Volume 13 | Issue 4 | April 2020

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

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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 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, 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.

March is Hashimoto's Thyroiditis Awareness Month.

Please see the Statement on COVID-19 on page 3 and the FAQs on the Effect of COVID-19 on the Thyroid on page 4.

In this issue, the studies ask the following questions:

- Is there a risk of cancer following radioactive iodine therapy for hyperthyroidism?
- Do steroids prevent thyroid eye disease after radioactive iodine?
- Does thyroid surgery cause depression?
- Does obesity cause thyroid cancer?
- Does extension of thyroid cancer outside of the thyroid affect prognosis?
- Does exposure to flame retardants during pregnancy cause thyroid problems?

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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STATEMENT ON COVID-19

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. As we try to do with *Clinical Thyroidology for the Public*, 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.

We recommend the following websites:

- **Centers for Disease Control (CDC) —** https://www.cdc.gov/coronavirus/2019-ncov/index.html
- **US Department of State —** https://www.state.gov/coronavirus/
- **World Health Organization —** https://www.who.int/
- **U.S. Food and Drug Administration (FDA) —** https://www.fda.gov/patients/coronavirus-disease-2019-covid-19-resources-patients
- ***Apple COVID-19 Screening tool app***, developed in conjunction with the CDC, FEMA and the White House. This is free and available in the App Store. Unfortunately, there is not yet an android version of this app.

We all can, and must, do our part to slow the spread of COVID-19 and to "flatten the curve". COVID-19 is thought to spread mainly from person-to-person who are in close contact with one another. Because of this, we all have the power to attack this pandemic by:

- Practicing Social Distancing (6 feet apart) — This is the **best way** to avoid being exposed to, or spreading, this virus.
- Cleaning our hands often with soap or hand sanitizer. Avoid touching our eyes, nose and mouth.
- Avoiding close contact with people who are sick.
- Staying home if we are sick, except to get medical care.
- Cleaning AND disinfecting frequently touched surfaces daily.

Take care and stay safe — we will get through this, together.

Alan P. Farwell, MD
Editor, *Clinical Thyroidology for the Public*

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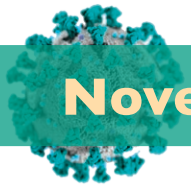

Novel Coronavirus (COVID-19) and the Thyroid

Frequently Asked Questions (FAQs)

Over the past days and weeks, the American Thyroid Association and its members have heard many important concerns raised by both patients and their providers about how the novel coronavirus (COVID-19) pandemic might impact people living with thyroid conditions. Here, we address the most frequently asked questions thus far.

HASHIMOTO'S THYROIDITIS AND HYPOTHYROIDISM

Are people with autoimmune thyroid disease, such as Hashimoto's thyroiditis or Graves' disease, at more risk for acquiring COVID-19 or having a more serious COVID-19 infection?

The U.S. Centers for Disease Control (CDC) advises that people who are immunocompromised are at higher-risk of severe illness from COVID-19. Immunocompromised people have a weaker immune system and have a harder time fighting infections. However, the immune system is complex, and having autoimmune thyroid disease does not mean that a person is immunocompromised or will be unable to fight off a viral infection.

Thus far, there is no indication that patients with autoimmune thyroid disease are at greater risk of getting COVID-19 or of being more severely affected should they acquire the COVID-19 infection.

Everyone should continue to practice the recommended hand hygiene and social distancing recommendations to avoid COVID-19 infection.

Are there any shortages of levothyroxine?

Levothyroxine is one of the most widely used medications in the United States, and there are many brand and generic types available.

At this time, there are no identified shortages of any types of these thyroid hormone replacement medications. However, in order to maintain social distancing and limit exposure to COVID-19, patients should consider obtaining a 90-day supply of prescriptions, or receiving their thyroid medications through a mail-order service instead of picking them up at the local pharmacy.

HYPERTHYROIDISM

How do patients taking methimazole for hyperthyroidism tell the difference between a COVID-19 infection or side effects of methimazole?

Many patients with Graves' disease and other types of hyperthyroidism are treated with the medication known as methimazole (or a similar medication called propyl-thiouracil [PTU]). A rare side effect of these antithyroid medications is a condition called agranulocytosis (occurring in 0.2-0.5% of people taking the medication), in which the number of the immune cells that fight infection decrease. Patients may have symptoms such as fever or sore throat. If these occur, patients are often told to stop the methimazole and go to a laboratory to have blood testing done.

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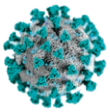

Novel Coronavirus (COVID-19) and the Thyroid FAQS, continued

As fever and signs of illness can also overlap with the symptoms of COVID-19 infection, many patients who happen to also be taking methimazole may be concerned that they have become infected with COVID-19. Should they quarantine at home if they have some of these symptoms?

Because agranulocytosis with fever can represent a serious infection, the possibility should not be ignored. Agranulocytosis is less common in patients who have been taking methimazole for a long time or when the dose of the medication is low (e.g. 15 mg in one study), but it can still occur. If a fever or other symptoms of an infection start while taking methimazole, it is best to contact your endocrinologist or other provider to determine how best to be evaluated.

Patients should always seek medical attention for symptoms that seem urgent or life-threatening. Any patient with new fever, cough, or other typical symptoms of COVID-19 infection should seek medical attention immediately, regardless of methimazole use.

How can methimazole be given to patients with critical illness?

Methimazole is an oral medication, and stopping these medications can lead to worsening of hyperthyroidism. During a critical respiratory illness, especially when a ventilator (breathing machine) is required, a patient may not be able to take medications by mouth. When treatment of hyperthyroidism is necessary, different routes for giving methimazole may be used. Providers taking care of patients with critical illnesses will be able to determine the best approach for making sure that a patient with hyperthyroidism continues to receive treatment as needed.

The placement of a naso-gastric tube or a Dobhoff tube allows the same methimazole pill to be delivered to the gut (digestive system) in a patient who is unable to swallow.

If the enteric route (through the stomach) is not available, these medications can be prepared for intravenous (IV) use:

- IV methimazole has been given by adding 500mg of methimazole powder to 0.9% sodium chloride solution to a final volume of 50mL and administering the correct dose as a slow IV push over 2 minutes.
- PTU is relatively insoluble. An IV formulation used in one report was made by dissolving tablets in isotonic saline with an alkaline pH (pH 9.25).

Enema or suppository formulations have also been used and require specific preparation.

THYROID NODULES AND THYROID CANCER

Is it safe to delay a biopsy of my thyroid nodule?

Most thyroid nodules are benign (not cancerous), but some nodules of a certain size that also have suspicious features on ultrasound may be advised to undergo a biopsy. Even if the thyroid nodule is found to be cancerous, there is usually little risk in delaying surgery to have it removed. Thus, it would also be generally safe to delay biopsy of the nodule unless your clinician strongly advises that it be done urgently.

Are people with thyroid cancer at greater risk for COVID-19 infection because they are immunocompromised?

The U.S. Centers for Disease Control (CDC) generally states that people who are undergoing cancer treatment meet the definition of being immunocompromised.

However, unlike many other types of cancer, the majority of thyroid cancer patients are not receiving chemotherapy or other treatment that would deplete the immune system

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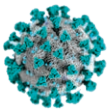

Novel Coronavirus (COVID-19) and the Thyroid FAQS, continued

and cause them to be immunocompromised. Having a previous diagnosis of thyroid cancer and receiving thyroid hormone medication is not a known risk factor for getting COVID-19 or being more severely affected by it.

For the rare thyroid cancer patients who are receiving chemotherapy medications for your thyroid cancer treatment, you would be considered at higher risk for severe illness due to COVID-19.

To read more about people who are at higher risk: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fspecific-groups%2Fhigh-risk-complications.html

Is it safe to delay thyroid cancer surgery because of the current COVID-19 pandemic?

The most common initial treatment for thyroid cancer is surgery to remove the thyroid tumor. Because of the current COVID-19 pandemic, many surgeries that were scheduled for thyroid cancer have had to be delayed, raising concerns about receiving timely care for thyroid cancer.

While surgery is necessary, most thyroid cancers are very slow-growing tumors, and the chance of thyroid cancer worsening if surgery is delayed by several months is extremely low. This is true even if there is spread of the thyroid cancer to local lymph nodes in the neck.

However, thyroid surgery would be essential and should be performed more urgently for patients with symptoms due to the size of the thyroid tumor, such as difficulty breathing or swallowing, cancers that are invading other parts of the neck, or if the biopsy showed aggressive forms of thyroid cancer, including anaplastic thyroid cancer and medullary thyroid cancer.

Is it safe to delay radioactive iodine treatment because of the current COVID-19 pandemic?

Radioactive iodine (RAI) therapy is often used for thyroid cancer patients after having surgery and typically involves several visits to a doctor or healthcare facilities. These treatments are frequently being rescheduled during the current COVID-19 pandemic, causing worry about these delays for patients scheduled to receive RAI.

RAI is often used to eliminate any remaining normal (non-cancerous) thyroid tissue or to decrease the chance of recurrence even when all thyroid cancer appears to have been surgically removed. Delays of six months or even longer do not appear to negatively affect the course of thyroid cancer in patients. Therefore, the short delays expected from waiting until the current COVID-19 pandemic is over are unlikely to lower the effectiveness of the RAI treatment.

In general, treatment with RAI is more urgent for patients who have papillary or follicular thyroid cancer who have distant metastases to the lungs or other body parts, particularly if growth of the metastases have been observed. Your health care provider will advise you when it is better to delay RAI treatment or when it is better to proceed with treatment despite the current pandemic.

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HYPERTHYROIDISM

Is there a risk of cancer following radioactive iodine therapy for hyperthyroidism?

BACKGROUND

Radioactive iodine therapy can be a valuable option to treat hyperthyroidism. It is taken as a pill, absorbed in the stomach and carried in the blood to the thyroid, where it is taken up into the overactive thyroid cells. The radiation then causes destruction of the overactive thyroid tissue. However, the non-overactive thyroid cells that may remain are also exposed to radiation, as are well as many tissues in the body. While radioactive iodine is very useful in treating hyperthyroidism due to Graves' disease, other treatments are available such as antithyroid drugs or surgery. Therefore, it is important to consider whether there is any potential harm from the radiation exposure.

A number of studies have been done to look for any association between radioactive iodine therapy and subsequent cancers. The results from previous studies have been varied for many reasons including the need to evaluate a large group of patients when looking for small differences, difficulty in identifying the proper comparison group, the need for long follow up and limited information regarding the radiation exposure. This study was performed to evaluate the risk of cancers in patients who were diagnosed with hyperthyroidism and then treated with radioactive iodine therapy, either with or without exposure to antithyroid drugs. The risk was compared to hyperthyroidism treated with antithyroid drugs alone over a 13 year period. In this way, the study was able to have a comparison group of patients with the same condition, but who were treated in a different way.

THE FULL ARTICLE TITLE

Gronich N et al 2019 Cancer risk following radioactive iodine treatment for hyperthyroidism: A cohort study. Thyroid 2020 Feb;30(2):243-250.

SUMMARY OF THE STUDY

This study used a large health care database covering more half of the Israeli population and includes all diagnoses for these patients. They identified all adult patients from 1/2002-6/2015 with a new diagnosis of hyperthyroidism who were treated with any anti-thyroid medication or radioactive iodine therapy. Patients were excluded if there was less than 6 months of medical history or if they had any previous cancer. Cancer diagnoses were obtained from the database and from the Israeli National Cancer Registry through 6/2016. End points were the first, new diagnosis of cancer appearing at least 1 year after entry, death or end of registration in the database.

A total of 16,637 patients were included in the study with an average follow up of 7.3 years. The majority of patients (13,808) were treated with anti-thyroid drugs alone, while 2829 patients received radioactive iodine therapy (1808 of whom also had anti-thyroid drugs). Most patients were treated with radioactive iodine therapy only once (95.3%), 4.6% received radioactive iodine therapy twice and only 3 patients received 3 or 4 treatments. A total of 825 new cancers were diagnosed during follow up.

The authors did not find any difference in the risk of any cancer at all and specifically no increased risk for breast cancer, colorectal cancer, prostate cancer, stomach cancer or urinary tract cancer which are areas with potential higher exposure to the radioactivity. There was a lower risk for thyroid cancer and a slightly higher risk for non-Hodgkin's lymphoma that did not reach statistical significance once other factors were included.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that there was no increased risk for subsequent cancers in patients treated with radioactive iodine for hyperthyroidism as compared to patients treated with antithyroid drugs. While the study is not randomized it is one of the largest studies evaluating this question. However, it does suffer from the problems of using a large database for analysis. Some of the possible confounding information is not available, such as actual doses of radioactive iodine used and concerns that information can be misclassified. However, overall, it supports the use of radioactive iodine as a safe treatment option for hyperthyroidism.

— Marjorie Safran, MD

HYPERTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/

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

ABBREVIATIONS & DEFINITIONS

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

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

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. **I-131** is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. **I-123** is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (*Thyroid Scan*) or to take pictures of the whole body to look for thyroid cancer (*Whole Body Scan*).

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GRAVES' DISEASE

Steroids are effective for preventing thyroid eye disease after radioactive iodine therapy in patients with Graves' disease for less than 5 years

BACKGROUND

Thyroid eye disease, also known as Graves' orbitopathy, is most often seen in association with Graves' disease. The eye disease includes inflammation of the eyes, eye muscles and the surrounding tissues and produces symptoms of dry eyes, red eyes, bulging of the eyes and double vision. Most patients with thyroid eye disease have minimal or no symptoms but ~10% have significant disease that requires treatment. Unfortunately, thyroid eye disease remains very difficult to treat.

Graves' disease, the most common cause of hyperthyroidism in the United States, can be treated with antithyroid drugs, radioactive iodine therapy or surgery. Radioactive iodine therapy can make thyroid eye disease worse, with increased risk in patients with pre-existing significant eye symptoms and those who smoke, have severe hyperthyroidism or high serum TSH-receptor antibody levels (the cause of Graves' disease). After radioactive iodine therapy, eye disease can worsen if the resulting hypothyroidism is not corrected promptly after the treatment. Some studies suggest that worsening of thyroid eye disease after radioactive iodine therapy may be prevented by high dose oral steroids.

Prior studies have also showed that patients with Graves' disease for less than 5 years have a higher risk to develop thyroid eye disease after radioactive iodine therapy. The goal of this study was to assess whether steroid therapy at the time of the radioactive iodine therapy prevents the development of thyroid eye disease in patients with Graves' disease for less than 5 years who do not have active eye disease.

THE FULL ARTICLE TITLE

Vannucchi G et al 2019 Prevention of orbitopathy by oral or intravenous steroid prophylaxis in short duration Graves' disease patients undergoing radioiodine ablation: A prospective randomized control trial study. Thyroid 29:1828–1833. PMID: 31860407.

SUMMARY OF THE STUDY

The study included patients with Graves' disease without clinical thyroid eye disease (20%) or with preexisting but inactive thyroid eye disease (80%) who received radioactive iodine therapy for relapsing hyperthyroidism after discontinuing antithyroid drug therapy. All patients received a fixed radioactive iodine dose of 600 MBq (16 mCi). A total of 121 patients with Graves' disease for less than 5 years were randomly assigned to start oral or intravenous (IV) steroid treatment at the time of radioactive iodine therapy for the prevention of thyroid eye disease development or reactivation. The oral steroid group received a starting dose of 35 mg/day of prednisone that was tapered off over 10 weeks, while the IV steroid group received weekly methylprednisolone for 4 weeks (500 mg/week for 2 weeks, then 250 mg/week for 2 more weeks). A second group of 22 patients who had Graves' disease for more than 5 years and did not receive preventive steroid therapy represented the control group. The patients were followed in the clinic for up to 5 years after the radioactive iodine therapy.

In the preventive steroid group, none of the patients developed new thyroid eye disease or had thyroid eye disease reactivation within 6 months after the radioactive iodine therapy. Oral and IV steroid treatment had the same effect in preventing thyroid eye disease. Two patients with preexisting thyroid eye disease (1 patient received oral steroid and 1 patient received IV steroid treatment) reactivated at 12 and 20 months, respectively; the reactivation was thought to be related to the natural course of the disease rather than the radioactive iodine therapy itself. In the control group, none of the patients developed new thyroid eye disease, and only 1 patient had thyroid eye disease reactivation 3 months after the radioactive iodine therapy. This patient developed severe hypothyroidism at that time, and the thyroid eye disease improved when thyroid levels normalized on thyroid hormone treatment.

GRAVES' DISEASE, continued

More than 80% of the patients who answered the side-effects questionnaire reported symptoms possibly related to steroid therapy (weight gain, dyspepsia, fatigue, mood disorder, etc.); those treated with oral steroids were more likely to develop symptoms as compared with those who received IV steroids.

Serum TRAb levels, the cause of Graves' disease and which are thought to play a major role in development of thyroid eye disease, increased as expected in all groups after the radioactive iodine therapy; however, it showed a delayed rise in steroid-treated patients with a peak at 6 months instead of 3 months in patients who did not receive this treatment. The duration of Graves' disease, serum TRAb titers, and steroid use did not affect the effectiveness of the radioactive iodine therapy in treating the hyperthyroidism.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that steroid treatment can prevent thyroid eye disease induced by radioactive iodine therapy in patients with Graves' disease for less than 5 years. Steroid therapy might not be necessary in patients who had Graves' disease for more than 5 years, since their risk of new or reactivated thyroid eye disease related to the radioactive iodine therapy is extremely low. The known increase in serum TRAb levels following radioactive iodine therapy is delayed by steroid treatment, which likely plays a role in the thyroid eye disease benefit noted from this treatment.

— Alina Gavrila, MD, MMSC

ATA THYROID BROCHURE LINKS

Graves' Disease: https://www.thyroid.org/graves-disease/
Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/
Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/

ABBREVIATIONS & DEFINITIONS

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

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

TRAb: antibodies often present in the serum of patients with Graves' disease that are directed against the TSH receptor located on the thyroid cell surface. Stimulation of this receptor by TRAb results in increased thyroid hormone production within the thyroid cells and hyperthyroidism.

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

Antithyroid drugs (ATDs): medications that block the thyroid from making thyroid hormone and are used to treat hyperthyroidism (methimazole, propylthiouracil).

GRAVES' DISEASE, continued

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

Hypothyroidism: a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Radioactive iodine treatment for hyperthyroidism usually results in hypothyroidism. Treatment requires taking thyroid hormone pills.

Steroids/Glucocorticoids: general anti-inflammatory and immunosuppressive drugs that are commonly used for the treatment of many autoimmune diseases associated with inflammation.

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THYROID SURGERY

Depression is associated with having a history of thyroid surgery

BACKGROUND

Thyroid surgery is usually recommended for thyroid cancer and can be to remove one lobe of the thyroid (partial thyroidectomy) or to remove the entire thyroid (total thyroidectomy). Thyroidectomy may also be recommended for certain non-cancerous disorders including hyperthyroidism and large goiters. The results of a total thyroidectomy is hypothyroidism which requires lifelong treatment with a thyroid hormone pill. Several recent reports have highlighted a decrease in the quality of life and an increase in depression in some patients with hypothyroidism due to thyroid surgery. Therefore, the authors have examined if there is an association between thyroid surgery and a new onset of depression.

THE FULL ARTICLE TITLE

Choi KW et al 2019 Increased morbidity of major depressive disorder after thyroidectomy: A nationwide population-based study in South Korea. Thyroid 29:1713–1722.

SUMMARY OF THE STUDY

Medical claims data of patients that underwent a partial or total thyroidectomy in South Korea from 2009-2016 was analyzed. They looked for associations between thyroid surgery, the extent of thyroid surgery, and the development of major depressive disorder either before or after surgery, controlling for other medical conditions.

Of the 187,176 patients who underwent partial or total thyroidectomy during the study period, 16,744 (8.9%) were diagnosed with depression either before or after their surgery. Of these, 77% had a total thyroidectomy (compared to a partial thyroidectomy) and 88% were female. The data show that there was a 68% increased risk of depression before a partial thyroidectomy and an 81% increased risk of depression before a total thyroidectomy. However, at 1 year after thyroid surgery, only patients that had a total thyroidectomy experienced higher rates of depression (11% increased risk). This was regardless of a thyroid cancer diagnosis.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The risk for developing a depression is increased around the time of having thyroid surgery, regardless of the extent of thyroid surgery. The risk can persist up to one year after a patient has a total thyroidectomy. This is important to increase awareness of physicians and patients to identify and treat this illness.

— Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/
Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/

ABBREVIATIONS & DEFINITIONS

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

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*.

THYROID SURGERY, continued

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.

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THYROID CANCER

Increasing obesity is associated with rising papillary thyroid cancer incidence and development of larger thyroid cancers

BACKGROUND

The number of patients with papillary thyroid cancer has been rising since the mid 1970's. Initially, this was attributed to more frequent use of neck ultrasound and CT scans which could identify new cases of thyroid cancer that would not have otherwise been found. More frequent neck imaging can certainly account for the increase in incidence of small, early stage papillary thyroid cancers; however, it cannot explain a reported rise in the incidence of large (>4 cm) papillary thyroid cancers as well as increase in death from thyroid cancer. As such, it is likely that other environmental factors may also be contributing to the changing incidence of papillary thyroid cancer.

The epidemic of obesity over this period mirrors the rise in papillary thyroid cancer; therefore, there may be a positive relationship between thyroid cancer and obesity. In fact, recent studies have shown a relationship between one's fat mass and diagnosis of papillary thyroid cancer. Further, obesity has already been linked to many other types of cancers such as gastrointestinal, breast, kidney and endometrial cancers.

The goal of the current study was to quantify the impact of rising rates of obesity on the incidence of papillary thyroid cancer.

THE FULL ARTICLE TITLE

Kitahara CM et al. 2019, Impact of overweight and obesity on U.S. papillary thyroid cancer incidence trends (1995–2015) J Natl Cancer Inst. Epub 2019 Oct 22.

SUMMARY OF THE STUDY

The authors used data from a large US study called the ***National Institutes of Health (NIH)—AARP diet health study***, which started in 1995 when members of the American Association of Retired Persons (AARP) between ages 51-70 completed a questionnaire about health and lifestyle characteristics which included questions about weight and body mass index (BMI) . Then, using local cancer registries and databases they identified 604 people from the study that were diagnosed with new papillary thyroid cancer between 1995-2005.

Compared with normal weight (BMI 18.5-24.9 kg/m2), being overweight (BMI 25.0-29.0 kg/m2) and obese (BMI > 30.0 kg/m2) was associated with a 1.26-fold and 1.30-fold increase in the risk of papillary thyroid cancer. Being overweight or obese was not associated with an increased risk of small papillary thyroid cancers, but rather with a 3-fold (for overweight) and 5-fold (for obese) risk of large papillary thyroid cancers. Overall, the association between BMI and risk of papillary thyroid cancer was stronger in men then women.

Due to the rising incidence of overweight and obesity in the USA between 1995 and 2015, the proportion of cases of papillary thyroid cancer that were attributed to either of these conditions also increased from 11.4 % to 16.2% (any size papillary thyroid cancer) and from 51.4% to 63.2% (large papillary thyroid cancers) by the end of the study period. In other words by 2015 one in every 6 of all papillary thyroid cancers, a nearly two-thirds of large papillary thyroid cancers among adults older than 60 years were attributable to overweight and obesity.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While historically not thought of as a strong risk factor for thyroid cancer, adiposity has now been implicated in the rise of papillary thyroid cancer, particularly large cancers. The exact mechanism of obesity in thyroid cancer development is still unknown, but one wonders if a substantial number of papillary thyroid cancers can be avoided by implementing public health interventions targeting overweight and obesity in the population.

— Phillip Segal, MD

THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

Body-mass index (BMI): a standardized measure of obesity calculated by dividing the weight in kilograms by the square of the height. A normal BMI is 18.5-24.9, overweight is 25-30 and obese is >30.

Papillary thyroid cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 4 | April 2020

Clinical Thyroidology® for the Public

THYROID CANCER

Extension of thyroid cancer into the muscles in the neck does not affect survival or predict recurrence in papillary thyroid cancer

BACKGROUND

Papillary thyroid cancer is the most common type of thyroid cancer. The overall prognosis of papillary thyroid cancer is excellent and, for most patients, the concern is for cancer recurrence as opposed to death from cancer. Papillary thyroid cancer that grows out of the thyroid and invades the tissues and/or muscles in the neck (extrathyroidal extension) is considered a more advanced stage with a higher risk for cancer recurrence. However, if the extension is not visible to the surgeon at the time of surgery and only seen under the microscope, the outcomes are not changed significantly. Additionally, there are few studies looking at isolated visible invasion into the neck muscles laying over the outer edges of the thyroid in the front of the neck (the strap muscles). This study examined patients with these types of cancers to see if outcomes were worse than those cancers without invasion into the strap muscles.

THE FULL ARTICLE TITLE

Li G et al 2019 Implications of extrathyroidal extension invading only the strap muscles in papillary thyroid carcinomas. Thyroid. Epub 2019 Dec 13. PMID: 31830859.

SUMMARY OF THE STUDY

This study reviewed the medical records of 4045 patients between the ages of 18 and 80 with papillary thyroid cancer who had surgery at one hospital in Chengdu, China between 2011 and 2016. Patients were divided into groups based on thyroid cancer invasion outside the thyroid. This included no invasion, invasion into soft tissue around the thyroid (not muscle), invasion into the strap muscles laying over the thyroid, or invasion to even more neck structures beyond those muscles (the most invasive).

The average follow up time was almost 3 years (1-5 years) and the outcomes evaluated included overall survival and survival without evidence of any thyroid cancer. Evidence of cancer recurrence was defined by seeing it on imaging studies or increased blood levels of the thyroid cancer marker thyroglobulin.

There were 9.2% of patients with thyroid cancer invasion into strap muscles. These cancers tended to be larger in size, be one of multiple cancers, involved lymph nodes more often and spread outside the neck more often than cancers without invasion outside the thyroid.

Cancer recurrence occurred in just over 20% of the patients with invasive cancers but there was no difference in thyroid cancer death compared to cancers that did not invade outside the thyroid. When controlling for other factors such as age, gender, lymph node involvement and other thyroid cancer features, the invasion into strap muscles did not seem to be related to increased risk of thyroid cancer recurrence. In contrast, the cancers that were the most invasive had worse outcomes for both recurrence and death from thyroid cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that, when papillary thyroid cancer invaded into neck strap muscles, there was an association with other aggressive thyroid cancer features and an increased rate of thyroid cancer recurrence. However, overall survival was no different than for those patients whose cancer did not invade strap muscles. Also, when other thyroid cancer risk factors were similar across cases (male gender, larger cancer sizes and lymph node involvement), survival with no thyroid cancer recurrence was similar.

This study is important for patients in that it helps provide more understanding of the risk of thyroid cancer invasion into neck strap muscles and may decrease some fear of a worse outcome when this feature is seen under the microscope, especially when there are no other significant high risk features for cancer recurrence.

— Joshua Klopper, MD

THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

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.

Lymph node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

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

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THYROID FUNCTION TESTS

Early-life exposure to flame retardants is associated with lower FT_4 but higher FT_3 during later life

BACKGROUND

Many things that we use in daily modern life such as plastics, personal care products, electronic waste, pesticides and flame retardants are known to contain chemicals that interfere with the normal functioning of the glands of the endocrine system. These chemicals are called endocrine-disrupting compounds (EDCs). Exposure to such chemicals has been associated with the development of cancer, hormone dysfunction and reproductive problems. Children are believed to be particularly susceptible, even if the exposure has happened before birth. Many of the studies that have been done to investigate these effects do not have a clear dose-response relationship between higher EDC exposure and health problems and different studies have inconsistent results.

A particular type of these EDCs, polybrominated biphenyls (PBB) are flame retardants used commonly in electrical appliances and textiles. Once they enter the human body, they attach to fat and remain detectable for many years. In pregnant women, EDCs are also able to pass through the placenta and are found in breast milk.

In 1973, millions of Michigan residents were exposed to PBB when it was accidentally added to livestock feed. During the 10 month period before this was discovered, people were exposed by eating contaminated meat and dairy. In the aftermath, people who were believed to have had the highest exposure because they lived in or obtained their food from the affected farms were recruited to investigate the long term health effects of PBB exposure. These participants, their children and other members of the community have been followed for the past 40 years as part of the Michigan PBB Registry and have had their levels of PBB regularly assessed. The levels of other similar substances, known as PCBs were also assessed, as the participants were continuously exposed to from typical environmental sources. This study examined the effect that this exposure had on thyroid hormone levels in children.

THE FULL ARTICLE TITLE

Curtis SW et al 2019 Thyroid hormone levels associate with exposure to polychlorinated biphenyls and polybrominated biphenyls in adults exposed as children. Environ Health **18:**75. PMID: 31443693.

SUMMARY OF THE STUDY

For this study, 717 participants in the Michigan PBB Registry provided serum samples between 2004 and 2015. In these samples, 4 types of PBB and 4 types of PCBs were measured. Participants who were known to take thyroid medications were excluded. To evaluate outcomes, serum TSH, free T_4, T_4 and free T_3 were measured.

The study population was 61.6% female, average age of exposure was 14 years, 446 were exposed before puberty and 269 after completion of puberty. The participants were found to have PCBs levels similar to those found in representative samples of the United States. However, 92% of participants had higher PBB levels when comparing to the rest of the U.S population. Older participants had higher levels of PBB and PCB; men had higher levels of both than women.

A higher PBB concentration was associated with a lower free T_4 and a higher free T_3 and this association was observed mainly in participants who were exposed before completion of puberty. A higher PCB concentration was associated with a higher free T_4. There was no association of either chemical with TSH, total T_4 or total T_3.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The conclusion of this study is that exposure to PBBs during early life is associated with lower free T_4 and higher free T_3 concentrations during later life. Although the associations between thyroid hormone levels and PBB in this study are not consistent with actual clinical thyroid disease (the majority of the samples were within usual ranges for

THYROID FUNCTION TESTS, continued

population), variation in thyroid hormone levels within their normal ranges can still impact health. Therefore, people with higher exposure to PBBs may be at greater risk for metabolic and reproductive problems even if their hormone levels are still within the usual population range. This is especially true about the people exposed as children. Further study of this population is needed to determine the health implications of this exposure.

— Jessie Block-Galarza, MD

ATA THYROID BROCHURE LINKS

Thyroid Function Tests: https://www.thyroid.org/thyroid-function-tests/

ABBREVIATIONS & DEFINITIONS

Thyroxine (T4): the major hormone produced by the thyroid gland.

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

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

Endocrine disruptors (EDCs): chemical pollutants in the environment that can affect the action of endocrine glands. Examples include bisphenol A (BPA), polychlorinated biphenols (PCBs), perfluoroalkyl substances (PFAs), polybrominated biphenyls (PBB) and organochlorines (OCs).

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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 toward the improvement of thyroid education and resources for patients.

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Graves' Disease & Thyroid Foundation

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www.thyroid.org/thyroid-information/
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Bite Me Cancer
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info@ngdf.org

Light of Life Foundation
www.checkyourneck.com
info@checkyourneck.com

MCT8 – AHDS Foundation
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Contact@mct8.info

Thyca: Thyroid Cancer Survivors' Association, Inc.
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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

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.

Hashimoto's Thyroiditis
(Lymphocytic Thyroiditis)

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 hormones help the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

WHAT IS HASHIMOTO'S THYROIDITIS?

The term "Thyroiditis" refers to "inflammation of the thyroid gland". There are many possible causes of thyroiditis (see *Thyroiditis brochure*). Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis, is the most common cause of hypothyroidism in the United States. It is an autoimmune disorder involving chronic inflammation of the thyroid. This condition tends to run in families. Over time, the ability of the thyroid gland to produce thyroid hormones often becomes impaired and leads to a gradual decline in function and eventually an underactive thyroid (Hypothyroidism). Hashimoto's thyroiditis occurs most commonly in middle aged women, but can be seen at any age, and can also affect men and children.

WHAT ARE THE SYMPTOMS OF HASHIMOTO'S THYROIDITIS?

There are no signs or symptoms that are unique to Hashimoto's thyroiditis.

Because the condition usually progresses very slowly over many years, people with Hashimoto's thyroiditis may not have any symptoms early on, even when the characteristic thyroid peroxidase (TPO) antibodies are detected in blood tests. TPO is an enzyme that plays a role in the production of thyroid hormones. If Hashimoto's thyroiditis causes cell damage leading to low thyroid hormone levels, patients will eventually develop symptoms of hypothyroidism (see *Hypothyroidism brochure*). Hypothyroid symptoms may include fatigue, weight gain, constipation, increased sensitivity to cold, dry skin, depression, muscle aches and reduced exercise tolerance, and irregular or heavy menses. In some cases, the inflammation causes the thyroid to become enlarged (goiter), which rarely may cause neck discomfort or difficulty swallowing.

HOW IS THE DIAGNOSIS OF HASHIMOTO'S THYROIDITIS MADE?

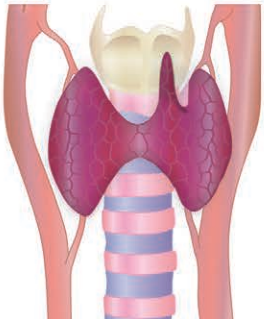
The diagnosis of Hashimoto's thyroiditis may be made when patients present with symptoms of hypothyroidism, often accompanied by a goiter (an enlarged thyroid gland) on physical examination, and laboratory testing of hypothyroidism, which is an elevated thyroid stimulating hormone (TSH) with or without a low thyroid hormone (Free thyroxine [Free T4]) levels. TPO antibody, when measured, is usually elevated.

Occasionally, the disease may be diagnosed early, especially in people with a strong family history of thyroid disease. TPO antibody may be positive, but thyroid hormone levels may be normal or there may only be isolated mild elevation of serum TSH is seen. Symptoms of hypothyroidism may be absent.

HOW IS HASHIMOTO THYROIDITIS TREATED?

Patients with elevated TPO antibodies but normal thyroid function tests (TSH and Free T4) do not require treatment. Patient with only a slightly elevated TSH (mild hypothyroidism) may not require medication and should have repeat testing after 3-6 months if this has not already been done. For patients with overt hypothyroidism (elevated TSH and low thyroid hormone levels) treatment consists of thyroid hormone replacement (see *Thyroid Hormone Treatment brochure*). Synthetic levothyroxine taken orally at an appropriate dose, is inexpensive, very effective in restoring normal thyroid hormone levels, and results in an improvement of symptoms of hypothyroidism. Most patients with Hashimoto's thyroiditis will require lifelong treatment with levothyroxine. Finding the appropriate dose, particularly at the beginning, may require testing with TSH every 6-8 weeks after any dose adjustment, until the correct dose is determined. After that, monitoring of TSH once a year is generally sufficient.

When levothyroxine is taken in the appropriate dose, it has no side effects. However, when an insufficient dose is taken, serum TSH remains elevated and patients may have persistent symptoms of hypothyroidism (see *Hypothyroidism brochure*). If the dose is excessive, serum TSH will become suppressed and patients may develop symptoms of hyperthyroidism or have other side effects (see *Hyperthyroidism brochure*).



FURTHER INFORMATION

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*