

Clinical Thyroidology® for the Public



AMERICAN THYROID ASSOCIATION

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Personalized treatment of anaplastic thyroid cancer has resulted in significant improvement in survival over the past two decades

Although rare, anaplastic thyroid cancer accounts for more than half of thyroid cancer-related death every year. In the last several years, there has been an increasing number of clinical trials investigating targeted, combination drug therapies in patients with anaplastic thyroid cancer. The goal of this study was to evaluate whether there has been an improvement in the overall survival of patients with anaplastic thyroid cancer over the past two decades, given the recent advances in the field.

Maniakas A et al. 2020 Evaluation of Overall Survival in Patients with Anaplastic Thyroid Carcinoma, 2000-2019. JAMA Oncol Aug 6;e203362. PMID: 32761153.

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Most small thyroid cancers are low-risk for both recurrence and spread outside of the thyroid and have an excellent prognosis. Because of this, experts wonder if it would be appropriate to change the terminology for the diagnosis. The current study is an analysis of 3 community focus groups of the general public conducted in Australia to consider a terminology change for small low-risk papillary thyroid cancer.

Shih P et al 2020 Terminology change for small low-risk papillary thyroid cancer as a response to overtreatment: Results from three Australian community juries. Thyroid. Epub 2020 Nov 25. PMID: 33238815.

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Can the emotions about having papillary thyroid cancer or just the possibility of cancer affect how we make treatment decisions?

Patients with papillary thyroid cancer generally have excellent outcomes no matter how much of the thyroid is removed. However, we do not know much about how patients feel when diagnosed with papillary thyroid cancer or possibility of cancer, their concerns and how these emotions might affect treatment decisions. This study was done to understand the reactions of patients who were diagnosed with papillary thyroid cancer.

Pitt SC et al. 2020 Patients' reaction to diagnosis with thyroid cancer or an indeterminate thyroid nodule. Thyroid. Epub 2020 Oct 3. PMID: 33012267

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Quality of life after thyroid cancer surgery is decreased if parathyroid hormone levels are low after surgery

If all four of the parathyroid glands are damaged, or accidentally removed, during surgery, calcium levels will be too low after surgery. This complication is usually only seen after a total thyroidectomy. The research described here studied people who had low parathyroid hormone levels after thyroid cancer surgery to better understand how these low levels effect the quality of a person's life.

Büttner M et al. 2020 Quality of life in patients with hypoparathyroidism after treatment for thyroid cancer. J Clin Endocrinol Metab. Epub 2020 Dec 1. PMID: 32918085.

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Frequency of low white blood cells in hyperthyroidism and the response to hyperthyroidism treatment

Uncontrolled hyperthyroidism can cause a decrease in the total count of one type of white blood cell known as neutrophils. As with the other systems, the low neutrophil counts return to normal once the thyroid hormone levels return to normal. What can be confusing in treating patients with hyperthyroidism is that a very low neutrophil count is a rare but dangerous side effect of antithyroid drugs used to control hyperthyroidism. This systematic review was done to evaluate how frequently low neutrophil counts are seen in patients with newly diagnosed and untreated hyperthyroidism.

Scappaticcio L 2020 Neutropenia in patients with hyperthyroidism: Systematic review and meta-analysis. Clin Endocrinol (Oxf). Epub 2020 Aug 16. PMID: 32799342.

HYPERTHYROIDISM13

Liver enzymes are commonly high in patients with untreated hyperthyroidism and improve after treatment of hyperthyroidism

When thyroid hormone levels are very high in hyperthyroidism, blood liver function tests can be also be increased to levels that suggest damage to the liver, even though severe liver problems from hyperthyroidism is extremely rare. What can be confusing is that the medications used to control hyperthyroidism can cause increased liver function tests that may indicate liver damage. This systematic review was done to evaluate how frequently elevated liver function tests levels are seen in patients with newly diagnosed and untreated hyperthyroidism.

Scappaticcio L et al 2020. Abnormal liver blood tests in patients with hyperthyroidism: Systematic review and meta-analysis. Thyroid. Epub 2020 Dec 16. PMID: 33327837.

ATA ALLIANCE FOR THYROID PATIENT EDUCATION15



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Clinical Thyroidology for the Public

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EDITOR'S COMMENTS

Welcome to another issue of *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through [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.

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

February is [Hypothyroidism Awareness month](#).

In this issue, the studies ask the following questions:

- Are newer treatments for anaplastic thyroid cancer increasing survival?
- Should low risk thyroid cancer even be called a cancer?
- How do patients respond psychologically to a diagnosis of thyroid cancer?
- How does post-op hypoparathyroidism affect thyroid cancer patient's quality of life?
- How often are liver function tests increased in patients with uncontrolled hyperthyroidism?
- How often is a low neutrophil count seen in patients with uncontrolled hyperthyroidism?

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,



THYROID CANCER

Personalized treatment of anaplastic thyroid cancer has resulted in significant improvement in survival over the past two decades

BACKGROUND:

Unlike papillary and follicular thyroid cancer, which have a good prognosis, anaplastic thyroid cancer is a very aggressive type of thyroid cancer. Although rare, representing less than 2% of all thyroid cancers, anaplastic thyroid cancer accounts for more than half of thyroid cancer-related death every year. In the most recent analysis of the Surveillance, Epidemiology, and End Results (SEER) database (1986-2015), the average survival of patients with anaplastic thyroid cancer was only 4 months and 98-99% of patients eventually died of the cancer. Patients with anaplastic thyroid cancer usually present with a rapidly growing and locally invading neck mass, lymph node involvement and often spread to other parts of the body. This means that surgery is often not helpful. Historically, these patients have been offered comfort treatment or hospice. However, in the last several years, there has been an increasing number of clinical trials investigating targeted, combination drug therapies in patients with anaplastic thyroid cancer.

In 2014, the University of Texas MD Anderson Cancer Center developed the Facilitating Anaplastic Thyroid Cancer Specialized Treatment (FAST) team to allow fast access to a multidisciplinary, highly specialized care and cancer molecular testing, such as the BRAF V600E mutation. The program has enrolled anaplastic thyroid cancer patients in clinical trials to receive targeted combination therapies. The patients who achieve significant response to initial targeted therapy receive additional treatments, including surgery and radiation. The goal of this study was to evaluate whether there has been an improvement in the overall survival of patients with anaplastic thyroid cancer over the past two decades, given the recent advances in the field.

THE FULL ARTICLE TITLE:

Maniakas A et al. 2020 Evaluation of Overall Survival in Patients with Anaplastic Thyroid Carcinoma, 2000-2019. JAMA Oncol Aug 6;e203362. PMID: 32761153.

SUMMARY OF THE STUDY:

The study included 479 patients with anaplastic thyroid cancer who presented at the University of Texas MD Anderson Cancer Center between January 2000 and October 2019. The average age was 65 years (21-93 years), and 51% of the patients were men. A total of 11% patients had stage IVA, 36% stage had IVB and 53% had stage IVC anaplastic thyroid cancer at presentation, all very advanced. The patients were divided into three subgroups: January 2000-December 2013 (227 patients), January 2014-December 2016 (the FAST program started in 2014) (100 patients), and January 2017-October 2019 (surgery and radiation started to be performed after neoadjuvant therapy in 2017) (152 patients). BRAF-V600E mutation testing to guide therapy increased over time from 17% of the patients in the 2000-2013 group, to 82% of the patients in the 2014-2016 group and 97% of those in the 2017-2019 group.

The average survival was 8 months in the 2000-2013 group, 10.6 months in the 2014-2016 group, and 15.7 months in the 2017-2019 group. There was a 1-year survival improvement of 12% in the 2014-2016 group (from 35% to 47%) and 24% in the 2017-2019 group (from 35% to 59%) as compared to the initial 2000-2013 group. Similarly, there was a 2-year survival improvement of 7% in the 2014-2016 group (from 18% to 25%) and 24% in the 2017-2019 group (from 18% to 42%).

The use of targeted therapy in patients with anaplastic thyroid cancer increased over time and resulted in an improvement in ~2-fold in overall survival. The study also reported a significant increase in the use of immunotherapy in recent years, with significantly better overall survival in patients who received targeted therapy with immunotherapy versus those who received targeted therapy alone. In addition, the use of additional BRAF-directed chemotherapy before surgery since 2017 was associated with an improved overall survival (94% at 1 year) in patients with the BRAF-V600E mutation.



THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This large, single-institution study showed a significant improvement in survival of patients with anaplastic thyroid cancer over the past two decades, regardless of disease stage. This remarkable progress is attributed to advances in the care of anaplastic thyroid cancer

patients, including comprehensive genetic testing and highly specialized, personalized treatment with integrated, multimodal therapies. The study highlights the importance of immediate recognition and referral of anaplastic thyroid cancer patients to specialty cancer centers of excellence.

— Alina Gavrilă, MD, MMSc

ATA THYROID BROCHURE LINKS

Anaplastic Thyroid Cancer - <https://www.thyroid.org/anaplastic-thyroid-cancer/>

ABBREVIATIONS & DEFINITIONS

Anaplastic thyroid cancer (ATC): a very rare, but very aggressive type of thyroid cancer. In contrast to all other types of thyroid cancer, most patients with anaplastic thyroid cancer die of their cancer within a few years.

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

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

Clinical trial: study designed to investigate the safety and effectiveness of a new medical treatment using human subjects, who consent to participate in research.

Molecular tests: detect specific molecules, or biomarkers, associated with cancer in a patient's tissue and fluid samples. Molecular diagnostic tests can help to select a specific cancer therapy and monitor the results of a treatment based on changes in the biomarker level.

Cancer-associated genes: genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these

genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC and RAS.

BRAF gene: this is a gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.

Mutation: a permanent change in one of the genes.

Targeted therapy: a type of cancer treatment that interferes with specific molecules found in cancer cells that are involved in the growth, progression, and spread of cancer.

Immunotherapy: a type of cancer treatment that boosts the immune system to fight cancer by detecting and destroying abnormal cells.

SEER: Surveillance, Epidemiology and End Results program, a nation-wide anonymous cancer registry generated by the National Cancer Institute that contains information on 26% of the United States population. Website: <http://seer.cancer.gov/>



THYROID CANCER

Should small, low-risk thyroid cancers even be called “cancer”?

BACKGROUND

Thyroid cancer is the fastest rising cancer in the United States. Most of this increase is due to the identification of small (<1 cm) thyroid cancers. Most small thyroid cancers are low-risk for both recurrence and spread outside of the thyroid and have an excellent prognosis. However, many patients still experience some psychological harm from being diagnosed with even a low-risk cancer because the word evokes certain fears and anxieties. Clinicians now offer to watch these small cancers with regular ultrasound exams instead of surgery to appropriate patients (active surveillance). However, this is still considered a cancer. Experts wonder if it would be appropriate to change the terminology for the diagnosis so as not to evoke the same patient reaction but also not minimize the need for surveillance and follow-up, since a small percentage do recur and spread outside of the thyroid.

The current study is an analysis of 3 community focus groups of the general public conducted in Australia to consider a terminology change for small low-risk papillary thyroid cancer.

THE FULL ARTICLE TITLE

Shih P et al 2020 Terminology change for small low-risk papillary thyroid cancer as a response to overtreatment: Results from three Australian community juries. *Thyroid*. Epub 2020 Nov 25. PMID: 33238815.

SUMMARY OF THE STUDY

Three community focus groups were conducted in Australia. Participants were recruited from social media

advertising and random phone calling from a diverse sample of 3 separate communities (Sydney, Wodonga and Cairns). Over a 2 day period that consisted of presentations by experts as well as live question and answer sessions, 40 participants voted on keeping or changing the “cancer” terminology and provided their reasoning.

Participants were divided on whether to change the terminology for small low-risk thyroid cancers. Many changed their opinion over the course of the two day focus group. All participants agreed that there should be increased education for patients and the public and that health professionals have a responsibility to reduce the harms of overtreatment.

Reasons to support terminology changes are potential reduction of psychological harm from cancer diagnosis, would lead to health systems changes, and potentially have positive social and financial implications. Reasons for not supporting a terminology change include need for truth as to the malignant nature of the disease as well as lack of strong evidence and research.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Currently, from the patient perspective, there is no consensus on whether to change the terminology of a low risk thyroid cancer diagnosis. More evidence and research is needed over larger geographic areas.

— Melanie Goldfarb, MD, MS, FACS, FACE

ATA THYROID BROCHURE LINKS

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

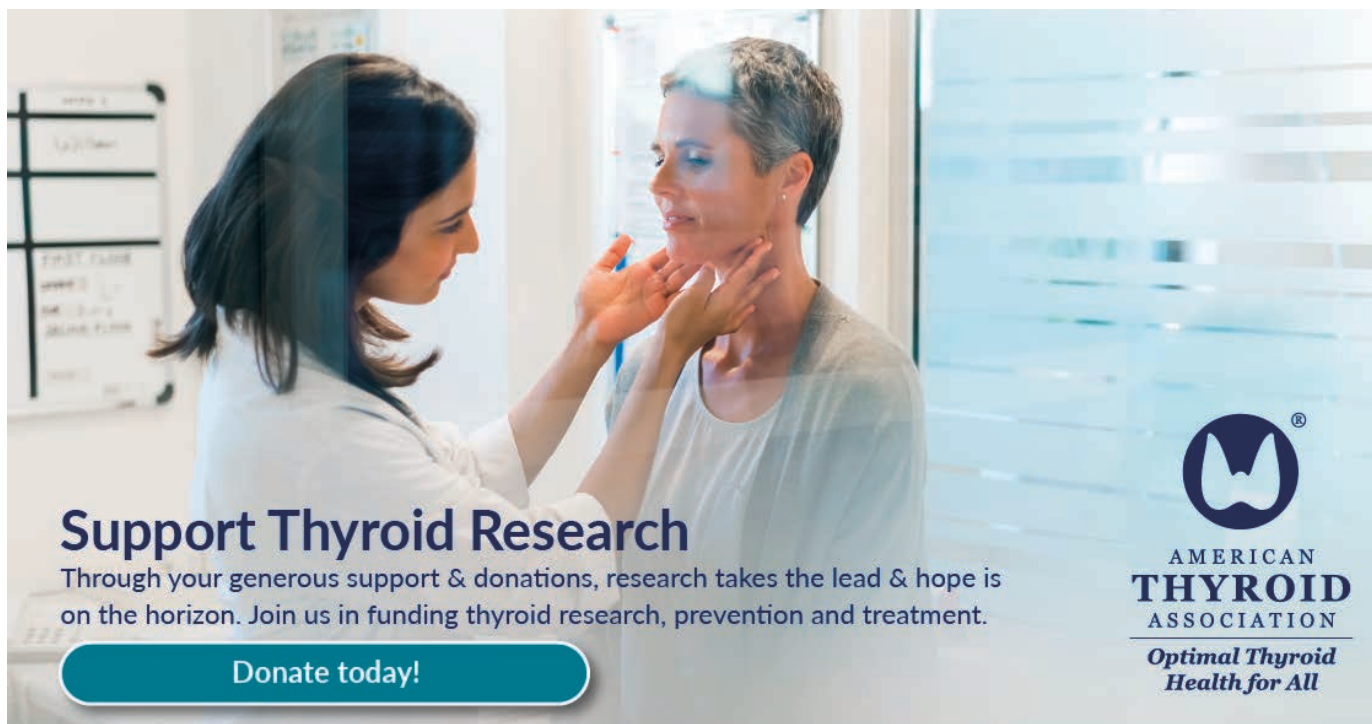


THYROID CANCER, continued

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).


Papillary microcarcinoma: a papillary thyroid cancer smaller than 1 cm in diameter.



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THYROID CANCER

Can the emotions about having papillary thyroid cancer or just the possibility of cancer affect how we make treatment decisions?

BACKGROUND

Many people have thyroid nodules and most of these nodules are not cancer. Thyroid ultrasound and needle biopsy are used to find out which nodules may be cancer. The most common thyroid cancer is the papillary thyroid cancer and surgery has been the standard treatment for many years. Sometimes the biopsy cannot tell whether there is cancer and these nodules are called indeterminate. Surgery or additional testing may be needed to make a diagnosis. Patients with papillary thyroid cancer generally have excellent outcomes no matter how much of the thyroid is removed. Because of this, recent guidelines give us more treatment options, such as removing only half of the thyroid or not removing very small thyroid cancers. These options also decrease the risk for complications from surgery and improve the quality of life.

This information is helpful, but it may not be enough to make the best treatment decision. We do not know much about how patients feel when diagnosed with papillary thyroid cancer or possibility of cancer, their concerns and how these emotions might affect treatment decisions. This study was done to understand the reactions of patients who were diagnosed with papillary thyroid cancer or indeterminate nodules.

THE FULL ARTICLE TITLE

Pitt SC et al. 2020 Patients' reaction to diagnosis with thyroid cancer or an indeterminate thyroid nodule. *Thyroid*. Epub 2020 Oct 3. PMID: 33012267

SUMMARY OF THE STUDY

This study was done in the United States as part of a prospective, randomized clinical trial. Researchers interviewed adult patients who were diagnosed with an indeterminate thyroid nodule or papillary thyroid cancer between August 2014 and February 2019. The interviews were done after the providers explained the results and discussed the plan with their patients but before the surgery. Patients also received educational materials explaining

the nodules and thyroid cancer, reasons to have surgery, associated risks and expected recovery from surgery. The study was designed to understand the emotional responses to these diagnoses as well as how other factors like reactions of family and friends effected these responses.

Study included 85 patients and 50 had papillary thyroid cancer. Both the diagnosis of cancer or possibility of cancer caused fear and anxiety. The most common reaction was the same for majority of the patients. They had an urgent need to get the cancer out of their body because "it was cancer". They also wanted to reassure themselves and their family before returning to a normal life. Patients were worried that the cancer could spread even though they were counseled that this was very unlikely, and this type of cancer had an excellent outcome. Patients who had cancer diagnosis and those with indeterminate results had very similar reactions. Other concerns were surgery related scarring, damage to voice or swallowing and the recovery period. The need to remove the cancer was so strong that the potential risks played a smaller role in their decision.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In conclusion, this study showed that patients had strong emotions, especially worry and anxiety, when diagnosed with papillary thyroid cancer or indeterminate nodules. Patients felt a need to "get it out" in response to the word cancer, even though they had information about the generally very good nature of the disease.

These results are important for both patients and providers. Providers need to understand the responses caused by these diagnoses so they can better inform and guide their patients. Patients need to be aware of the natural emotions they may feel and how these may affect their decisions. This would help them to consider all the information about their disease so they can choose the best treatment option.

— Ebru Sulanc, MD



THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

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

Thyroid Nodules: <https://www.thyroid.org/thyroid-nodules/>

ABBREVIATIONS & DEFINITIONS

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

Indeterminate thyroid biopsy: this happens a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

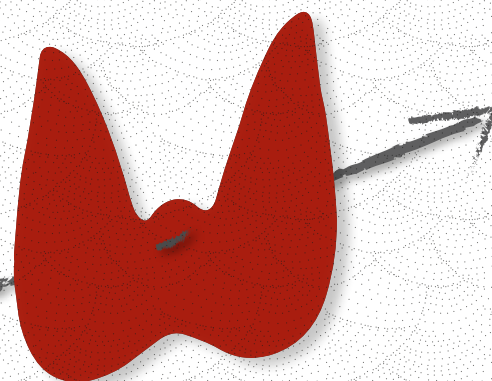
Papillary thyroid cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

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

FEBRUARY Hypothyroidism Awareness Month



AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All





THYROID CANCER

Quality of life after thyroid cancer surgery is decreased if parathyroid hormone levels are low after surgery

BACKGROUND

Surgery to remove the thyroid gland is usually needed to treat thyroid cancer. When this is done by a surgeon who specializes in this kind of surgery, thyroid surgery is safe and effective. One potential problem that can happen after thyroid surgery is damage to the parathyroid glands that results in a low parathyroid hormone level. The parathyroids are four very small glands (each about the size of a grain of rice) that live on the surface of the thyroid. Other than living on the thyroid gland surface, the parathyroid glands have nothing to do with the thyroid. They do have an important job, however: they make a single hormone that controls the body's calcium level. In fact, everyone must have at least one functioning parathyroid gland to have normal body calcium levels.

It is very important that the parathyroid glands be carefully peeled away from the thyroid and left in the neck by the surgeon during thyroid surgery. If all four of the parathyroid glands are damaged, or accidentally removed, during surgery, calcium levels will be too low after surgery. This can be very serious. Some people with low calcium levels will have bad side effects, like numbness and tingling in their hands, feet and around their mouths, serious muscle cramps and even full body seizures. Such people will have to take very large amounts of calcium every day after surgery, often for the rest of their lives. This complication is usually only seen after a total thyroidectomy, as a lobectomy does not disturb the parathyroid glands on the opposite side and parathyroid hormone levels should remain normal.

The research described here studied people who had low parathyroid hormone levels after thyroid cancer surgery to better understand how these low levels effect the quality of a person's life.

FULL ARTICLE TITLE

Büttner M et al. 2020 Quality of life in patients with hypoparathyroidism after treatment for thyroid cancer.

J Clin Endocrinol Metab. Epub 2020 Dec 1. PMID: 32918085.

SUMMARY OF THE STUDY

Thyroid cancer patients who underwent thyroid surgery at any one of 14 different treatment centers in Europe were evaluated for post-surgery permanent low parathyroid hormone levels. Among the 89 thyroid cancer patients who had thyroid surgery at one of these centers during the study, 17 had permanently low parathyroid hormone levels after surgery and 72 had normal post-surgery parathyroid hormone levels. After surgery, all 89 patients filled out a questionnaire designed to gather information about quality of life. The results of this questionnaire were then compared between patients having permanently low parathyroid hormone levels after surgery and patients with normal post-surgery parathyroid levels.

Not surprisingly, this study found that people having permanently low parathyroid hormone levels following thyroid cancer surgery had a worse quality of life compared to people with normal post-surgery parathyroid hormone levels. This included worse physical functioning, emotional functioning and social functioning, as well as more tingling/numbness, more restlessness, more fatigue, more difficulty breathing and more difficulty sleeping. People having low parathyroid hormone levels following thyroid surgery were not more likely to experience joint pain, muscle cramps or racing heartbeat. The study also found that more extensive surgery (neck dissection/lymph node removal during thyroid surgery) was more likely to result in permanently low parathyroid hormone levels.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study authors concluded that low parathyroid hormone levels following thyroid cancer surgery significantly decrease quality of life. It is very important for people who need thyroid cancer surgery to understand this possible surgical complication and take steps to minimize



THYROID CANCER, continued

the risk that this will happen to them. The best way to minimize this risk is to choose a surgeon who specializes in thyroid surgery and thus has lots of experience in recognizing and preserving the parathyroid glands during surgery. Such surgeons are also more likely to understand just how extensive a surgery should be for each individual person diagnosed with thyroid cancer and so should be able to minimize the amount of surgery needed in each

case. This understanding should also decrease risk of low parathyroid hormone levels following thyroid surgery. This is important information, since a person diagnosed with thyroid cancer should know the possible side effects of thyroid surgery, and be able to discuss these side effects, when choosing a thyroid surgeon.

— Jason D. Prescott, MD PhD

ATA Thyroid Brochure Links

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

Thyroid Surgery: <https://www.thyroid.org/thyroid-surgery/>

ABBREVIATIONS & DEFINITIONS

Parathyroid glands: usually four small glands located around the thyroid that secrete parathyroid hormone (PTH) which regulates the body's calcium levels.

Parathyroid hormone (PTH): the hormone that regulates the body's calcium levels. High levels of PTH cause hypercalcemia, or too much calcium in the blood. Low levels of PTH cause hypocalcemia, or too little calcium in the blood.

Lobectomy: surgery to remove one lobe of the thyroid.

Total thyroidectomy: surgery to remove the entire thyroid gland.



HYPERTHYROIDISM

Frequency of low white blood cells in hyperthyroidism and the response to hyperthyroidism treatment

BACKGROUND

Uncontrolled hyperthyroidism has widespread effects on most of the body's functions. Most of the body's functions return to normal with the thyroid hormone levels return to normal during treatment of the hyperthyroidism. One such system affected is the immune system and the white blood cells that are involved in the immune response. The high levels of thyroid hormone can cause a decrease in the total count of one type of white blood cell known as neutrophils. Very low counts of neutrophils often increase the risk of getting a severe infection. As with the other systems, the low neutrophil counts return to normal once the thyroid hormone levels return to normal.

What can be confusing in treating patients with hyperthyroidism is that a very low neutrophil count, including an extreme form of low neutrophil count called agranulocytosis, is a rare but dangerous side effect of antithyroid drugs used to control hyperthyroidism. With methimazole, the risk of agranulocytosis is higher with a higher dose of the drug while there is no dose effect with propylthiouracil (PTU). If agranulocytosis occurs, the antithyroid drugs should be stopped and alternative treatments (surgery, radioactive iodine therapy) need to be considered. Therefore, it may be difficult to start antithyroid drugs in a patient with hyperthyroidism when their neutrophil count is already low.

This systematic review was done to evaluate how frequently low neutrophil counts are seen in patients with newly diagnosed and untreated hyperthyroidism.

THE FULL ARTICLE

Scappaticcio L 2020 Neutropenia in patients with hyperthyroidism: Systematic review and meta-analysis. Clin Endocrinol (Oxf). Epub 2020 Aug 16. PMID: 32799342.

SUMMARY OF THE STUDY

The authors reviewed over 1800 medical articles and of those, they included 13 studies in their analysis. Combining all 13 reports, they studied a total of 1144 patients with hyperthyroidism. Almost 90% of these patients had hyperthyroidism due to Graves' disease. Of these, 10% patients had neutropenia before receiving any treatment. The majority had mild to moderate neutropenia. In the 84 patients for whom the counts were measured, the low neutrophil counts resolved after receiving antithyroid treatment, which included antithyroid drugs and/or radioactive iodine therapy. It took about 2 to 8 weeks for the neutrophil count to return to normal. None of the patients developed severe neutropenia or agranulocytosis following antithyroid drug treatment.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This review shows that mild to moderate decreases in the neutrophil count is common in hyperthyroidism and almost always resolves after treatment of the hyperthyroidism. Further, patients with mild neutropenia are not at increased risk of developing severe neutropenia or agranulocytosis after starting antithyroid drugs.

The American Thyroid Association guidelines currently recommend checking baseline white blood cell counts in patients with newly diagnosed hyperthyroidism. These studies show that antithyroid drugs can be safely used in patients with mild to moderate decreases in the neutrophil count and will usually result in return of the neutrophil count to normal. However, as the guidelines also note a baseline moderate to severe neutropenia "should prompt serious reconsideration of initiating antithyroid drug therapy".

— Susana Ebner MD



HYPERTHYROIDISM, continued

ATA BROCHURE LINKS

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

Graves' Disease: <https://www.thyroid.org/graves-disease/>

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.

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

White blood cells: blood cells involved with the immune response and fighting infections. Neutrophils, lymphocytes, eosinophils as basophils are all types of white blood cells.

Neutrophils: one of the white blood cells involved with the immune response and fighting infections.

Agranulocytosis: a marked decrease in the neutrophil 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.



HYPERTHYROIDISM

Liver enzymes are commonly high in patients with untreated hyperthyroidism and improve after treatment of hyperthyroidism

BACKGROUND

Uncontrolled hyperthyroidism has widespread effects on most of the body's functions. Most of the body's functions return to normal with the thyroid hormone levels return to normal during treatment of the hyperthyroidism. One system affected by hyperthyroidism is the liver system, as the liver and thyroid are closely related. The liver makes proteins that bind and carry thyroid hormone in blood and helps the body break down thyroid hormone. When thyroid hormone levels are very high in hyperthyroidism, blood liver function tests can be also be increased to levels that suggest damage to the liver, even though severe liver problems from hyperthyroidism is extremely rare. These abnormal liver function tests return to normal when the hyperthyroidism is controlled and the thyroid hormone levels return to normal.

What can be confusing is that the medications used to control hyperthyroidism, the antithyroid drugs methimazole and propylthiouracil (PTU), both can cause increased liver function tests that may indicate liver damage. When this occurs, the antithyroid drugs should be stopped and alternative treatments (surgery, radioactive iodine therapy) need to be considered. Therefore, it may be difficult to start antithyroid drugs in a patient with hyperthyroidism when their liver function tests are also high.

This systematic review was done to evaluate how frequently elevated liver function tests are seen in patients with newly diagnosed and untreated hyperthyroidism.

THE FULL ARTICLE TITLE

Scappaticcio L et al 2020. Abnormal liver blood tests in patients with hyperthyroidism: Systematic review and meta-analysis. *Thyroid*. Epub 2020 Dec 16. PMID: 33327837.

SUMMARY OF THE STUDY

The authors evaluated combined results from 25 studies, each of which looked at liver function tests in at least 10 patients with newly diagnosed and untreated hyperthyroidism. They did not include any patients who had underlying liver disease or very severe hyperthyroidism. Patients in the study had hyperthyroidism from Graves' disease, toxic multinodular goiter, and toxic adenoma. Liver function tests measured in each study included alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), total bilirubin (BIL), glutamyl transferase (GGT), prothrombin time, lactate dehydrogenase, and albumin.

A total of 6345 patients (age 19-77 years; 3061 females and 898 males) were included. Overall, 55% of patients had at least one abnormal liver function test at diagnosis. In patients with Graves' disease, 60% of patients had at least one liver function test at diagnosis. Frequency of abnormal levels of each liver function tests were 33% for ALT, 23% for AST, 44% for ALP, 12% for BIL, and 24% for GGT. Liver function tests improved in many patients after treatment of hyperthyroidism with antithyroid drugs and the return of thyroid hormone levels to normal. Frequency of normalization of each of abnormal liver function tests after treatment were 83% for ALT, 87% for AST, 53% for ALP, 50% for BIL, and 70% for GGT.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This systematic review showed that high blood liver function tests are common in patients with newly diagnosed and untreated hyperthyroidism. Frequency of having at least one abnormal liver function test in patients was 55%, much higher than 32% as reported in previous studies. In most cases, liver function tests were only mildly elevated, up to 5 times the normal range. However,



HYPERTHYROIDISM, continued

high liver function tests became normal in most of these patients after they were treated with antithyroid drugs and thyroid hormone levels became normal.

The American Thyroid Association currently recommends checking baseline liver function tests in patients with newly diagnosed hyperthyroidism. These studies show

that antithyroid drugs can be safely used in patients with mild liver function test increases and will usually result in resolution of the liver abnormalities. However, these patients should be monitored carefully to make sure liver function tests improve with improvement of hyperthyroidism.

— Sun Y. Lee, MD

ATA THYROID BROCHURE LINKS

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

Graves' Disease: <https://www.thyroid.org/graves-disease/>

ABBREVIATIONS & DEFINITIONS

Thyrotoxicosis: a condition where thyroid hormone levels are elevated. It can be caused by either increased production of thyroid hormone from the thyroid gland, increased release of stored thyroid hormone from the thyroid gland, or taking too much of thyroid hormone.

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.



Clinical Thyroidology® for the Public

ATA Alliance for Thyroid Patient Education

GOAL The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases. We look forward to future collaborations and continuing to work together toward the improvement of thyroid education and resources for patients.



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Survivors' Association, Inc.TM
www.thyca.org



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checkyourneck.com



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Foundation

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Thyroid
Federation
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American Thyroid Association

www.thyroid.org

ATA Patient Resources:

www.thyroid.org/thyroid-information/

Find a Thyroid Specialist: www.thyroid.org

(Toll-free): 1-800-THYROID

thyroid@thyroid.org

Bite Me Cancer

www.bitemecancer.org

info@bitemecancer.org

Graves' Disease and Thyroid Foundation

www.gdatf.org

(Toll-free): 877-643-3123

info@ngdf.org

Light of Life Foundation

www.checkyourneck.com

info@checkyourneck.com

MCT8 – AHDS Foundation

mct8.info

Contact@mct8.info

Thyca: Thyroid Cancer Survivors' Association, Inc.

www.thyca.org

(Toll-free): 877-588-7904

thyca@thyca.org

Thyroid Cancer Alliance

www.thyroidcanceralliance.org

www.thyroidcancerpatientinfo.org

Rotterdam, The Netherlands

Thyroid Cancer Canada

www.thyroidcancercanada.org

416-487-8267

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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 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

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.

Hypothyroidism in Pregnancy

WHAT IS THE THYROID GLAND?

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

WHAT ARE THE NORMAL CHANGES IN THYROID FUNCTION ASSOCIATED WITH PREGNANCY?

HORMONE CHANGES. Thyroid function tests change during normal pregnancy due to the influence of two main hormones: human chorionic gonadotropin (hCG) and estrogen. Because hCG can weakly stimulate the thyroid, the high circulating hCG levels in the first trimester may result in a low TSH that returns to normal throughout the duration of pregnancy. Estrogen increases the amount of thyroid hormone binding proteins, and this increases the total thyroid hormone levels but the "Free" hormone (the amount that is not bound and can be active for use) usually remains normal. The thyroid is functioning normally if the TSH and Free T4 remain in the trimester-specific normal ranges throughout pregnancy.

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

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

For the first 18-20 weeks of pregnancy, the baby is completely dependent on the mother for the production of thyroid hormone. By mid-pregnancy, the baby's thyroid begins to produce thyroid hormone on its own. The baby,

however, remains dependent on the mother for ingestion of adequate amounts of iodine, which is essential to make the thyroid hormones. The World Health Organization recommends iodine intake of 250 micrograms/day during pregnancy to maintain adequate thyroid hormone production. Because iodine intakes in pregnancy are currently low in the United States, the ATA recommends that US women who are planning to become pregnant, who are pregnant, or breastfeeding, should take a daily supplement containing 150 mcg of iodine.

HYPOTHYROIDISM & PREGNANCY

WHAT ARE THE MOST COMMON CAUSES OF HYPOTHYROIDISM DURING PREGNANCY?

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

WHAT ARE THE RISKS OF HYPOTHYROIDISM TO THE MOTHER?

Untreated, or inadequately treated, hypothyroidism has increased risk of miscarriage, and has been associated with maternal anemia, myopathy (muscle pain, weakness), congestive heart failure, pre-eclampsia, placental abnormalities, and postpartum hemorrhage (bleeding). These complications are more likely to occur in women with severe hypothyroidism. Some risks also appear to be higher in women with antibodies against thyroid peroxidase (TPO). Women with mild hypothyroidism may have no symptoms or attribute symptoms they have to the pregnancy.



Hypothyroidism in Pregnancy

WHAT ARE THE RISKS OF MATERNAL HYPOTHYROIDISM TO THE BABY?

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

Untreated severe hypothyroidism in the mother can lead to impaired brain development in the baby. Recent studies have suggested that mild developmental brain abnormalities also may be present in children born to women who had mild untreated hypothyroidism during pregnancy. At this time, there is no general consensus of opinion regarding screening all women for hypothyroidism during pregnancy. However, the ATA recommends checking a woman's TSH as soon as pregnancy is confirmed in women at high risk for thyroid disease, such as those with prior treatment for hyper- or hypothyroidism, a family history of thyroid disease, a personal history of autoimmune disease, and those with a goiter.

Women with established hypothyroidism should have a TSH test as soon as pregnancy is confirmed. They also should immediately increase their levothyroxine dose, because thyroid hormone requirements increase during pregnancy. (See below for specific dosing recommendations.) If new onset hypothyroidism has been detected, the woman should be treated with levothyroxine to normalize her TSH values (see *Hypothyroidism brochure*).

WHO SHOULD BE TREATED FOR HYPOTHYROIDISM DURING PREGNANCY?

Women found to have a TSH level greater than 10 mIU/L in the first trimester of pregnancy should be treated for hypothyroidism. Conversely, women with a TSH of 2.5 or less, do not need levothyroxine treatment. For women with TSH measured between these (2.5-10), ATA recommendations for treatment vary and may depend on whether or not the mother has TPO antibodies. When TPO antibodies are positive, treatment is recommended when the TSH is above 4 and should be considered when the TSH is between 2.5-4.0. However, when

there are no TPO antibodies (i.e. negative), current ATA recommendations are less strong and suggest that treatment 'may be considered' when TSH is between 2.5-10.0 mIU/L. These recommendations are based on the degree of evidence that exists that treatment with levothyroxine would be beneficial.

HOW SHOULD A WOMAN WITH HYPOTHYROIDISM BE TREATED DURING PREGNANCY?

The goal of treating hypothyroidism in a pregnant woman is adequate replacement of thyroid hormone. Ideally, hypothyroid women should have their levothyroxine dose optimized prior to becoming pregnant. Levothyroxine requirements frequently increase during pregnancy, usually by 25 to 50 percent. Hypothyroid women taking levothyroxine should independently increase their dose by 20%–30% as soon as pregnancy is diagnosed and should notify their doctor for prompt testing and further evaluation. One means of accomplishing the dose increase is to take two additional tablets weekly of their usual daily levothyroxine dosage. Thyroid function tests should be checked approximately every 4 weeks during the first half of pregnancy to ensure that the woman has normal thyroid function throughout pregnancy. As soon as delivery of the child occurs, the woman may go back to her usual pre-pregnancy dose of levothyroxine. It is also important to recognize that prenatal vitamins contain iron and calcium that can impair the absorption of thyroid hormone from the gastrointestinal tract. Consequently, levothyroxine and prenatal vitamins should not be taken at the same time and should be separated by at least 4 hours.

SPECIAL CONSIDERATIONS FOR WOMEN WITH A HISTORY OF GRAVES' DISEASE

In addition to the dosing and testing considerations explained in this brochure, women with a history of *Graves' disease* who were treated with radioiodine (RAI) or surgical thyroidectomy should also have Graves' antibodies (TRAb) tested early in pregnancy to assess the risk of passing antibodies on to the fetus. If antibodies are elevated, follow-up testing is recommended at weeks 18-22, and if antibodies are still elevated, additional follow-up is recommended at weeks 30-34 to evaluate the need for fetal and neonatal monitoring.



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

