american thyroid association

Clinical Thyroidology for the Public

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Earlier this year, the American Thyroid Association published updated guidelines for the diagnosis, evaluation and management of hyperthyroidism. Kimberly Dorris, Executive Director/CEO of the Graves' Disease and Thyroid Foundation has reviewed these guidelines from the patient's point a view and highlights the main points of the guidelines.

Ross, D et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and other causes of Thyrotoxicosis. Ross, Burch, et al., Thyroid. Oct 2016, 26(10): 1343-1421.

Hyperthyroidism is more common in women than men, especially in women of childbearing age. During pregnancy, the current American Thyroid Association guidelines recommend propylthiouracil as the drug of choice as the risk of birth defects is lower and the defects appear to be less severe with propylthiouracil. The goal of this study was to determine the frequency of these two adverse side effects as compared to birth defects in the general population and in pregnant women in an effort to guide the treatment of hyperthyroidism in pregnancy.

Andersen SL et al. Antithyroid drug side effects in the population and in pregnancy. J Clin Endocrinol Metab 2016; 101 (4): 1606-14. Epub January 27, 2016.

Antithyroid drugs (ATDs) are frequently used to treat Graves' disease. Agranulocytosis (low white blood cells) is a rare complication of ATDs occurring in 0.1-0.3% of patients. Graves' disease itself can cause mild decreases in WBCs. The goal of this study is to evaluate the how common low WBCs are seen in patients newly diagnosed with hyperthyroidism due to Graves' disease before starting ATD treatment and the effect of this treatment on the WBC count.

Aggarwal A et al. Treatment of hyperthyroidism with antithyroid drugs corrects mild neutropenia in Graves' disease. Clin Endocrinol (Oxf). June 13, 2016 [Epub ahead of print]

Agranulocytosis (low white blood cells) is a rare complication of antithyroid drugs occurring in 0.1-0.3% of patients. Severe infections occur in approximately two out of three patients and up to 5% of these patients will die of this complication. Previous studies have shown that certain genetic variants are associated with a high risk of antithyroid drug–induced agranulocytosis. These two studies examine the association of a specific genetic marker with antithyroid drug–induced agranulocytosis in a population of ethnic Chinese people and the pattern of genetic variants in a European population.

—Cheung CL et al. HLA-B*38:02:01 predicts carbimazole/methimazole-induced agranulocytosis. Clin Pharmacol Ther 2016;99:555-61. Epub January 12, 2016.

—Hallberg P et al for the EuDAC collaborators. Genetic variants associated with antithyroid drug-induced agranulocytosis: a genome-wide association study in a European population. Lancet Diabetes Endocrinol 2016;4:507-16. Epub May 3, 2016.

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

We also provide even faster updates of late-breaking thyroid news through Twitter at @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*.

November is Hyperthyroidism Awareness Month. In honor of this topic, our lead summary in this issue is a review of the recent ATA Hyperthyroidism guidelines provided by Kimberly Dorris, Executive Director/CEO of the Graves' Disease and Thyroid Foundation

In this issue, the studies ask the following questions:

1. What do the new American Thyroid Association Hyperthyroidism guidelines mean for patients?
2. What are the risks of taking antithyroid drugs for hyperthyroidism during pregnancy?
3. Are low WBC counts in Graves' disease due to antithyroid drugs or the inderlying disease?
4. Can molecular markers identify patients with Graves' disease at risk for agranulocytosis?

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

— Alan P. Farwell, MD, FACE

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HYPERTHYROIDISM

American Thyroid Association Task Force Updates Treatment Guidelines for Hyperthyroidism

FULL JOURNAL TITLE

Ross, D et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and other causes of Thyrotoxicosis. Ross, Burch, et al., Thyroid. Oct 2016, 26(10): 1343-1421.

American Thyroid Association Task Force Updates Treatment Guidelines for Hyperthyroidism

Kimberly Dorris, Executive Director/CEO
Graves' Disease and Thyroid Foundation

A task force organized by the American Thyroid Association (ATA) has updated the organization›s *"Guidelines for Diagnosis and Management of Hyperthyroidism and other causes of Thyrotoxicosis."* The Guidelines, published in *Thyroid*, a peer-reviewed journal from Mary Ann Liebert, Inc., publishers and the official journal of the ATA, are available free on the *Thyroid* website.

Thyrotoxicosis refers to having excessive levels of thyroid hormone in the body and can occur because of hyperthyroidism (overactive thyroid), inflammation of the thyroid, ingesting too much thyroid hormone from external sources, or other causes. Graves' disease is the most common cause of hyperthyroidism.

The task force was chaired by Dr. Douglas Ross (Massachusetts General Hospital, Boston, MA) and included Dr. Henry Burch (Walter Reed National Military Center, Bethesda, MD), Dr. David Cooper (Johns Hopkins Medicine in Baltimore, MD), Dr. M. Carol Greenlee (Western Slope Endocrinology Grand Junction, CO), Dr. Peter Laurberg (Aalborg University, Aalberg, Denmark), Dr. Ana Luiza Maia (Federal University of Rio Grande do Sul, Porto Alegre, Brazil), Dr. Scott Rivkees (University of Florida College of Medicine, Gainsville, FL), Dr. Mary Samuels (Oregon health and Science University, Portland, Oregon), Dr. Julie Ann Sosa (Duke University School of Medicine, Durham, North Carolina), Dr. Marius Stan (Mayo Clinic, Rochester, MN) and Dr. Martin Walter (University Hospital Bern, Switzerland). Drs. Cooper and Greenlee are GDATF Physician Advisory Board members and Dr. Rivkees is a GDATF newsletter contributor. The new guidelines include 124 evidence-based recommendations.

Much of the information in the 2011 guidance has been retained, including the following:

- Critical information on diagnostic testing, as the specific diagnosis will determine the available treatment options. For hyperthyroidism due to Graves' disease, treatment options include antithyroid medications (ATDs), radioiodine therapy (RAI) and thyroidectomy. However, none of these options are recommended for thyroiditis, an inflammation of the thyroid; rather, treatment usually involves the prescription of beta blockers (medications which slow the heart rate), with additional measures recommended depending on the type of thyroiditis. For overactive nodules, RAI or thyroidectomy are commonly used, with ATDs less frequently prescribed.

- A discussion of treatment options for patients living with thyroid eye disease; antithyroid drugs or surgery are still recommended over RAI for patients with active and moderate-to-severe or sight-threatening eye involvement.

- An emphasis on the importance of incorporating the patient's values and wishes into the final treatment decision.

ATA Task Force Updates Treatment Guidelines for Hyperthyroidism, continued

The guidance notes the increasing popularity in the United States of ATDs for the treatment of Graves' disease. ATDs are the preferred treatment option in Europe, Latin America, and Japan. Although RAI remains the most common treatment option in the USA, this option has been used with decreasing frequency over the last 20 years.

The updated guidance includes a review of newly published research studies and how the findings impact clinical care decisions; key areas of interest are discussed below.

Diagnostic Testing. Although both antibody testing and a radioactive uptake test can distinguish Graves' disease from other sources of thyrotoxicosis, a recent study found that the use of antibody testing resulted in reduced costs and a quicker time to diagnosis. In addition, physicians have discovered that biotin, a supplement frequently touted for its benefits to hair and skin, can interfere with thyroid function tests. For patients who are taking biotin and are found to have low TSH and/or high T_4, the guidance recommends discontinuing the supplement and retesting in two days.

Treatment with Radioactive Iodine. For individuals at risk of complications due to worsening hyperthyroidism (specifically the elderly and those with other medical conditions), consideration should be given to re-starting ATDs 3-7 days following RAI treatment. For women who are breast-feeding, the new guidance recommends delaying RAI treatment until three months after lactation stops. The new guidance also mentions cancer risk, noting that, *"A recent meta-analysis found no increase in the overall cancer risk after RAI treatment for hyperthyroidism; however, a trend towards increased risk of thyroid, stomach and kidney cancer was seen, requiring further research."*

Treatment with Antithyroid Medications. The new guidance includes an expanded section on the initial dosing for ATDs, based on the severity of hyperthyroidism. The goal is to prescribe a high enough dose to normalize thyroid function, while minimizing the risk of side effects. Although methimazole can be taken once a day, split dosing (for example, taking 15 mg twice per day instead of 30 mg once per day) may be more effective for patients with severe hyperthyroidism.

The new guidance also goes into greater detail on potential side effects with antithyroid medications. Minor reactions include rash and itching; more serious reactions are rare, but can include damage to the liver and a severe reduction in white blood cell count. The vast majority of reactions occur within the first 90 days of stopping or re-starting the medications. The one exception is vasculitis, a dangerous inflammation of blood vessels that is more common with increased duration of ATD dosing (More risk with PTU than Tapazole). Children and patients of Asian ethnicity are at particular risk for vasculitis.

Monitoring recommendations have changed slightly, with thyroid function testing now recommended at 2-6 weeks instead of four weeks. As with the 2011 guidance, the new document notes that, *"Serum TSH may remain suppressed for several months after starting therapy and is therefore not a good parameter for monitoring therapy early in the course."* Once thyroid levels have stabilized, a dose reduction of 30-50% is recommended, with testing repeated in 4-6 weeks.

The 2016 guidelines place new emphasis on antibody testing, noting that ATDs should be discontinued if TSH and TRAb are normal. *"TRAb assessment at the end of the course of ATD therapy is a useful method of dividing patients into two groups: one with persistent elevations who are unlikely to be in remission, and another group with low or undetectable TRAb, who have a higher probability of permanent remission. In the group with elevated TRAb, relapse rates approach 80-100%, while in the latter group, relapse rates are in the 20-30% range."* Even in patients with negative TRAb, relapses can still occur, so thyroid levels *"should be monitored at 2 to 3-month intervals for the first 6 months, then at 4 to 6-month intervals for the next 6 months, then every 6 to 12 months, in order to detect relapses as early as possible. The patient should be counseled to contact the treating physician if symptoms of hyperthyroidism are recognized."*

ATA Task Force Updates Treatment Guidelines for Hyperthyroidism, continued

Additional information is provided regarding the long-term use of antithyroid medications for patients with persistently elevated TRAb, particularly those who have *"mild stable disease on a low dose of MMI."* Recent studies have found long-term use of ATDs to be safe, and one study found that this approach was superior to RAI in terms of avoiding thyroid eye disease, maintaining euthyroidism, and stabilizing weight.

The new guidance also discusses the possible use of potassium iodide as "adjunct" to ATD therapy; recent studies indicate that this may result in more rapid control of hyperthyroidism with fewer side effects.

Treatment with Thyroidectomy. The new guidance notes that the availability of local surgical expertise affects the decision to move forward with thyroidectomy. The use of a high-volume surgeon results in a reduced risk of complications, reduced hospital stays, and reduced costs. Low blood calcium due to damaged parathyroid glands is a common complication of thyroid surgery and can cause symptoms such as tingling and muscle spasms. Although the prior guidelines recommended testing calcium levels following thyroidectomy, recent research has demonstrated a value in testing calcium levels prior to surgery; advance supplementation should be considered in patients at increased risk for hypoparathyroidism.

Following surgery, the new guidance recommends testing Free T_4 in patients with previously suppressed TSH in order to determine the correct dosing of thyroid hormone. In addition, the new guidance stresses the importance of communication among the patient's entire medical team – both prior to surgery and during the postoperative period.

Thyroid Storm. The new guidelines include an expanded section on the diagnosis and management of thyroid storm, a life-threatening emergency that can occur in patients with untreated or inadequately treated hyperthyroidism. Thyroid storm can also occur in patients who abruptly stop ATDs, experience an acute nonthyroidal illness, or undergo surgery or childbirth without adequate control of hyperthyroidism. Treatment of thyroid storm can include the use of ATDs (PTU is preferred over methimazole, as it can prevent the conversion of T_4 into T_3), steroids, beta blockers, iodine, and more extreme measures such as plasma exchange and emergency surgery.

Children and Graves' disease. The new guidance tweaks the time frames for monitoring thyroid levels for children taking antithyroid drugs. Testing is now recommended 2-6 weeks after starting antithyroid medications with a subsequent follow up 4-6 weeks later, and then at 2-3 month intervals. The new guidance also mentions the need to be vigilant for weight gain in children taking ATDs, with nutritional consultation considered for children experiencing excessive weight gain.

Subclinical hyperthyroidism. This section has been expanded to include a discussion regarding the controversy over whether to treat subclinical hyperthyroidism (SH). Patients with SH have TSH levels below the normal range, but normal range T_3 and T4. Although the research has produced conflicting results, some studies have found an increased risk of cardiovascular issues, osteoporosis, cognitive decline, and overall mortality for patients with untreated subclinical hyperthyroidism. The 2011 guidance noted that treatment of subclinical hyperthyroidism should be "strongly considered" in *"all individuals ≥ 65 years of age; in patients with cardiac risk factors, heart disease or osteoporosis; in postmenopausal women who are not on estrogens or bisphosphonates; and in individuals with hyperthyroid symptoms."* The new guidance now lists treatment as recommended for these individuals.

Graves' disease and pregnancy. The 2016 guidance includes a significantly expanded section on Graves' disease and pregnancy. Physicians are advised to initiate a discussion of future pregnancy plans with patients of child-bearing age: *"the physician providing care to a young woman with newly diagnosed GD should include discussion and guidance on GD and pregnancy. The severely hyperthyroid patient may not be in a position to fully comprehend many simultaneous messages, and a more detailed discussion may be appropriate when the patient has become euthyroid."*

ATA Task Force Updates Treatment Guidelines for Hyperthyroidism, continued

The 2016 guidance includes an expanded discussion of the risk of birth defects with methimazole and PTU. PTU has long been the mainstay of anti-thyroid drug therapy for women in the first trimester of pregnancy, as methimazole has been associated with an increased risk of birth defects. However, new research has identified an increased risk of birth defects with PTU as well, although these tend to be less serious than those associated with methimazole. Options for women with Graves' who are taking methimazole and planning a future pregnancy include switching to PTU while trying to conceive; switching to PTU after a pregnancy is confirmed; choosing definitive therapy prior to trying to conceive; or withdrawing antithyroid drugs when pregnancy is confirmed. If antithyroid medications are withdrawn, the guidance recommends checking levels weekly throughout the first trimester, and then monthly thereafter. It must be noted that while discontinuation of ATDs at this point in pregnancy is discussed there remains a need for additional research in this area. During the second trimester, patients can remain on PTU or switch back to methimazole.

If large doses of antithyroid medications are required for the patient to remain euthyroid, definitive therapy is the preferred option. For those who choose to remain on antithyroid medications while trying to conceive, patients are advised to test for pregnancy *"within the first days after a missed or unusually light menstrual period"* and to contact their endocrinologist or managing physician within 24 hours of a positive test.

For women who are pregnant and have not yet achieved euthyroidism, treatment with propranolol or metoprolol is considered safe for "short periods of time" to help alleviate symptoms such as tremors and rapid heart rate.

The new guidance also mentions the short-term increase in antibodies that can occur following treatment with RAI. "This is a potential argument in favor of surgical thyroidectomy in women with high TRAb titers that may become pregnant within the years to come, especially those planning therapy within the next year. However, the importance of this difference in autoimmune activity for pregnancy outcome has not been studied, and it should be weighed against the other benefits and harms of surgery and RAI therapy."

Guidelines for antibody testing in pregnancy have been updated, with testing now recommended during the first trimester and then again at 18-22 weeks if levels are elevated.

For women with severe disease, the new guidelines recommend frequent monitoring of maternal thyroid function as well as "non-invasive assessment of fetal thyroid function (e.g. fetal heart rate, bone maturity, and fetal goiter on ultrasound)".

ADDITIONAL UPDATES:

- Iodine could potentially be a treatment option for patients who are unable to tolerate ATDs and who are not candidates for surgery or RAI; this approach might also be effective in patients who have had one failed RAI.

- The new guidance discusses the use of ethanol and radiofrequency for ablation of overactive nodules, options that have been used primarily outside the United States. The guidance notes that these approaches "can be considered in select patients where RAI, surgery or long-term ATD are inappropriate, contraindicated, or refused, and expertise in these procedures is available."

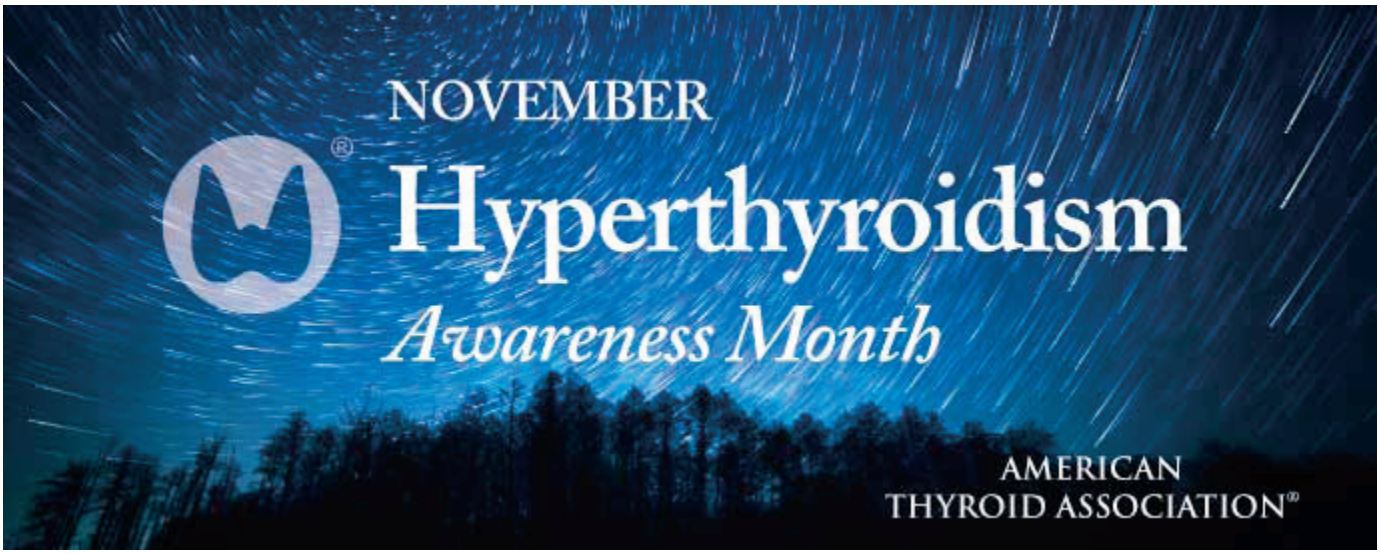
- For patients taking medications known to potentially cause thyrotoxicosis (such as lithium or amiodarone), thyroid function testing is recommended at 6 month intervals.

In conclusion, it's important to note that these guidelines are just that – guidelines. As the task force members note, *"It is not the intent of these guidelines to replace clinical judgment, individual decision making, or the wishes of the patient*

ATA Task Force Updates Treatment Guidelines for Hyperthyroidism, continued

or family. Rather, each recommendation should be evaluated in light of these elements in order that optimal patient care is delivered." If your own provider's recommendations differ from what is outlined here, these guidelines should be used as a starting point for an open discussion. Each patient has a unique experience with thyroid dysfunction as well as a unique medical and family history, and any treatment recommendations should be tailored accordingly.

Would you like to review the guidance in full? Please visit the Professional Guidelines page of the American Thyroid Association's website at http://www.thyroid.org/professionals/ata-professional-guidelines/.



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THYROID AND PREGNANCY

Birth defects are more common than other complications in pregnant women treated with anti-thyroid drugs

BACKGROUND

Hyperthyroidism, particularly Graves' disease, is more common in women than men, especially in women of childbearing age. Untreated hyperthyroidism in pregnancy can affect both the mother and the developing baby. The preferred antithyroid drug in non-pregnant women is Methimazole. During pregnancy, the current American Thyroid Association guidelines recommend propylthiouracil as the drug of choice for newly diagnosed Graves' disease and to switch to propylthiouracil if already on therapy. The reason for this is that, while both of these medications have been associated with birth defects when used in the first trimester, the risk is lower and the defects appear to be less severe with propylthiouracil. Both antithyroid drugs also have similar side effects, including the rare, but potentially serious, side effect of agranulocytosis (low white blood cells) that can lead to potentially serious infections, and the more rare side effect of liver failure. The goal of this study was to determine the frequency of these two adverse side effects as compared to birth defects in the general population and in pregnant women in an effort to guide the treatment of hyperthyroidism in pregnancy.

THE FULL ARTICLE TITLE

Andersen SL et al. Antithyroid drug side effects in the population and in pregnancy. J Clin Endocrinol Metab 2016; 101 (4): 1606-14. Epub January 27, 2016.

SUMMARY OF THE STUDY

Children born from January 1st, 1973 until December 31, 2008 and their parents were identified using the Danish Medical Birth Register. Exposure to antithyroid drugs was obtained from the Danish National Prescription Register, which contains information from January 1st, 1995. Information on the outcomes was obtained from the Danish National Hospital Register, which contains inpatient diagnoses since 1977 and inpatient and outpatient diagnoses since January 1995. All visits from January 1st 1995 until December 31, 2010 were included. Birth defects registered before the age of 2 years were included. To study the pregnant women, the population was restricted to women who gave birth to a live-born child between 1996-2008. The study population included 2,299,952 people, out of which 28,998 people were treated with antithyroid in the study period.

Results showed there were 41 cases of agranulocytosis and 11 cases of liver failure per 5 millions inhabitants during a 10 year period. Among all people exposed to antithyroid drugs, there were 45 cases of antithyroid drug-associated agranulocytosis (0.16%) and 10 cases of antithyroid drug-associated liver failure (0.03). There were 830,680 pregnancies and 848,022 live born babies, of which 2206 were exposed to antithyroid drugs during pregnancy. One case of agranulocytosis occurred during pregnancy and one case of liver failure was associated with pregnancy, both while treated with propylthiouracil. A total of 75 children (3.4% of exposed babies) were estimated to have birth defects associated with antithyroid drugs. Unfortunately, the types and severity of birth defects were not reported.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In the Danish Population, antithyroid drug-associated birth defect and agranulocytosis were more common than antithyroid drug-associated liver failure. In pregnant Danish women, birth defects were the most frequent associated complication of antithyroid drugs. This study is important for patients because restricting the use of these medications in early pregnancy, when clinically possible, can decrease antithyroid drug-related side effects in pregnant women and likely will prevent birth defects related to antithyroid drugs. In addition, planning definitive treatment of hyperthyroidism with either surgery or radioactive iodine prior to pregnancy in women of childbearing age is an option that would also prevent birth defects associated with the use of antithyroid drugs in pregnancy.

— Liuska Pesce, MD

ATA THYROID BROCHURE LINKS

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

Graves' disease: http://www.thyroid.org/graves-disease/

Hyperthyroidism: http://www.thyroid.org/hyperthyroidism/

THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

Agranulocytosis: a marked decrease in the white blood cell count that causes a patient to be more likely to develop an infection. This is commonly associated with a fever and/or a sore throat.

Liver failure: Loss of liver function that occurs rapidly, usually in a person who has no history of liver disease.

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

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

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.

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HYPERTHYROIDISM

Low white blood cell counts are common in patients with Graves' disease and improve with antithyroid drug treatment

BACKGROUND

Graves' disease is the most common type of hyperthyroidism in the United States. Antithyroid drugs (ATDs) are frequently used to treat Graves' disease. These drugs (Methimazole and Propylthiouracil in the United States, Carbimazole in Europe) are usually very well tolerated. However, agranulocytosis (low white blood cells) is a rare complication of ATDs occurring in 0.1-0.3% of patients. White blood cells (WBCs) help fight infections, so agranulocytosis can result in severe and even deadly infections. Graves' disease itself can cause mild decreases in WBCs that do not lead to infections, so it is important not to confuse this with agranulocytosis The goal of this study is to evaluate the how common low WBCs are seen in patients newly diagnosed with hyperthyroidism due to Graves' disease before starting ATD treatment and the effect of this treatment on the WBC count.

THE FULL ARTICLE TITLE

Aggarwal A et al. Treatment of hyperthyroidism with antithyroid drugs corrects mild neutropenia in Graves' disease. Clin Endocrinol (Oxf). June 13, 2016 [Epub ahead of print]

SUMMARY OF THE STUDY

The study included 206 consecutive patients newly diagnosed with Graves' disease followed in an outpatient endocrinology clinic in Newcastle, United Kingdom between 2010 and 2014. Samples for complete blood count (CBC) that includes WBC counts were obtained prior to starting ATD treatment and then a few months later after the thyroid tests returned to normal on drug treatment. All patients started treatment with Carbimazole and about 10% of the patients were later switched to Propylthiouracil because of side effects from the carbimazole, including itching and joint pain. The majority of study participants were white (94.7%).

Mild low WBCs were found in 29 of the 206 (14%) study patients before starting ATD treatment. Interestingly, more than half of the 11 non-white patients (54.5%) but only 11.8% of the white patients had a low WBCs at diagnosis. The patients who had baseline low WBCs had more severe hyperthyroidism and also had other low CBC tests such as low platelets and mild anemia. Interestingly, current smokers had a lower risk of having baseline low WBCs and had higher baseline CBC tests in general as compared with non-smokers.

The WBC count returned to normal in all patients with baseline low WBC count after starting ATD treatment. The WBC also increased in patients that had a normal WBC at baseline. In addition, platelet levels increased and anemia improved on ATD treatment. The time period required to normalize the thyroid function on ATD treatment and the ATD dose used were similar in patients with low and normal baseline WBC levels. None of the patients with a normal baseline WBC count developed a low count on ATD treatment. No study patient had agranulocytosis at baseline or developed this on treatment.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

A significant proportion of newly diagnosed patients with Graves' disease have a low baseline WBC count before starting ATD treatment, particularly non-white patients and patients with severe hyperthyroidism. The low WBC count and other blood abnormalities normalize once the thyroid function returns to normal on ATD treatment. The American Thyroid Association recommends performing a complete CBC, including WBC count before starting ATD treatment. It is important to diagnose a pre-exiting low neutrophil count before starting treatment to differentiate it from the ATD-induced agranulocytosis, which can results in life-threatening infections and requires prompt ATD discontinuation.

— Alina Gavrila, MD, MMSC

ATA THYROID BROCHURE LINKS

Hyperthyroidism: http://www.thyroid.org/hyperthyroidism/

Graves' disease: http://www.thyroid.org/graves-disease/

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 medications (methimazole, carbimazole, propylthiouracil), radioactive iodine or surgery.

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

Antithyroid drugs (ATDs): medications that block the thyroid from making thyroid hormone. Methimazole, carbimazole and propylthiouracil (PTU) are used to treat hyperthyroidism, especially when it is caused by Graves' disease.

Triiodothyronine (T3): the active thyroid hormone. Thyroxine (T_4), the major hormone produced by the thyroid gland gets converted to the active hormone T_3 in various tissues in the body.

Complete blood count (CBC): test that analyzes the blood cells: red blood cells which carry oxygen, white blood cells which protect the body against infection and platelets which help with blood clotting.

Hemoglobin: the protein in red blood cells that binds oxygen to carry around to all the cells in the body. Hemoglobin levels are low with anemia.

Lymphocytes: type of white blood cells that are part of the immune system and produce antibodies to fight infection.

Neutrophils (WBCs): the most abundant type of white blood cells that fight infection by ingesting germs (micro-organisms) and releasing enzymes that kill germs.

Agranulocytosis: a marked decrease in the WBC count that causes a patient to be more likely to develop an infection. This is commonly associated with a fever and/or a sore throat.

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HYPERTHYROIDISM

Can we predict which patients with hyperthyroidism will develop agranulocytosis with antithyroid drugs?

BACKGROUND

Graves' disease is the most common type of hyperthyroidism in the United States. Antithyroid drugs (ATDs) are frequently used to treat Graves' disease. These drugs (Methimazole and Propylthiouracil in the United States, Carbimazole in Europe) are usually very well tolerated. However, agranulocytosis (low white blood cells) is a rare complication of ATDs occurring in 0.1-0.3% of patients. White blood cells (WBCs) help fight infections, so agranulocytosis can result in severe and even deadly infections. Presenting symptoms include sore throat, fever, and muscle aches, but severe infections occur in approximately two out of three patients and up to 5% of these patients will die of this complication.

The mechanism through which antithyroid drugs cause agranulocytosis is currently unknown, but studies suggest an autoimmune cause. Certainly, if patients at risk for this severe side effect could be identified, other options for treatment such as surgery or radioactive iodine could be chosen. Molecular tests have been used to identify patients at risk for other medical disorders and have been used in some patients with agranulocytosis. Previous studies have shown that certain genetic variants are associated with a high risk of antithyroid drug–induced agranulocytosis in ethnic Chinese people in Taiwan and Hong Kong. They analyzed molecular markers known as single-nucleotide polymorphisms (SNPs) in their study.

The Cheung study used SNPs to examine whether a specific genetic marker was associated with antithyroid drug–induced agranulocytosis in a population of ethnic Chinese people. The Hallberg study used SNPs to examine whether a similar pattern of genetic variants are associated with agranulocytosis in a European population.

THE FULL ARTICLE TITLE

Cheung CL et al. HLA-B*38:02:01 predicts carbimazole/methimazole-induced agranulocytosis. Clin Pharmacol Ther 2016;99:555-61. Epub January 12, 2016.

SUMMARY OF THE STUDY

Since 2013 in specialist or regional hospitals in Hong Kong, agranulocytosis was found to have developed in 19 female and 5 male Chinese patients with Graves' disease. Genetic studies were performed on 24 of these patients. Agranulocytosis developed 19 patients taking methimazole or carbimazole and in 5 patients taking. Controls (those without thyroid disease or agranulocytosis) included 387 randomly selected women from various other studies as well an additional group of 57 patients with Graves' disease who had been treated with methimazole or carbimazole for at least 3 months without agranulocytosis.

The initial discovery screen detected a strong signal known as SNP rs185386680(G) in the HLA region. This identified HLA-B*38:02:01 variant is a susceptibility locus for agranulocytosis. Further, they found that HLA-DRB1*08:03 that had been found in the earlier studies did not meet the threshold for significance in this study.

THE FULL ARTICLE TITLE

Hallberg P et al for the EuDAC collaborators. Genetic variants associated with antithyroid drug-induced agranulocytosis: a genome-wide association study in a European population. Lancet Diabetes Endocrinol 2016;4:507-16. Epub May 3, 2016.

SUMMARY OF THE STUDY

Patients were recruited through national registries and hospitals collaborating in the European Drug-induced Agranulocytosis Consortium (EuDAC), a network of investigators in Sweden, Spain, France, Germany, the United Kingdom, and the Netherlands. Cases included patients in whom agranulocytosis developed during antithyroid drug treatment or within 7 days after stopping treatment. Each patient was required to have complete recovery after stopping of the drug. A total of 39 patients had agranulocytosis that was induced by antithyroid drugs (methimazole, 74%; carbimazole, 13%: and propylthiouracil, 13%). Researchers selected 5170 controls (people without agranulocytosis) from several Swedish national registries. In addition, 49 patients who had been treated for hyperthyroidism without developing agranulocytosis were selected. Roughly 600,000 SNPs were genotyped for final analyses.

HYPERTHYROIDISM, continued

The results identified three genetic variants to be associated with antithyroid-induced agranulocytosis: rs652888 located in an intron of EHMT2, HLA-B*27:05 and HLA-B*08:01. The predictive ability for all three variants combined was high. Using this analysis, the authors concluded that one case of antithyroid-induced agranulocytosis would be avoided for each 238 patients genotyped.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These two studies present preliminary information that patients that have certain genetic variants are at increased risk for antithroid-induced agranulocytosis. Screening for these variants would help choose the best treatment for Graves' disease. However, at present, these markers are not ready to be put into general clinical use but suggest that this may be the case in the future. Further, these studies provide information that may help to determine what causes antithroid-induced agranulocytosis.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

Hyperthyroidism: http://www.thyroid.org/hyperthyroidism/

Graves' disease: http://www.thyroid.org/graves-disease/

ABBREVIATIONS & DEFINITIONS

Agranulocytosis: a marked decrease in the white blood cell count that causes a patient to be more likely to develop an infection. This is commonly associated with a fever and/or a sore throat.

White blood cells: the infection-fighting cells of the blood.

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.

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.

AMERICAN THYROID ASSOCIATION
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SPOTLIGHT ON: GRAVES' DISEASE & THYROID FOUNDATION

It's been a busy year for the Graves' Disease & Thyroid Foundation!

In April 2016, the GDATF headed to Baltimore, MD to host a patient education event and to exhibit at the annual meeting of the American Association of Endocrine Surgeons. Endocrinologist Dr. David Cooper, MD, Director, Thyroid Clinic, Johns Hopkins Medicine and Dawn M. Elfenbein, MD, MPH, Clinical Instructor, Surgery, University of California, Irvine School of Medicine fielded questions from patients on Graves' disease, autoimmunity, and thyroid eye disease. Attendees traveled from New York, New Jersey, and Washington DC to attend.

In May, the GDATF hosted a full-day patient education event at University of California Shiley Eye Institute. The first part of the event was devoted to presentations on Graves' eye disease (also called thyroid eye disease) from physicians at UC San Diego Shiley Eye Institute. Presentations included:

- "Ophthalmic manifestations of thyroid eye disease and update on medical therapy" from Bobby S. Korn, MD, PhD
- "Orbital and Eyelid Surgery in Thyroid Eye Disease" from Don O. Kikkawa, MD
- "Strabismus in Thyroid Eye Disease" from David B. Granet, MD

The presentations on thyroid eye disease were followed with a question and answer session featuring all three presenters.

The morning session concluded with two patient panels, featuring patients who were living with Graves' disease and thyroid eye disease.

The afternoon presentations focused on treatment options for Graves' disease. An attendee question and answer session followed each presentation. Presentations included:

- "An Endocrinologist's view of Graves Disease" from Karen McCowen, MD
- "Radioactive Iodine for Diagnosis and Treatment of Graves' Disease" from Farshad Moradi, MD, PhD
- "Thyroid Surgery for Graves Disease" from Kevin Brumund, MD

All three afternoon presenters are affiliated with University of California San Diego.

The program concluded with a support group session where attendees were allowed to discuss their questions and concerns in a small group setting. There were separate groups for Graves' patients, thyroid eye disease patients, and for family members of patients. Facilitators were GDATF Board Co-Chairs Steve and Kathleen Flynn and GDATF Executive Director/CEO Kimberly Dorris.

Out of state participants traveled from as far as Oregon and North Dakota. Attendees had an opportunity to connect outside of the formal sessions over dinner at some excellent local restaurants. Attendees called the program "informative" and even "life-changing". We are grateful to the County of San Diego for helping to fund this important event via their Community Reinhancement Program!

In September, the American Thyroid Association hosted its 86th Annual Meeting in Denver, CO. The GDATF had an opportunity to attend presentations from Dr. Rebecca S. Bahn and Dr. Michele Morino on thyroid eye disease; by Dr. David Cooper and Dr. Susan Mandel on Graves' disease in pregnancy; and by Dr. Douglas Ross and Dr. George Kahaly on

SPOTLIGHT ON: Graves' Disease & Thyroid Foundation, continued

the pros and cons of methimazole versus definitive therapy for Graves' disease. On the final Saturday of the meeting, the ATA and the Alliance for Patient Education hosted a public forum for patients and family members.

In October, we headed to Chicago, IL for the Fall Symposium of the American Society of Ophthalmic, Plastic, and Reconstructive Surgery (ASOPRS). This meeting gave us the opportunity to let eye surgeons know about our education and support services, as living with thyroid eye disease is challenging both physically and emotionally. We also hosted a patient support group meeting at Dollop, a local coffee shop.

The following week, our friends at ThyCa: Thyroid Cancer Survivors, Inc. invited us to host a satellite symposium on Graves' disease and thyroid eye disease as part of their annual patient conference in Los Angeles. This was a successful collaboration between fellow members of the ATA's Alliance for Patient Education! Several conference attendees stopped by to listen to the presentation or to pick up materials for friends and family members. We are grateful to ThyCa for the opportunity, as well as to the presenters who donated their time on a Saturday to help promote patient education: Dr. Raymond Douglas (speaking about thyroid eye disease), Dr. Ira Lesser (speaking about the emotional aspects of thyroid dysfunction), and Dr. Andrew Gianoukakis (speaking about Graves' disease treatments).

We have some exciting events in the works for 2017! To get the latest news, please visit us at gdatf.org, follow us on social media, or sign up for our free monthly e-newsletter by e-mailing info@gdatf.org.

In addition to in-person patient education events and local support group meetings, GDATF advocates are available to speak one-on-one with patients and family members. Our staff will not give medical advice (such as interpreting labs or making treatment recommendations), but we are happy to share general information and resources. Advocates can be contacted at 877-643-3123 or info@gdatf.org. We are also active on Facebook and Twitter, and we have an online support forum on our website at gdatf.org. (There is no cost to participate in the online forum, although users who wish to post or reply on the forum must register with a valid e-mail address.)

GDATF Board Updates

The Graves' Disease & Thyroid Foundation extends our best wishes to Dr. Lawrence C. Wood, who announced his retirement from the GDATF Board of Directors after serving two three-year terms. GDATF Founder and Chair Emeritus Nancy Hord Patterson, Ph.D., noted, "Dr. Wood has been a pioneer in the area of patient support and education for decades. He is known and respected throughout the world, and has been my/our friend, mentor and colleague through all these years." As we say a fond farewell to Dr. Wood, Carla DiMare and Ashok Bhaseen join the GDATF as the organization's newest Board members. Carla is a trial attorney in California and Massachusetts who specializes in civil litigation and social justice issues. Ashok worked with Abbott Pharmaceuticals (Canada and International) for 12 years and has served as the Global President of Thyroid Federation International since 2011.

— Kimberly Dorris, Executive Director/CEO
Graves' Disease and Thyroid Foundation

AMERICAN THYROID ASSOCIATION
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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-portal/
Find a Thyroid Specialist: www.thyroid.org
Phone (toll-free): 1-800-THYROID
e-mail: thyroid@thyroid.org

ATA Mission: The ATA leads in promoting thyroid health and understanding thyroid biology.
ATA Vision: The ATA is the leading organization focused on thyroid biology and the prevention and treatment of thyroid disorders through excellence and innovation in research, clinical care, education, and public health.
ATA Values: The ATA values scientific inquiry, clinical excellence, public service, education, collaboration, and collegiality.

To further our mission, vision and values the ATA sponsors "Friends of the ATA" online to advance the information provided to patients and the public such as this publication, *Clinical Thyroidology for the Public*. We welcome your support.

continued on next page

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

Light of Life Foundation
checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

Thyroid Federation International

BITE ME CANCER!

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

Thyroid Cancer Canada
Cancer de la thyroïde Canada

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.

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AMERICAN THYROID ASSOCIATION
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Light of Life Foundation
checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

Thyroid Federation International

BITE ME CANCER!

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

Thyroid Cancer Canada
Cancer de la thyroïde Canada

ATA Alliance for Thyroid Patient Education

Continued...

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

www.thyca.org
Phone (toll-free): 877 588-7904
e-mail: thyca@thyca.org

ThyCa: Thyroid Cancer Survivors' Association, Inc., founded in 1995, is an international nonprofit organization, guided by a medical advisory council of renowned thyroid cancer specialists, offering support and information to thyroid cancer survivors, families, and health care professionals worldwide.

THYROID CANCER CANADA

www.thyroidcancercanada.org
Phone: 416-487-8267
Fax: 416-487-0601
e-mail: info@thyroidcancercanada.org

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

THYROID FEDERATION INTERNATIONAL

www.thyroid-fed.org
e-mail: tfi@thyroid-fed.org

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

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ThyCa: Thyroid Cancer Survivors' Association, Inc.
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Thyroid Cancer Canada
Cancer de la thyroïde Canada

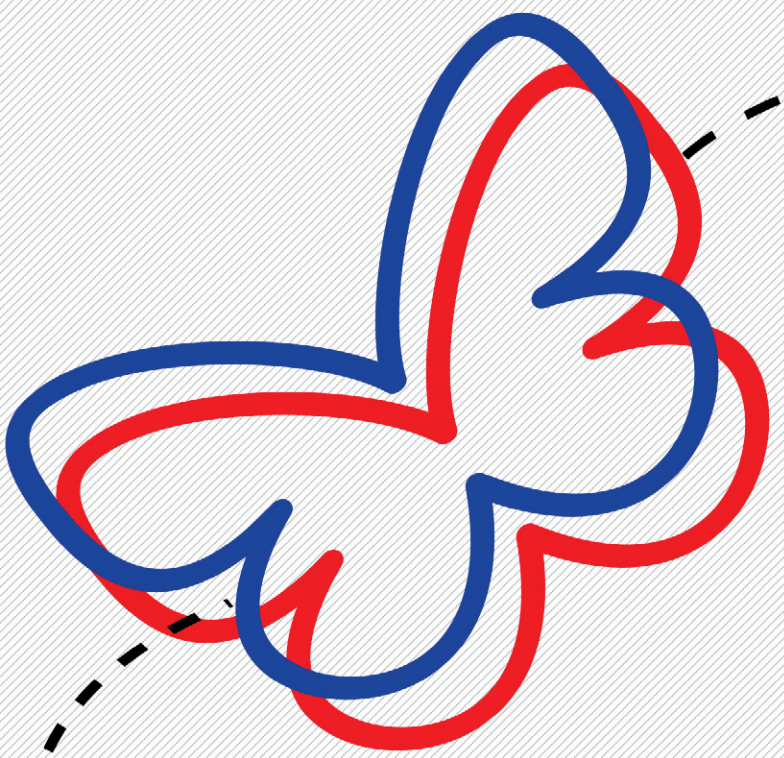
Reasons to #GIVE2THYROID

American Thyroid Association

#GIVINGTUESDAY

November 29, 2016

www.thyroid.org/donate



Reason 1

Care for Thyroid Patients

Thyroid Specialists are dedicated to patient care and treatment. Clinician scientists develop evidence-based management guidelines on thyroid diseases and thyroid cancer. Support our continuing care about the thyroid.

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

Reason 2

Thyroid Research

Thyroid specialists are devoted to thyroid discovery: new science, new treatments, improved patient outcomes. Support the advancement of understanding your thyroid.

+clinical practice guidelines
+position statements
+early career training
+research and education grants
+leadership & service awards
+community for collaboration
+continuing education programs
+peer-review biomedical journals
+summarized medical literature
+up to date thyroid news & publications
+patient education

American Thyroid Association
www.thyroid.org/donate

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 perspiration, heart racing, hand tremors, anxiety, difficulty sleeping, thinning of your skin, fine brittle hair and weakness in your muscles—especially in the upper arms and thighs. You may have more frequent bowel movements, but diarrhea is uncommon. You may lose weight despite a good appetite and, for women, menstrual flow may lighten and menstrual periods may occur less often. Since hyperthyroidism increases your metabolism, many individuals initially have a lot of energy. However, as the hyperthyroidism continues, the body tends to break down, so being tired is very common.

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

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

WHAT CAUSES HYPERTHYROIDISM?

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

Hyperthyroidism

HOW IS HYPERTHYROIDISM DIAGNOSED?

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

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

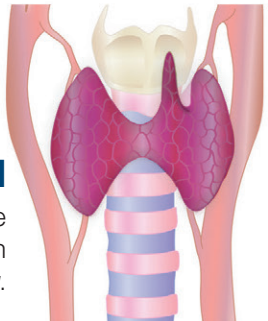
HOW IS HYPERTHYROIDISM TREATED?

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, bring quick control of hyperthyroidism and do not cause permanent damage to the thyroid gland. In about 20% to 30% of patients with Graves' disease, treatment with antithyroid drugs for a period of 12 to 18 months will result in prolonged remission of the disease. For patients with toxic nodular or multinodular goiter, antithyroid drugs are sometimes used in preparation for either 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 get an infection such as a fever or sore throat, you should stop the drug immediately and have a white blood cell count that day. Even if the drug has lowered your white blood cell count, the count will return to normal if the drug is stopped immediately. But if you continue to take one of these drugs in spite of a low white blood cell count, there is a risk of a more serious, even life-threatening infection. Liver damage is another very rare side effect. A very serious liver problem can occur with PTU use which is why this medication should not generally be prescribed. You should stop either methimazole or PTU and call your doctor if you develop yellow eyes, dark urine, severe fatigue, or abdominal pain.



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***.

Hyperthyroidism

RADIOACTIVE IODINE

Another way to treat hyperthyroidism is to damage or destroy the thyroid cells that make thyroid hormone. Because these cells need iodine to make thyroid hormone, they will take up any form of iodine in your blood stream, whether it is radioactive or not. The radioactive iodine used in this treatment is administered by mouth, usually in a small capsule that is taken just once. Once swallowed, the radioactive iodine gets into your blood stream and quickly is taken up by the overactive thyroid cells. The radioactive iodine that is not taken up by the thyroid cells disappears from the body within days. Over a period of several weeks to several months (during which time drug treatment may be used to control hyperthyroid symptoms), radioactive iodine destroys the cells that have taken it up. The result is that the thyroid or thyroid nodules shrink in size, and the level of thyroid hormone in the blood returns to normal. Sometimes patients will remain hyperthyroid, but usually to a lesser degree than before. For them, a second 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 most of your thyroid gland. This procedure is best performed by a surgeon who has much experience in thyroid surgery. An operation could be risky unless your hyperthyroidism is first controlled by an antithyroid drug (see above) or a beta-blocking drug (see below). Usually for some days before surgery, your surgeon may want you to take drops of nonradioactive iodine—either Lugol's iodine or supersaturated potassium iodide (SSKI). This extra iodine reduces the blood supply to the thyroid gland and thus makes the surgery easier and safer. Although any surgery is risky, major complications of thyroid surgery occur in less than 1% of patients operated on by an experienced thyroid surgeon. These complications include damage to the parathyroid glands that surround the thyroid and control your body's calcium levels (causing problems with low calcium levels) and damage to the nerves that control your vocal cords (causing you to have a hoarse voice).

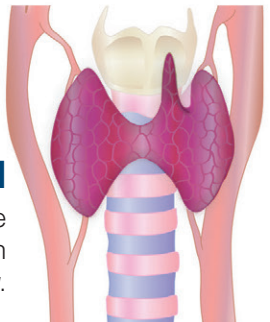
After your thyroid gland is removed, the source of your hyperthyroidism is gone and you will likely become hypothyroid. As with hypothyroidism that develops after radioiodine treatment, your thyroid hormone levels can be restored to normal by treatment once a day with a thyroid hormone supplement.

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 the *beta adrenergic blocking agents* that block the action of thyroid hormone on your body. They usually make you feel better within hours to days, even though they do not change the high levels of thyroid hormone in your blood. These drugs may be extremely helpful in slowing down your heart rate and reducing the symptoms of palpitations, shakes, and nervousness until one of the other forms of treatment has a chance to take effect. Propranolol (Inderal®) was the first of these drugs to be developed. Some physicians now prefer related, but longer-acting beta-blocking drugs such as atenolol (Tenormin®), metoprolol (Lopressor®), nadolol (Corgard®), and Inderal-LA® because of their more convenient once- or twice-a-day dosage.

OTHER FAMILY MEMBERS AT RISK

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



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***.