relatively uncommon in the United States, which is thought to be relatively iodine-sufficient. If very sensitive imaging techniques (ultrasound) are used, it is possible to detect an increase in thyroid volume in some women. This is usually only a 10-15% increase in size and is not typically apparent on physical examination by the physician. However, sometimes a significant goiter may develop and prompt the doctor to measure tests of thyroid function.

WHAT IS THE INTERACTION BETWEEN THE THYROID FUNCTION OF THE MOTHER AND THE BABY?

For the first 10-12 weeks of pregnancy, the baby is completely dependent on the mother for the production of thyroid hormone. By the end of the first trimester, the baby's thyroid begins to produce thyroid hormone on its own. The baby, however, remains dependent on the mother for ingestion of adequate amounts of iodine, which is essential to make the thyroid hormones. The World Health Organization recommends iodine intake of 200 micrograms/day during pregnancy to maintain adequate thyroid hormone production. The normal diet in the United States contains sufficient iodine so additional iodine supplementation is rarely necessary.

HYPERTHYROIDISM & PREGNANCY

WHAT ARE THE MOST COMMON CAUSES OF HYPERTHYROIDISM DURING PREGNANCY?

Overall, the most common cause (80-85%) of maternal hyperthyroidism during pregnancy is Graves' disease (see *Graves' Disease brochure*) and occurs in 1 in 1500 pregnant patients. In addition to other usual causes of hyperthyroidism (see *Hyperthyroidism brochure*), very high levels of hCG, seen in severe forms of morning sickness (hyperemesis gravidarum), may cause transient hyperthyroidism. The diagnosis of hyperthyroidism can be somewhat difficult during pregnancy, as 123I thyroid scanning is contraindicated during pregnancy due to the small amount of radioactivity, which can be concentrated by the baby's thyroid. Consequently, diagnosis is based on a careful history, physical exam and laboratory testing.

WHAT ARE THE RISKS OF GRAVES' DISEASE/ HYPERTHYROIDISM TO THE MOTHER?

Graves' disease may present initially during the first trimester or may be exacerbated during this time in a woman known to have the disorder. In addition to the classic symptoms associated with hyperthyroidism, inadequately treated maternal hyperthyroidism can result in early labor and a serious complication known as pre-eclampsia. Additionally, women with active Graves' disease during pregnancy are at higher risk of developing very severe hyperthyroidism known as thyroid storm. Graves' disease often improves during the third trimester of pregnancy and may worsen during the post partum period.

Thyroid Disease and Pregnancy

WHAT ARE THE RISKS OF GRAVES' DISEASE/ HYPERTHYROIDISM TO THE BABY?

The risks to the baby from Graves' disease are due to one of three possible mechanisms:

1) UNCONTROLLED MATERNAL HYPERTHYROIDISM: Uncontrolled maternal hyperthyroidism has been associated with fetal tachycardia (fast heart rate), small for gestational age babies, prematurity, stillbirths and possibly congenital malformations.This is another reason why it is important to treat hyperthyroidism in the mother.

2) EXTREMELY HIGH LEVELS OF THYROID STIMULATING IMMUNOGLOBLULINS (TSI): Graves' disease is an autoimmune disorder caused by the production of antibodies that stimulate thyroid gland referred to as thyroid stimulating immunoglobulins (TSI). These antibodies do cross the placenta and can interact with the baby's thyroid. Although uncommon (2-5% of cases of Graves' disease in pregnancy), high levels of maternal TSI's, have been known to cause fetal or neonatal hyperthyroidism. Fortunately, this typically only occurs when the mother's TSI levels are very high (many times above normal). Measuring TSI in the mother with Graves' disease is often done in the third trimester.

   In the mother with Graves' disease requiring antithyroid drug therapy, fetal hyperthyroidism due to the mother's TSI is rare, since the antithyroid drugs also cross the placenta. Of potentially more concern to the baby is the mother with prior treatment for Graves' disease (for example radioactive iodine or surgery) who no longer requires antithyroid drugs. It is very important to tell your doctor if you have been treated for Graves' Disease in the past so proper monitioring can be done to ensure the baby remains healthy during the pregnancy.

3) ANTI-THYROID DRUG THERAPY (ATD). Methimazole (Tapazole) or propylthiouracil (PTU) are the ATDs available in the United States for the treatment of hyperthyroidism (see *Hyperthyroidism brochure*). Both of these drugs cross the placenta and can potentially impair the baby's thyroid function and cause fetal goiter. Historically, PTU has been the drug of choice for treatment of maternal hyperthyroidism, possibly because transplacental passage may be less than with Tapazole. However, recent studies suggest that both drugs are safe to use during pregnancy. It is recommended that the lowest possible dose of ATD be used to control maternal hyperthyroidism to minimize the development of hypothyroidism in the baby or neonate. Neither drug appears to increase the general risk of birth defects.

   Overall, the benefits to the baby of treating a mother with hyperthyroidism during pregnancy outweigh the risks if therapy is carefully monitored.

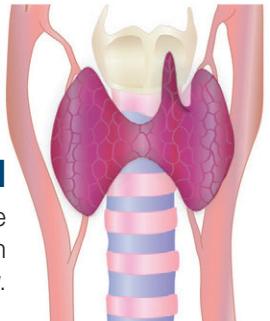
WHAT ARE THE TREATMENT OPTIONS FOR A PREGNANT WOMAN WITH GRAVES' DISEASE/ HYPERTHYROIDISM?

Mild hyperthyroidism (slightly elevated thyroid hormone levels, minimal symptoms) often is monitored closely without therapy as long as both the mother and the baby are doing well. When hyperthyroidism is severe enough to require therapy, anti-thyroid medications are the treatment of choice, with PTU being the historical drug of choice. The goal of therapy is to keep the mother's free T4 and free T3 levels in the high-normal range on the lowest dose of antithyroid medication. Targeting this range of free hormone levels will minimize the risk to the baby of developing hypothyroidism or goiter. Maternal hypothyroidism should be avoided. Therapy should be closely monitored during pregnancy. This is typically done by following thyroid function tests (TSH and thyroid hormone levels) monthly.

In patients who cannot be adequately treated with anti-thyroid medications (i.e. those who develop an allergic reaction to the drugs), surgery is an acceptable alternative. Surgical removal of the thyroid gland is only very rarely recommended in the pregnant woman due to the risks of both surgery and anesthesia to the mother and the baby.

Radioiodine is contraindicated to treat hyperthyroidism during pregnancy since it readily crosses the placenta and is taken up by the baby's thyroid gland. This can cause destruction of the gland and result in permanent hypothyroidism.

Beta-blockers can be used during pregnancy to help treat significant palpitations and tremor due to hyperthyroidism. They should be used sparingly due to reports of impaired fetal growth associated with long-term use of these medications. Typically, these drugs are only required until the hyperthyroidism is controlled with anti-thyroid medications.



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*.

Thyroid Disease and Pregnancy

WHAT IS THE NATURAL HISTORY OF GRAVES' DISEASE AFTER DELIVERY?

Graves' disease typically worsens in the postpartum period, usually in the first 3 months after delivery. Higher doses of anti-thyroid medications are frequently required during this time. At usual, close monitoring of thyroid function tests is necessary.

CAN THE MOTHER WITH GRAVES' DISEASE, WHO IS BEING TREATED WITH ANTI-THYROID DRUGS, BREASTFEED HER INFANT?

Yes. PTU is the drug of choice because it is highly protein bound. Consequently, lower amounts of PTU cross into breast milk compared to Tapazole. It is important to note that the baby will require periodic assessment of his/her thyroid function to ensure maintenance of normal thyroid status.

TABLE 1:

	1st Trimester	2nd Trimester	3rd Trimester
TSH	Normal or Decreased	Normal	Normal
Free T4	Normal	Normal	Normal
Free T3	Normal	Normal	Normal
Total T4	High	High	High
Total T3	High	High	High
T3 Resin Uptake (Inverse measure of protein binding)	Low	Low	Low
Free T4 Index (FT4I, FTI)	Normal	Normal	Normal

HYPOTHYROIDISM & PREGNANCY

WHAT ARE THE MOST COMMON CAUSES OF HYPOTHYROIDISM DURING PREGNANCY?

Overall, the most common cause of hypothyroidism is the autoimmune disorder known as Hashimoto's thyroiditis (see *Hypothyroidism brochure*). Hypothyroidism can occur during pregnancy due to the initial presentation of Hashimoto's thyroiditis, inadequate treatment of a woman already known to have hypothyroidism from a variety of causes, or over-treatment of a hyperthyroid woman with anti-thyroid medications. Approximately, 2.5% of women will have a slightly elevated TSH of greater than 6 and 0.4% will have a TSH greater than 10 during pregnancy.

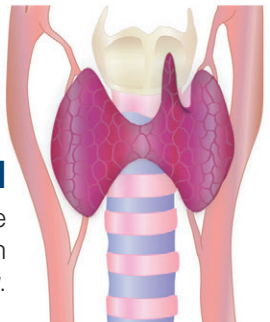
WHAT ARE THE RISKS OF HYPOTHYROIDISM TO THE MOTHER?

Untreated, or inadequately treated, hypothyroidism has been associated with maternal anemia (low red blood cell count), myopathy (muscle pain, weakness), congestive heart failure, pre-eclampsia, placental abnormalities, low birth weight infants, and postpartum hemorrhage (bleeding). These complications are more likely to occur in women with severe hypothyroidism. Most women with mild hypothyroidism may have no symptoms or attribute symptoms they may have as due to the pregnancy.

WHAT ARE THE RISKS OF MATERNAL HYPOTHYROIDISM TO THE BABY?

Thyroid hormone is critical for brain development in the baby. Children born with congenital hypothyroidism (no thyroid function at birth) can have severe cognitive, neurological and developmental abnormalities if the condition is not recognized and treated promptly. These developmental abnormalities can largely be prevented if the disease is recognized and treated immediately after birth. Consequently, all newborn babies in the United States are screened for congenital hypothyroidism so they can be treated with thyroid hormone replacement therapy as soon as possible.

The effect of maternal hypothyroidism on the baby's brain development is not as clear. Untreated severe hypothyroidism in the mother can lead to impaired brain development in the baby. This is mainly seen when the maternal hypothoidism is due to iodine deficiency, which also affects the baby However, recent studies have suggested that mild brain developmental abnormalities may be present in children born to women who had mild untreated hypothyroidism during pregnancy. At this time there is no general consensus of opinion regarding screening all women for hypothyroidism during pregnancy. However, some physician groups recommend checking a woman's TSH value either before becoming prenant (pre-pregnancy counseling) or as soon as pregnancy is confirmed. This is especially true in women at high risk for thyroid disease, such as those with prior treatment for hyperthyroidism, a positive family history of thyroid disease and those with a goiter. Clearly, woman with established hypothyroidism should have a TSH test once pregnancy is confirmed, as thyroid hormone requirements increase during pregnancy, often leading to the need to increase the levothyroxine dose. If the TSH is normal, no further monitoring is typically required. This issue should be discussed further with your health care provider, particularly if you are contemplating pregnancy. Once hypothyroidism has been detected, the woman should be treated with levothyroxine to normalize her TSH and Free T4 values (see *Hypothyroidism brochure*).



FURTHER INFORMATION

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Thyroid Disease and Pregnancy

HOW SHOULD A WOMAN WITH HYPOTHYROIDISM BE TREATED DURING PREGNANCY?

The treatment of hypothyroidism in a pregnant woman is the same as for a man or non-pregnant woman, namely, adequate replacement of thyroid hormone in the form of synthetic levothyroxine (see *Hypothyroidism brochure*). It is important to note that levothyroxine requirements frequently increase during pregnancy, often times by 25 to 50 percent. Occasionally, the levothyroxine dose may double. Ideally, hypothyroid women should have their levothyroxine dose optimized prior to becoming pregnant. Women with known hypothyroidism should have their thyroid function tested as soon as pregnancy is detected and their dose adjusted by their physician as needed to maintain a TSH in the normal range. Thyroid function tests should be checked approximately every 6-8 weeks during pregnancy to ensure that the woman has normal thyroid function throughout pregnancy. If a change in levothyroxine dose is required, thyroid tests should be measured 4 weeks later. As soon as delivery of the child occurs, the woman may go back to her usual pre-pregnancy dose of levothyroxine. It is also important to recognize that prenatal vitamins contain iron and calcium that can impair the absorption of thyroid hormone from the gastrointestinal tract. Consequently, levothyroxine and prenatal vitamins should not be taken at the same time and should be separated by at least 2-3 hrs.

FURTHER INFORMATION

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