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AMERICAN **THYROID** ASSOCIATION **Optimal Thyroid Health for All**

EDITOR'S COMMENTS2

HYPERTHYROIDISM

Risk of cancer after treatment of hyperthyroidism

The management of hyperthyroidism includes three primary options: radioactive iodine therapy, antithyroid drugs and thyroidectomy. There has been a concern about the long term risk of developing cancer after radioactive iodine therapy for hyperthyroidism. This study looked at the effects of all 3 of the treatment options for hyperthyroidism on the likelihood of getting cancer.

Kitahara CM et al 2020 Association of radioactive iodine, antithyroid drug, and surgical treatments with solid cancer mortality in patients with hyperthyroidism. JAMA Netw Open 3(7): e209660. PMID: 32701159.

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Longer duration of hyperthyroidism is associated with increased risk of dementia Dementia is common in older adults and can lead to difficulty in performing daily activities. Recent studies have focused on understanding whether risk factors that can be treated, such as thyroid function changes, affect the risk of developing dementia. The objective of this study was to assess the risk of dementia in patients with hyperthyroidism and understand whether duration of hyperthyroidism plays a role.

Folkestad L et al Graves' disease and toxic nodular goiter, aggravated by duration of hyperthyroidism, are associated with Alzheimer's and vascular dementia: A registry-based long-term follow-up of two large cohorts. Thyroid 2020; May;30(5):672-680.

HYPERTHYROIDISM

Early thyroidectomy may decrease death in amiodarone-induced thyrotoxicosis (AIT) Amiodarone-induced thyroxicosis (AIT) can be severe and difficult to treat. Some have recommended surgery, and possibly early surgery when the patient is still hyperthyroid, as the best and quickest treatment for AIT. The authors here look at what is the best timing of surgery for AIT to achieve to best outcomes.

Cappellani D et al 2020 Duration of exposure to thyrotoxicosis increases mortality of compromised AIT patients: The role of early thyroidectomy. J Clin Endocrinol Metab 105(9):dgaa464. PMID: 32678873

HYPOTHYROIDISM

How often is thyroid hormone needed after a lobectomy?

Removal of half of the thyroid gland has become an increasingly acceptable treatment option for thyroid disease, including some thyroid cancers. It can be challenging to predict which patients who have a thyroid lobectomy will still make enough thyroid hormone to avoid needing to take a thyroid hormone pill after surgery. This study aimed to determine factors associated with the need for thyroid hormone supplementation in patients following a thyroid lobectomy.

Wilson M et al 2020 Postoperative thyroid hormone supplementation rates following thyroid lobectomy. Am J Surg. Epub 2020 Jul 1. PMID: 32684294.

THYROID CANCER. II ATA risk stratification system correctly predicts the chances of thyroid cancer relapse at 1 year. The most recent ATA guidelines for the management of thyroid nodules and cancer categorizes patients at the time of diagnosis into three groups: low, intermediate and high risk for recurrence or relapse of thyroid cancer. Each category of risk is associated with an estimate of the chances of cancer relapse. This study evaluates how well these risk categories that were assigned at the time of diagnosis match the response to therapy after 1 year of treatment in a large group of thyroid cancer patients.

Giorgio Grani et al. Real-world performance of the American Thyroid Association risk Estimates in Predicting 1-year Differentiated Thyroid Cancer Outcomes: A prospective multicenter study of 2000 patients. Thyroid. Epub 2020 Jul1. PMID 32475305

THYROID AND PREGNANCY13 Developmental test scores were similar in children of mothers with hypothyroidism treated with levothyroxine before pregnancy versus early pregnancy

Recent studies suggested that there may be a link between mild hypothyroidism in mothers and brain development in children. However, clinical trials of mothers with subclinical hypothyroidism have not shown that levothyroxine treatment has any effect on improving outcomes, possibly because treatment was started too late in the pregnancy. The current study aimed to compare the brain developmental test scores of children born to mothers with hypothyroidism who were started on levothyroxine either before pregnancy or between 8 and 14 weeks of pregnancy.

Zhou Q, Wang C, Xu H, Li X. 2020 Impact of preconception treatment initiation for hypothyroidism on neurocognitive function in children. J Clin Endocrinol Metab. Epub 2020 Aug 25. PMID: 32841335.

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Clinical Thyroidology for the Public

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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 also provide even faster updates of late-breaking thyroid news through <u>Twitter</u> at *@* thyroidfriends and on <u>Facebook</u>. 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, MCT8 – AHDS Foundation, ThyCa: Thyroid Cancer Survivors' Association, Thyroid Cancer Canada, Thyroid Cancer Alliance* and *Thyroid Federation International*.

We invite all of you to join our **Friends of the ATA** community. It is for you that the American Thyroid Association (ATA) is dedicated to carrying out our mission of providing reliable thyroid information and resources, clinical practice guidelines for thyroid detection and treatments, resources for connecting you with other patients affected by thyroid conditions, and cutting edge thyroid research as we search for better diagnoses and treatment outcomes for thyroid disease and thyroid cancer. We thank all of the *Friends of the ATA* who support our mission and work throughout the year to support us. We invite you to help keep the ATA mission strong by choosing to make a donation that suits you — it takes just one moment to give online at: www.thyroid.org/donate and all donations are put to good work. The ATA is a 501(c)3 nonprofit organization and your gift is tax deductible.

The Covid-19 pandemic has caused an unprecedented upheaval in our daily lives and presented extremely difficult challenges to our healthcare system. There is a lot of information circulating around. We at the American Thyroid Association would like to make sure that you all have access to most accurate, reliable, fact-based and updated information. (https://www.thyroid.org/covid-19/)

November is Hyperthyroidism Awareness Month.

In this issue, the studies ask the following questions:

- What is the risk of cancer after treatment of hyperthyroidism?
- Does the duration of hyperthyroidism increase the risk of dementia?
- Does thyroidectomy increase survival in patient with amiodarone-induced thyrotoxicosis?
- How often is thyroid hormone supplementation needed after lobectomy?
- Does the ATA stratification system predicts the chances of thyroid cancer relapse?
- Are developmental test scores in children of hypothyroid mothers affected by when the mothers started treatment?

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

— Alan P. Farwell, MD, FACE

in You

HYPERTHYROIDISM

Risk of cancer after treatment of hyperthyroidism

BACKGROUND

The management of hyperthyroidism includes three primary options: radioactive iodine therapy, antithyroid drugs (ATDs) and thyroidectomy (surgery to remove some or all of the thyroid). Practice patterns have varied significantly over time and in different parts of the world, in part owing to potential adverse effects, both short- and long-term, of each of the treatment options. In particular, there has been a concern about the long term risk of developing cancer after radioactive iodine therapy for hyperthyroidism.

The Cooperative Thyrotoxicosis Therapy Follow-up Study (CTTFUS) is a large a large database of patients treated for hyperthyroidism in the United States and United Kingdom between the 1940s and 1960s. A 1998 study had initially examined the risk of death from for cancer in the CTTFUS group. A recent update from this groups reported a positive association between the dose of radioactive iodine and death from solid cancers, including breast cancers. This study expands to also include patients with hyperthyroidism who were treated with ATDs and surgery, in addition to those who received radioactive iodine therapy. This study was done to look at the effects of the treatment options for hyperthyroidism on the likelihood of getting cancer.

THE FULL ARTICLE TITLE

Kitahara CM et al 2020 Association of radioactive iodine, antithyroid drug, and surgical treatments with solid cancer mortality in patients with hyperthyroidism. JAMA Netw Open 3(7): e209660. PMID: 32701159.

SUMMARY OF THE STUDY

The original CTTFUS group included 35,593 patients with hyperthyroidism treated with radioactive iodine therapy, ATDs and thyroidectomy or a combination of these at 26 centers (25 in the United States, 1 in the United Kingdom) between January 1, 1946, and December 31, 1964. Of these, 31,583 were eligible for follow-up through 1990 and 31,363 U.S. patients were eligible for follow-up through December 31, 2014; these included 25,455 with death records available, 3089 found or presumed to be alive, and 2829 lost to follow-up. The study involved a review of medical charts to look at the risk of cancer in patients treated for hyperthyroidism. The data collected was studies to look at the differences if any based on age, gender and type of treatment.

Of the 31,363 patients, 22,357 (71.3%) were treated with ATDs (alone or in combination with other treatments), 19,589 (62.5%) with radioactive iodine therapy, 13,676 (43.6%) with surgery; 7474 (23.8%) were treated only with radioactive iodine therapy, 1138 (3.65%) only with ATDs, and 800 (2.6%) with surgery alone. For those treated with radioactive iodine therapy, 12,979 (66.3%) received one course of treatment and the overall average dose for all patients who received was 8 mCi.

The average follow-up was 26.0 years, with the shortest duration in the ATD-only group (20.2 years) and the longest in the ATD and surgery group (33.6 years). The highest proportion of cancer-related deaths occurred in the ATD-only (160 [18.3%]) and ATD and surgery (1413 [18.6%]) groups. Overall, 59 patients (5.2%) in the ATD-only group died of cancer in the first 5 years of follow-up, as compared with 74 (0.8%) in the ATD and surgery group and 193 (2.1%) in the other groups; there also was a higher rate of prior cancers in this group.

After excluding prior cancers and adjusting for patient age, sex, and underlying diagnosis, there was no significant difference in the likelihood of death from cancers (solid cancers such as breast and other solid organs) across treatment groups outlined above. For patients treated with radioactive iodine therapy, the risk of death from cancers increased with an increase in the dose.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that there was no significant difference in the likelihood of death from cancers (solid cancers such as breast and other solid organs) across different treatment groups for hyperthyroidism (ATDs,

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HYPERTHYROIDISM, continued

radioactive iodine therapy or surgery). However, the dose of radioactive iodine therapy was linked to a modestly increased risk of death from these cancers. It is important to understand this link so patients understand the long term effects of these treatments and make the right decision for themselves in consultation with their physician/health care provider.

—Vibhavasu Sharma, MD, FACE

ATA THYROID BROCHURE LINKS

Hyperthyroidism (Overactive): <u>https://www.thyroid.org/hyperthyroidism/</u> Radioactive Iodine Therapy: <u>https://www.thyroid.org/radioactive-iodine/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u>

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.

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.

Propylthiouracil (PTU): an antithyroid medication that blocks the thyroid from making thyroid hormone. Propylthiouracil is used to treat hyperthyroidism, especially in women during pregnancy.

Radioactive iodine: 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 nondestructive 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).

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

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HYPERTHYROIDISM

Longer duration of hyperthyroidism is associated with increased risk of dementia

BACKGROUND

Dementia, a decrease in memory and other brain functions, is common in older adults and can lead to difficulty in performing daily activities. Due to the worldwide growth of the older adult population, there is a significant projected increase in the number of dementia cases. Despite widespread research to understand risk factors for dementia, there is currently no cure. Because of this, recent studies have focused on understanding whether risk factors that can be treated, such as thyroid function changes, affect the risk of developing dementia. The objective of this study was to assess the risk of dementia in patients with hyperthyroidism and understand whether duration of hyperthyroidism plays a role.

THE FULL ARTICLE TITLES

Folkestad L et al Graves' disease and toxic nodular goiter, aggravated by duration of hyperthyroidism, are associated with Alzheimer's and vascular dementia: A registry-based long-term follow-up of two large cohorts. Thyroid 2020; May;30(5):672-680.

SUMMARY OF THE STUDIES

This study used data from two large registries in Europe, the Danish National Patient Registry (DNPR) and the OPENTHYRO. The DNPR includes all adult patients in Denmark with hyperthyroidism either due to Graves' disease or toxic nodular goiter since 1977. The OPENTHYRO registry consists of all individuals who had at least one thyroid stimulating hormone (TSH) measurement performed at the Odense University Hospital in Denmark between 1995 and 2012. Diagnosis of dementia was determined based on billing codes and diagnosis of hyperthyroidism was determined based on billing codes (DNPR) and laboratory data (OPENTHYRO). The authors compared events of dementia in hyperthyroid patients (both overt and subclinical) to patients with normal thyroid function, taking into account ongoing chronic conditions. Patients who had a diagnosis of dementia or were prescribed a

medication as treatment of dementia prior to the first TSH measurement were excluded.

The final study population from DNPR included 55,656 hyperthyroid individuals and 220,561 individuals with normal thyroid function. Patients were followed for an average of 7.9 years. Overall, a total of 2,217 (4.9%) of individuals were diagnosed with dementia compared with 7,907 (3.6%) in the individuals with normal thyroid function. The risk of dementia was significant even when adjusting for other medical problems. Both causes of hyperthyroidism (Graves' disease vs toxic nodular goiter) were associated with an increased risk of dementia.

In the OPENTHYRO study sample, 2,688 hyperthyroid individuals were identified and matched with 10,752 individuals from the euthyroid reference population. Average follow-up was 8.7 years. Overall, 190 (7.1%) of hyperthyroid individuals had dementia, compared to 473 (4.4%) in individuals with normal thyroid function. Additionally, there was a 4.4-fold increased risk of dementia over 5 years of decreased TSH compared to those with normal TSH.

WHAT ARE THE IMPLICATIONS OF THESE STUDIES?

This study suggests that there is a significantly higher risk by ~20% of dementia in hyperthyroid patients compared to individuals with normal thyroid function, with duration of hyperthyroidism further adding to that risk. These findings have important public health implications as hyperthyroidism may be a potential risk factor for the development of dementia that can be treated. It is therefore important for physicians to closely follow patients with consistently low TSH levels, as early recognition and treatment of hyperthyroidism may play a role in decreasing the risk for a decrease in brain. However, larger studies are needed to conclusively determine the effects of hyperthyroidism treatment on dementia risk.

— Maria Papaleontiou, MD

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HYPERTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Hyperthyroidism (Overactive): <u>https://www.thyroid.org/hyperthyroidism/</u> Graves' Disease: <u>https://www.thyroid.org/graves-disease/</u>

ABBREVIATIONS & DEFINITIONS

Dementia: a general term for loss of memory, language, problem-solving and other thinking abilities that are severe enough to interfere with daily life. Alzheimer's is the most common cause of dementia.

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

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

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.

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.

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.



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HYPERTHYROIDISM

Early thyroidectomy may decrease death in amiodaroneinduced thyrotoxicosis (AIT)

BACKGROUND

Amiodarone is a medication used to treat heart problems, mainly related to irregular heart rhythms. Amiodarone contains a lot of iodine and can affect the thyroid, causing hypothyroidism and hyperthyroidism. The hyperthyroidism caused by amiodarone (amiodarone-induced thyroxicosis, AIT) can be severe and difficult to treat. AIT greatly increases the risk of severe heart complications in patients that are already at high risk because of their irregular heart rhythms. It can take weeks to months to stabilize thyroid hormones with medication in patients with AIT, and the longer AIT is present, the greater the risk of heart complications and death. Surgery is an effective treatment for AIT if the patients are healthy enough to undergo an operation. Therefore, some have recommended surgery, and possibly early surgery with removal of the entire thyroid gland (total thyroidectomy), as the best and quickest treatment for AIT. One concern of early thyroidectomy is the risk of complications during the operation in a patient that is still hyperthyroid. The authors here look at what is the best timing of surgery for AIT to achieve to best outcomes.

THE FULL ARTICLE TITLE

Cappellani D et al 2020 Duration of exposure to thyrotoxicosis increases mortality of compromised AIT patients: The role of early thyroidectomy. J Clin Endocrinol Metab 105(9):dgaa464. PMID: 32678873

SUMMARY OF THE STUDY

The authors looked at 64 patients over a 20 year period in Pisa, Italy that had AIT and were treated with a total thyroidectomy. They compared outcomes (including death related to the surgery, the frequency of death from heart problems over the next 5 years and others) in patients that underwent an early thyroidectomy when the patient was still hyperthyroid vs late thyroidectomy after the hyperthyroidism was controlled.

Most patients were older and male and started with slightly decreased heart function. Patients that had a late thyroidectomy had a higher death rate both in the immediate post-operative period as well as over the next 5 years. However, in patients with the worst cardiac problems, death rate was higher in patients that had an early thyroidectomy. These results were without taking other patient factors into account. When all patient and treatment factors were accounted for, only patient age and duration of being hyperthyroid were important predictors of death from cardiovascular disease.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors conclude that in general, for patients with AIT, early thyroidectomy leads to decreased early and late death from heart problems. This is important because current guidelines and historical practice call for medical management of AIT and surgery as a last resort. Therefore the authors conclude that surgery needs to be considered early for these patients, except possibly those with the worst heart problems.

— Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

Hyperthyroidism (Overactive): <u>https://www.thyroid.org/hyperthyroidism/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u>

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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.

Euthyroid: a condition where the thyroid gland as working normally and producing normal levels of thyroid hormone.

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

Amiodarone: an iodine-rich drug that is commonly used for the treatment of irregular heart rhythms. Amiodarone can cause thyroid problems, including both hypothyroidism and hyperthyroidism.

Amiodarone induced Thyrotoxicosis (AIT): elevated thyroid hormone levels that can occur as a result of excessive iodine from amiodarone resulting in increased thyroid hormone production and secretion or to destruction of thyroid cells with release of thyroid hormone into the blood

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HYPOTHYROIDISM

How often is thyroid hormone needed after a lobectomy?

BACKGROUND

Surgery to remove all or part of part or all of the thyroid gland is commonly needed to treat both benign (noncancerous) and cancerous thyroid disease. The normal job of the thyroid gland is to produce thyroid hormone, which helps control the body's metabolism (how the body uses energy). This is a very important job - people who have no source of thyroid hormone will eventually become very sick, or even die. For this reason, people who undergo surgery to remove the entire thyroid gland will need to take a thyroid hormone pill after surgery (usually once a day, every day, for the rest of their lives).

Removal of half of the thyroid gland has become an increasingly acceptable treatment option for thyroid disease, including some thyroid cancers. One advantage of removing only part of the thyroid (usually one half of the thyroid gland, called a thyroid lobectomy), is that the half of the thyroid left behind will continue to produce thyroid hormone. If this is enough thyroid hormone to meet the body's normal needs, a thyroid hormone pill will not be needed following thyroid surgery. Unfortunately, it can be challenging to predict which patients who have a thyroid lobectomy will still make enough thyroid hormone to avoid needing to take a thyroid hormone pill after surgery.

The study described here tries to shed light on this question by looking at the medical records of people who previously underwent a thyroid lobectomy. By evaluating these records, including information from blood testing and imaging studies done before thyroid surgery, the study team hoped to learn how to predict which people having a thyroid lobectomy would need to take a thyroid hormone pill after surgery. This is important information, since a person needing thyroid surgery might choose to have the whole thyroid removed if they would still need to take a thyroid hormone pill after removing only half of the thyroid gland.

FULL ARTICLE TITLE

Wilson M et al 2020 Postoperative thyroid hormone

supplementation rates following thyroid lobectomy. Am J Surg. Epub 2020 Jul 1. PMID: 32684294.

SUMMARY OF THE STUDY

The study authors reviewed the medical records of 100 patients who underwent thyroid lobectomy surgery at their institution during a one-year period (between 2016 and 2017). Serum TSH levels were measured prior to surgery and at 6 weeks, 6 months, 12 months, and annually thereafter following thyroid lobectomy. The goal was a TSH in the normal range if the surgery was for benign disease and <2 of the surgery was for a thyroid cancer. The average age was 50.5 years, 74% were women and 84% were Caucasian. The average preoperative serum TSH was 1.50 mIU/L.

The study found that almost half of the people having a thyroid lobectomy (47%) needed a thyroid hormone pill after surgery and that this medicine was needed within six weeks of surgery in most cases. In addition, the investigators found that people having a thyroid lobectomy for treatment of thyroid cancer were more likely to need a thyroid hormone pill after surgery (73% of patients) compared to those undergoing this surgery for benign thyroid disease. This is not surprising, as people diagnosed with thyroid cancer generally need higher thyroid hormone levels after surgery than do patients with benign thyroid disease. In addition, people with low, but still normal, thyroid hormone levels before surgery were more likely need thyroid hormone, as were people found to have a small thyroid gland or evidence of thyroid inflammation prior to thyroid lobectomy. Patient age at the time of thyroid lobectomy, gender, race and size of thyroid cancer/benign overgrowth (nodule) did not predict need for a thyroid hormone pill after thyroid lobectomy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that the need for thyroid hormone supplementation is associated with a higher preoperative serum TSH level, a smaller thyroid gland to

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HYPOTHYROIDISM, continued

begin and either thyroiditis or thyroid cancer. The majority of patients with benign thyroid disease after a lobectomy did not require thyroid hormone replacement therapy. The results of this study are important because most people who need thyroid surgery would like to avoid having to take this medicine after surgery. This information might help some patients choose between having all or just half of their thyroid gland removed. For example, if a person needing thyroid surgery knew before

surgery that they would need to take a thyroid hormone pill regardless of whether all or only half of their thyroid was removed, they might choose to have their whole thyroid removed (which would eliminate any chance of needing additional thyroid monitoring or surgery in the future). Thus, this study provides information that can help a person who needs thyroid surgery choose which surgery would be best for them.

— Jason D. Prescott, MD PhD

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): <u>https://www.thyroid.org/hypothyroidism/</u> Thyroid Hormone Treatment: <u>https://www.thyroid.org/thyroid-hormone-treatment/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u>

ABBREVIATIONS & DEFINITIONS

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

Lobectomy: surgery to remove one lobe of the thyroid.

Completion thyroidectomy: surgery to remove the remaining thyroid lobe in thyroid cancer patients who initially had a lobectomy.

Total thyroidectomy: surgery to remove the entire thyroid gland.

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

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

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THYROID CANCER

ATA risk stratification system correctly predicts the chances of thyroid cancer relapse at 1 year.

BACKGROUND

In 2015, the American Thyroid Association (ATA) published the most recent guidelines for the management of thyroid nodules and cancer. In an effort to predict how patients with thyroid cancer will respond to the initial treatment, the ATA recommended to categorize the patients at the time of diagnosis into three risk groups: low, intermediate and high risk for recurrence or relapse of thyroid cancer. Patients will be placed on one of the three categories based on the characteristics of their initial thyroid cancer (for example, size of the cancer, presence or absence of special aggressive cancer variants, presence of large lymph nodes involving cancer, invasion of blood vessels and spread to other parts of the body. Each category of risk is associated with an estimate of the chances of cancer relapse). This study evaluates how well these risk categories that were assigned at the time of diagnosis match the response to therapy after 1 year of treatment in a large group of thyroid cancer patients.

THE FULL ARTICLE

Giorgio Grani et al. Real-world performance of the American Thyroid Association risk Estimates in Predicting 1-year Differentiated Thyroid Cancer Outcomes: A prospective multicenter study of 2000 patients. Thyroid. Epub 2020 Jul1. PMID 32475305

SUMMARY OF THE STUDY

The authors used an Italian database of almost 7000 patients with thyroid cancer. They included in their study over 2000 patients who were diagnosed with thyroid cancer between 2013 and 2019. The majority of the patients were women. Most patients (77%) have evidence of spread of the cancer to the neck lymph nodes. Most of the patients had a total thyroidectomy. A total of 57% of patients received radioactive iodine

therapy. The response to the treatment was evaluated at 1 year after the surgery. To evaluate presence or absence of cancer in these patients, they measured the thyroglobulin levels in the blood (thyroid cancer marker), they performed a thyroid ultrasound and some patients had a nuclear medicine radioactive scan done. The response to therapy was classified as: 1) *excellent*: if there was no evidence of cancer; 2) *biochemically incomplete*: if the thyroglobulin level was elevated; 3) *structurally incomplete*: if there was evidence of cancer or a mass in the thyroid ultrasound or on the nuclear scan (this group of patients is the one with highest chances of dying of the disease); and 4) *indeterminate*: it there were inconclusive ultrasound findings or thyroglobulin elevations.

Of all patients, 54% were classified as low risk, 38% were classified as intermediate risk and 8% were classified as high risk. In terms of their response to therapy: only 2% of the patient in the low risk group dah a structurally incomplete response (consistent with the presence of cancer), 6% of the intermediate risk group had a structurally incomplete response and 15% of the high risk group had a structurally incomplete response.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study supports the utility and value of the ATA stratification system. This means that by categorizing the patients with thyroid cancer at the time of diagnosis into low, intermediate and high risk groups one can adequately predict their chances of being on remission or having a relapse of thyroid cancer after 1 year of treatment. This classification system can also help guide treatment in a more individualized way and avoid needless aggressive therapies.

— Susana Ebner MD

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THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u> Radioactive Iodine Therapy: <u>https://www.thyroid.org/radioactive-iodine/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u>

ABBREVIATIONS & DEFINITIONS

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

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

Thyroglobulin: a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid

tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker in patients that do not have thyroglobulin antibodies

Total thyroidectomy: surgery to remove the entire thyroid gland.



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THYROID AND PREGNANCY

Developmental test scores were similar in children of mothers with hypothyroidism treated with levothyroxine before pregnancy versus early pregnancy

BACKGROUND

Thyroid hormone plays an important role in the baby's normal development during pregnancy. Because the baby does not make his or her own thyroid hormone until much later in pregnancy, he or she depends on mother's thyroid hormone crossing the placenta during early pregnancy. If the mother has severe hypothyroidism (low thyroid hormone levels) that is not treated, it can cause problems in brain development in the baby, leading to a lower IQ and problems in movement or language skills. In mothers with subclinical hypothyroidism (mild hypothyroidism), the effect on the baby's brain development have not been as clear.

Recent studies suggested that there may be a link between mild hypothyroidism in mothers and problems with brain development in children. However, clinical trials of mothers with subclinical hypothyroidism have not shown that levothyroxine treatment has any effect on improving outcomes. One problem of these clinical trials may have been that the treatment was started too late in pregnancy, after the first trimester when a lot of brain development happens. The current study aimed to compare the brain developmental test scores of children born to mothers with hypothyroidism who were started on levothyroxine either before pregnancy or between 8 and 14 weeks of pregnancy.

THE FULL ARTICLE TITLE

Zhou Q, Wang C, Xu H, Li X. 2020 Impact of preconception treatment initiation for hypothyroidism on neurocognitive function in children. J Clin Endocrinol Metab. Epub 2020 Aug 25. PMID: 32841335.

SUMMARY OF THE STUDY

A total of 466 women were recruited from a hospital in Shanghai, China, from 2012 to 2013. Of these women, 187 were diagnosed with hypothyroidism before pregnancy (**BC group**) and 279 were diagnosed at the first prenatal care visit at 8 to 14 weeks of pregnancy (AC group). Overt hypothyroidism was diagnosed if they had high thyroid-stimulating hormone (TSH) and low free thyroxine (FT₄) levels in blood tests, and subclinical hypothyroidism was diagnosed if they had high TSH levels and normal FT₄ levels. All women with overt hypothyroidism were treated with levothyroxine. Women with subclinical hypothyroidism were treated with levothyroxine if the serum thyroid peroxidase (TPO) antibody level was high. TSH levels were checked every month during pregnancy, and the levothyroxine dose was adjusted to keep TSH level in normal range for pregnancy. Children were tested for brain development using the Gesell Developmental Diagnosis Scale (GDDS) that tests motor function, adaptability, language, and social emotional response, at 6, 12, and 24 months of age.

The average TSH of the BC group before pregnancy was 4.30 mIU/L. At the first prenatal visit, 97.9% of the BC group were taking levothyroxine and had an average TSH of 3.89 mIU/L. In the BC group, 82.4% of women were diagnosed with overt hypothyroidism and 17.6% with subclinical hypothyroidism, and 27.3% had a positive TPO antibody. The average serum TSH of the AC group at the first prenatal visit was 5.47 mIU/L. In the AC group, 37.6% of these women were diagnosed with overt hypothyroidism and 62.4% with subclinical hypothyroidism, and 35.5% had a positive TPO antibody. At delivery, the average TSH was 1.84 mIU/L in the BC group and 2.71 mIU/L in the AC group. At delivery, 77.5% of women in the BC group and 74.2% of women in the AC group who were taking levothyroxine.

There were no significant differences in overall scores of the GDDS assessment in children at 6 and 24 months. The overall score was 2 points lower in the BC group than in the AC group at 12 months. Of the individual scores, the adaptability score was 5 points higher in children in the BC group at 6 months and the motor function score

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THYROID AND PREGNANCY, continued

was 2 points lower in children in the BC group at 12 months. There were no significant differences in GDDS scores at 6, 12 or 24 months when overtly hypothyroid women and subclinically hypothyroid women were compared separately, except that the motor function score was 9 points lower in the subclinically hypothyroid BC group than in the subclinically hypothyroid AC group at 12 months.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that the brain development scores in children born to hypothyroid mothers was the same whether the mothers started levothyroxine before pregnancy as compared to starting at 8 to 14 weeks of pregnancy. The finding of this study is similar to the results of previous clinical trials that showed no significant improvement in children's brain development test scores when mothers with subclinical hypothyroidism were treated with levothyroxine. This study showed no adverse effects of starting levothyroxine treatment of the mother in early pregnancy as compared with before pregnancy. All mothers with hypothyroidism were treated and there was no group of women with normal thyroid function to compare. Despite this limitation, it is important to show that the brain development scores in children of hypothyroid women were similar as long as levothyroxine therapy is started within the 1st trimester of pregnancy.

— Sun Y. Lee, MD

ATA THYROID BROCHURE LINKS

Thyroid Disease in Pregnancy: <u>https://www.thyroid.org/thyroid-disease-pregnancy/</u> Hypothyroidism (Underactive): <u>https://www.thyroid.org/hypothyroidism/</u>

ABBREVIATIONS & DEFINITIONS

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

Overt Hypothyroidism: clear hypothyroidism an increased TSH and a decreased T_4 level. All patients with overt hypothyroidism are usually treated with 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.

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

Thyroxine (T₄): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

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

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.

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Clinical Thyroidology[®] for the Public

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 toward the improvement of thyroid education and resources for patients.















American Thyroid Association

Foundation

www.thyroid.org

ATA Patient Resources: www.thyroid.org/thyroid-information/ Find a Thyroid Specialist: www.thyroid.org (Toll-free): I-800-THYROID thyroid@thyroid.org

Bite Me Cancer

www.bitemecancer.org info@bitemecancer.org

Graves' Disease and Thyroid Foundation

www.gdatf.org (Toll-free): 877-643-3123 info@ngdf.org

Light of Life Foundation

www.checkyourneck.com info@checkyourneck.com

MCT8 – AHDS Foundation

mct8.info Contact@mct8.info

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

(Toll-free): 877-588-7904 thyca@thyca.org

Thyroid Cancer Alliance

www.thyroidcanceralliance.org www.thyroidcancerpatientinfo.org Rotterdam. The Netherlands

Thyroid Cancer Canada

www.thyroidcancercanada.org 416-487-8267 info@thyroidcancercanada.org

Thyroid Federation International www.thyroid-fed.org tfi@thyroid-fed.org



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The ATA was a valuable resource for our family when my dad was diagnosed with Anaplastic Thyroid Cancer. When you're faced with a detrimental diagnosis where even a few days can make the difference in life or death, understanding your options quickly is critical. The ATA website offers a one-stop shop for patients and caregivers to find specialists, current clinical trials, general thyroid cancer information, and links to other patient support groups and information.

Mary Catherine Petermann

- Father who was diagnosed with Anaplastic Thyroid Cancer in 2006
- He was treated at Mayo Clinic
- He has clean scans as of October 2016

JOIN US

PLEASE JOIN OUR JOURNEY TO ADVANCED DISCOVERIES AND TREATMENT FOR THYROID DISEASE AND THYROID CANCER

As patients with thyroid disease navigate the challenges to their quality of life and researchers and physicians look for more effective directions, we at the ATA have our own destination– **funding for critical thyroid research, prevention, and treatment.** For 94 years, the ATA has led the way in thyroidology. It's a daily obstacle course to find new drugs, better treatments, advanced surgical methods, and more rapid diagnoses for the 20 million Americans who have some form of thyroid disease.

The ATA has paved the way with management guidelines for clinicians who diagnose and treat thyroid disease. For physicians treating pregnant women diagnosed with thyroid disease, our recent publication presents 97 evidence-based recommendations making sure that best practices are implemented with the latest, most effective treatment.



Through your generous support and donations, research takes the lead and hope is on the horizon. **Will you join us** in our campaign to raise **\$1.5 million** for thyroid research, prevention, and treatment? Your compassionate, tax-deductible gift will provide funds for:

- Research grants that pave the way for 1,700 ATA physicians and scientists who have devoted their careers to understanding the biology of and caring for patients affected by thyroid disease.
- Patient education for individuals and families looking for life-changing clinical trials, the best thyroid specialists, and cutting edge treatment and drugs.
- Professional education that offers a wealth of knowledge and leading-edge research for trainees and practitioners.
- A website that is the go-to resource for thyroid information for patients and practitioners alike. In 2016 alone, there were more than 3,700,000 website views of ATA's library of online thyroid information patient brochures.

Donations **of all sizes** will change the future for thyroid patients. You will make a direct impact on patients like Mary Catherine's father as he deals with Anaplastic Thyroid Cancer. You will help scientists like ATA Associate Member Julia Rodiger, Ph.D., a scientist at the National Institutes of Health, as she analyzes thyroid hormones for intestinal stem cell development.

Hyperthyroidism

WHAT IS THE THYROID GLAND?

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

WHAT IS 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.

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 sweating, 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* (also known as *Basedow's 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).

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. In these last two forms. there is excess thyroid hormone but the thyroid is not overactive.

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 fingers. Your reflexes are likely to be fast, and your eyes may have some abnormalities if you have Graves' disease.

Hyperthyroidism

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 measure levels of thyrotropin receptor antibodies (TRAbs), which when elevated confirm the diagnosis of Graves disease. Your doctor may also 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.

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 unconvinced 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, 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 radioiodine 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 develop 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 lodine: 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 bloodstream, 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 bloodstream 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.



FURTHER INFORMATION

2 This page and its contents are Copyright © 2018 the American Thyroid Association Further details on this and other thyroid-related topics are available in the patient thyroid information section on the American Thyroid Association[®] website at *www.thyroid.org*. For information on thyroid patient support organizations, please visit the *Patient Support Links* section on the ATA website at *www.thyroid.org*

Hyperthyroidism

For them, a second radioiodine 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 radioiodine.

Surgery: Your hyperthyroidism can be permanently cured by surgical removal of all or most of your thyroid gland. This procedure is best performed by a surgeon who has 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 rarely in patients operated on by an experienced thyroid surgeon. These complications include damage to the parathyroid glands that are next to 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 become hypothyroid. As with hypothyroidism that develops after radioiodine 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 beta-blockers 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

FURTHER INFORMATION

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

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Further details on this and other thyroid-related topics are available in the patient thyroid information section on the American Thyroid Association[®] website at *www.thyroid.org*. For information on thyroid patient support organizations, please visit the *Patient Support Links* section on the ATA website at *www.thyroid.org*