AMERICAN THYROID ASSOCIATION
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Clinical Thyroidology® for the Public

VOLUME 10 | ISSUE 11 | NOVEMBER 2017

Thyroid cancer is one of the fastest rising cancers, especially in women. National guidelines have provided recommendations on the management of thyroid cancer. While the prognosis of thyroid cancer is usually excellent, decreased survival has been observed among the minority of patients who receive thyroid cancer care that is not aligned with either of the guidelines. This study was done to compare differences in the care of patients with thyroid cancer between the years 1998 to 2012.

Jaap K et al Disparities in the care of differentiated thyroid cancer in the United States: exploring the National Cancer Database. Am Surg 2017;83:739-46.

While mild/subclinical hypothyroidism in the mother is associated with pregnancy complications, the effects on brain development in the baby is less clear. This is also true with hypothyroxemia in pregnancy. The current study was designed to examine the results of treatment for subclinical hypothyroidism or hypothyroxinemia detected in early pregnancy on the basis of IQ assessed in children at 5 years of age.

Casey et al for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Treatment of subclinical hypothyroidism or hypothyroxinemia in pregnancy. N Engl J Med 2017;376:815-25.

Hypothyroid women on thyroid hormone replacement often require adjustments in levothyroxine dosing during pregnancy, usually a higher dose. The best protocol for managing this dose change is unknown, including the magnitude and timing of the dose change. These authors performed a clinical trial to compare two protocols for adjusting thyroid hormone doses in hypothyroid women during pregnancy.

Sullivan SD et al. Randomized trial comparing two algorithms for levothyroxine dose adjustment in pregnant women with primary hypothyroidism. J. Clin Endocrinol. Metab. 2017. 102: 3499-3507.

Overall, thyroid blood testing has steadily increased over the past few decades, corresponding with rising healthcare costs. Many thyroid tests are overused and may be inappropriate for the type of thyroid condition suspected. This study was done to assess how frequently certain thyroid blood tests were ordered in the U.S. across multiple healthcare organizations.

Lin, DC et al for the Thyroid Benchmarking Group. Multicenter Benchmark Study Reveals Significant Variation in Thyroid Testing in the United States. Thyroid 27(10): 1232-1245, 2017.

Medullary thyroid cancer is a rare cancer and is caused by mutations in the RET oncogene. The 2015 ATA guidelines categorize RET mutations into 3 categories – low, moderate, and high risk. This study examined the association of these mutations and the aggressiveness of the cancer.

Voss RK et al Medullary thyroid carcinoma in MEN2A: ATA moderate- or high-risk RET mutations do not predict disease aggressiveness. J Clin Endocrinol Metab 2017;102:2807-13.

When a patient is diagnosed with medullary thyroid cancer, quite often other members of their family are screened for the same cancer. Most patients with non-medullary thyroid do not have any family members with the same cancer but some do have a familial form. The benefit of screening family members after an individual gets diagnosed with non-medullary thyroid cancer is not known. The objective of this study was to identify criteria that would predict benefit of screening family members of patients with non-medullary thyroid cancer.

Klubo-Gwiezdzinska J Results of screening in familial non-medullary thyroid cancer. Thyroid 2017 Aug;27(8):1017-1024.

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EDITOR'S COMMENTS

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

We also provide even faster updates of late-breaking thyroid news through Twitter at @thyroidfriends and on Facebook. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room.

Also check out our friends in the Alliance for Thyroid Patient Education. The Alliance member groups consist of: the *American Thyroid Association*, *Bite Me Cancer*, the *Graves' Disease and Thyroid Foundation*, the *Light of Life Foundation*, *ThyCa: Thyroid Cancer Survivors Association*, *Thyroid Cancer Canada and Thyroid Federation International*.

November is Hyperthyroidism Awareness Month.

In this issue, the studies ask the following questions:

- Do racial or insurer-based disparities exist in the treatment of thyroid cancer?
- Does treatment of subclinical hypothyroidism in the mother improve brain development in the baby?
- What is the best way to adjust levothyroxine doses during pregnancy?
- What are the best thyroid tests to order in the treatment of thyroid disease?
- Does the type of cancer mutation affect the outcome in patients with medullary thyroid cancer?
- Does the number of family members affected matter when screening for familial non-medullary thyroid cancer?

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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THYROID CANCER

Are there racial differences in the care of patients with thyroid cancer?

BACKGROUND

Thyroid cancer is one of the fastest rising cancers, especially in women. A total of 62,000 new cases were diagnosed in 2016 alone. Fortunately, most of these cancers are low risk and, in these patients, the thyroid cancer is usually treated with surgery alone. Patients with intermediate and higher risk cancers are treated with radioactive iodine after surgery, which has shown to decrease cancer recurrence and improve survival in these higher risk patients. Guidelines from the American Thyroid Association and the National Comprehensive Cancer Network have each provided recommendations on the management of thyroid cancer. While the prognosis of thyroid cancer is usually excellent, decreased survival has been observed among the minority of patients who receive thyroid cancer care that is not aligned with either of the guidelines. This study was done to compare differences in the care of patients with thyroid cancer between the years 1998 to 2012.

THE FULL ARTICLE TITLE

Jaap K et al Disparities in the care of differentiated thyroid cancer in the United States: exploring the National Cancer Database. Am Surg 2017;83:739-46.

SUMMARY OF THE STUDY

The source of data for this study was the National Cancer Database. There were more than 250,000 patients with thyroid cancer included in the study; 78% of the patients were female, more than 80% were white and the average age was 48 years. Most of the patients (73.5%) had private insurance. Each of the geographic regions of the United States were represented fairly equally. Most patients had undergone a total thyroidectomy (83.3%), but only about half (48.5%) received postoperative radioactive iodine therapy. A total of 52% of patients had received care at a Comprehensive Community Cancer Program, while 41% received care from an academic medical center as designated by the Commission on Cancer.

Patients were more likely to receive a total thyroidectomy and central neck dissection at academic medical centers. Black patients were less likely to receive central neck dissection than white patients. Those more likely to receive postoperative radioactive iodine ablation were whites, privately insured individuals, and those receiving care at an academic medical center, demonstrating the disparities in care for differentiated thyroid cancer in this data set.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that those at risk for receiving less aggressive treatment of their thyroid cancer were more likely to be black, uninsured, and treated at Community Cancer Programs. The results of this study show racial and income based differences in the care of patients with thyroid cancer. There is also a difference noted between the academic medical centers and community cancer programs. The care of patients with thyroid cancer needs to be more uniform and the thyroid cancer care guidelines maybe helpful in this regard.

—Vibhavasu Sharma, MD

ATA THYROID BROCHURE LINKS:

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

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

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

ABBREVIATIONS & DEFINITIONS

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.

Radioactive iodine therapy: 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

THYROID CANCER, continued

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).

Thyroid Awareness Monthly Campaigns

The ATA will be highlighting a distinct thyroid disorder each month and a portion of the sales for Bravelets™ will be donated to the ATA. The month of **November** is **Hyperthyroidism Awareness Month** and a bracelet is available through the **ATA Marketplace** to support thyroid cancer awareness and education related to thyroid disease.

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THYROID AND PREGNANCY

Levothyroxine therapy of subclinical hypothyroidism or hypothyroxinemia in pregnancy does not affect brain function in the offspring

BACKGROUND

Thyroid hormone is essential for normal brain development in the baby during pregnancy. Hypothyroidism in the mother during pregnancy has been associated with multiple complications of pregnancy. Overt hypothyroidism in the mother (high TSH and low FT_4) has been shown to cause a lower IQ and impaired brain development in their children. While it is clear that mild/subclinical hypothyroidism in the mother (high TSH, normal FT_4) also is associated with pregnancy complications, the effects on brain development in the baby is less clear. This is also true with hypothyroxemia in pregnancy, where the mother's FT_4 is low but the TSH is normal. Further, while screening mothers early in pregnancy will identify individuals with subclinical hypothyroidism and hypothyroxinemia, it is uncertain whether treatment with levothroxine would have any effect on pregnancy outcomes on the baby's brain development.

The current study was designed to examine the results of treatment for subclinical hypothyroidism or hypothyroxinemia detected in early pregnancy on the basis of IQ assessed in children at 5 years of age.

THE FULL ARTICLE TITLE

Casey et al for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Treatment of subclinical hypothyroidism or hypothyroxinemia in pregnancy. N Engl J Med 2017;376:815-25.

SUMMARY OF THE STUDY

The study was a randomized, placebo-controlled trial at 15 centers. All women who presented before 20 weeks of pregnancy were invited to be screened for TSH and FT_4. In the first year, TSH >3.0 was used as the basis for inclusion, but this was subsequently adjusted to >4.0 because only 6% of women had TSH >3.0. Hypothyroxinemia was set as FT_4 <0.86 ng/dl. Measurement of anti-TPO antibodies and urine iodine were performed. Women with subclinical hypothyroidism were randomly assigned to receive either 100 µg of levothroxine or a matching placebo capsule daily. Women with hypothyroxinemia were given 50 µg of levothroxine or placebo. The treated women had monthly measurements of TSH and FT_4. On the basis of the results of these measurements, doses were adjusted, with sham adjustments in the placebo groups. The goal of the levothroxine therapy was a TSH of 0.1 to 2.5 mU/L with maximum dose of 200 µg. For the hypothyroxinemia trial, the goal was FT_4 between 0.86 and 1.90 ng/dl. The primary outcome was the full-scale IQ at age 5 years.

From October 2006 to October 2009, a total of 97,228 pregnant women underwent thyroid screening; 3057 had subclinical hypothyroidism; 800 of these women were eligible and consented to participate. A total of 677 of them underwent randomization for the study. Hypothyroxinemia was diagnosed in 805 women, of whom 632 were eligible and 526 underwent randomization. In the subclinical hypothyroidism trial, randomization occurred before 17 weeks and 93% of the L-T_4-treated group achieved a TSH between 0.1 and 2.5 mU/L by 21 weeks. In the hypothyroxinemia trial, randomization occurred at 18 weeks, and 83% of women treated with levothyroxine achieved an FT4 between 0.86 and 1.90 ng/dl by 23 weeks.

In the subclinical hypothyroidism trial, the average IQ at 5 years was 97 in the levothyroxine treated group and 94 placebo group. In the hypothyroxinemia trial, the average IQ at 5 years was 94 in the levothyroxine treated group and 91 in the placebo group. None of these differences were significant. Further, there were no differences in adverse pregnancy events or outcomes between the levothyroxine treated and placebo groups in either trial.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that levothyroxine therapy for subclinical hypothyroidism or hypothyroxinemia diagnosed during pregnancy beginning at an average of 17 to 19 weeks of

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THYROID AND PREGNANCY, continued

pregnancy had no effect on pregnancy outcomes or on brain development in children through 5 years of age than no treatment for these conditions. Because treatment has no effect, these data suggest that screening pregnant women for subclinical hypothyroidism or hypothyroxinemia is not helpful.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

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

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

Hypothyroidism: 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.

Subclinical Hypothyroidism: a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

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

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.

Levothyroxine (T_4): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tyrosint™ and generic preparations.

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THYROID AND PREGNANCY

Thyroid dysfunction in pregnancy

BACKGROUND

Thyroid hormone is essential during pregnancy for the baby to develop normally. Maintaining normal thyroid function in the mother during pregnancy is important for the pregnancy to have the best outcomes. Hypothyroidism that is inadequately treated in the mother during pregnancy can lead to premature delivery and other pregnancy complications. Hypothyroid women on thyroid hormone replacement often require adjustments in levothyroxine dosing during pregnancy, usually a higher dose. The best protocol for managing this dose change is unknown, including the magnitude and timing of the dose change. These authors performed a clinical trial to compare two protocols for adjusting thyroid hormone doses in hypothyroid women during pregnancy.

THE FULL ARTICLE TITLE

Sullivan SD et al. Randomized trial comparing two algorithms for levothyroxine dose adjustment in pregnant women with primary hypothyroidism. J. Clin Endocrinol. Metab. 2017. 102: 3499-3507.

SUMMARY OF THE STUDY

These investigators conducted a study of hypothyroid pregnant women living in Washington DC. Pregnant women with hypothyroidism of many causes were enrolled in the study before 11 weeks of the pregnancy and assigned to one of two thyroid hormone adjustment protocols. In Group 1, women increased their thyroid hormone dose by taking two extra doses per week at first presentation during pregnancy, followed by adjustments every two weeks in the first two trimesters then every 4 weeks in the third trimester based on their TSH values. The first dose increase was not based on TSH values but subsequent dose changes did take into account the woman's TSH. Women in Group 2 had their initial thyroid hormone dose change based on their TSH value at presentation and the dose either increased or decreased depending on the result. Dose changes were at the same intervals as Group 1, but instead of changing by dose (or pill number) per week, the dose was changed by micrograms of levothyroxine depending on the TSH.

The average time of study entry was 6.4 weeks of pregnancy for the 34 women that participated in the study. Most women (97%) were less than 10 weeks pregnant at the time of enrollment. The average TSH during the study was 1.5. More women in Group 1 had a suppressed TSH in the first trimester than women in Group 2. However, overall both groups of women had high rates of normal TSH values during their pregnancies (75% of pregnant hypothyroid women were to TSH goal in all 3 trimesters in Group 1 and 81% were to goal in Group 2, difference was not statistically significant). Both groups of women had an average of 3.5 thyroid hormone dose changes per pregnancy. Women with thyroid cancer and Graves' disease required more thyroid hormone dose adjustments than women with Hashimoto's disease or subclinical hypothyroidism.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Many hypothyroid women on thyroid hormone replacement therapy require dose adjustments to maintain normal TSH levels during pregnancy. The majority of women in both study groups had TSH values in the desired range during pregnancy. Although more women who had a standard dose increase in early pregnancy (Group 1) by two doses per week had a suppressed TSH in the first trimester, both groups had similar overall success in keeping the TSH in the normal range for each trimester. This study underscores the concept that the overall goal is to maintain a normal TSH during pregnancy in hypothyroid women and that multiple protocols for thyroid hormone dose adjustment can be effective and the choice can be individualized for the woman and the health care provider taking care of her.

— Whitney W. Woodmansee MD

ATA THYROID BROCHURE LINKS

Hypothyroidism: https://www.thyroid.org/hypothyroidism/

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

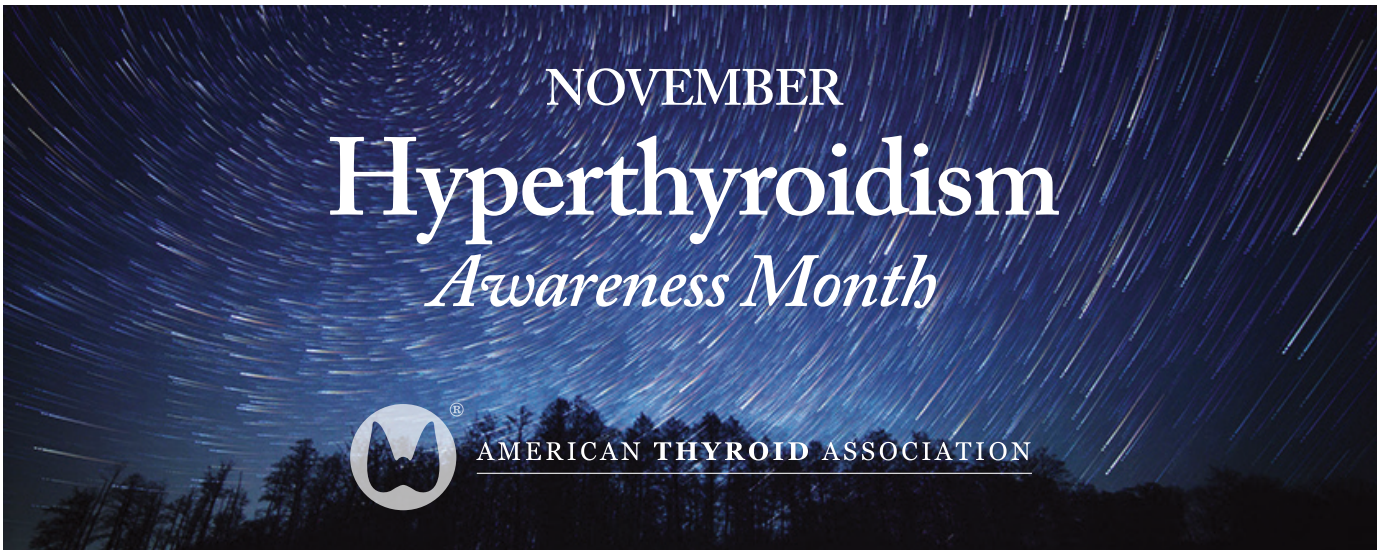
THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

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

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.

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal. The goal is a TSH in the normal range and is the usual therapy.



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THYROID BLOOD TESTS

Inconsistent ordering of thyroid blood tests in the U.S.

BACKGROUND

There are many options for thyroid blood testing. Many thyroid tests are overused and may be inappropriate for the type of thyroid condition suspected. Recommendations for which thyroid tests should be ordered are different in patients who are not currently taking thyroid-related medications, compared to those who are. TSH is usually the initial test if either hypothyroidism or hyperthyroidism are suspected. Further, screening for thyroid disease is currently controversial with no universally accepted recommendations.

Overall, thyroid blood testing has steadily increased over the past few decades, corresponding with rising healthcare costs. This study was done to assess how frequently certain thyroid blood tests were ordered in the U.S. across multiple healthcare organizations.

THE FULL ARTICLE TITLE

Lin, DC et al for the Thyroid Benchmarking Group. Multicenter Benchmark Study Reveals Significant Variation in Thyroid Testing in the United States. Thyroid 27(10): 1232-1245, 2017.

SUMMARY OF THE STUDY

The researchers studied data obtained from 82 laboratories associated with 24 U.S. unique healthcare organizations. The study reports on how often the following thyroid blood tests in each of these laboratories were ordered over the entire 2015 calendar year: thyroid stimulating hormone (TSH), free T_4 (fT_4), total T_4 (TT_4), free T_3 (fT_3), total T_3 (TT_3), T_3 uptake (T_3u), and reverse T_3 (rT_3).

TSH was the most frequent blood test ordered, consistent with its role as the usual the initial screening test if either hypothyroidism or hyperthyroidism are suspected. The study reported the order of subsequent thyroid tests following an initial serum TSH result. For every 100 TSH tests ordered, there were 14 fT_4's, three TT_4's, four fT_3's, two TT_3's, 0.1 rT_3's, and 0.1 T_3u's. Tests for fT_4 were nine times as common as those for TT_4, while those for fT_3 and TT_3 were mostly evenly split. One of the most variable thyroid tests was whether a rT_3 level was obtained following an initially abnormal TSH.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

From this sample of 82 U.S. clinical laboratories, there is considerable variation in the type of thyroid blood tests ordered by clinicians. This suggests that there is a need for better guidance in selecting the appropriate thyroid blood tests to obtain. Such measures would improve patient care and reduce unnecessary testing costs.

— Angela M. Leung, MD, MSc

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

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

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.

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

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THYROID CANCER

Specific RET mutations and cancer outcomes in MEN2A medullary thyroid cancer

BACKGROUND

Medullary thyroid cancer is a rare cancer and comprises 1-2% of the thyroid cancers in the US. Importantly, medullary thyroid cancer has a clear genetic component with RET oncogene and mutations in the RET gene cause this cancer. Medullary thyroid cancer can occur by itself (sporadic) or can run in families by itself or as part of a genetic syndrome. One important genetic syndrome is Multiple Endocrine Neoplasia type 2A, which includes medullary thyroid cancer, an adrenal tumor known as a pheochromocytoma, and parathyroid adenomas that lead to hyperparathyroidism. Almost all patients with MEN2A develop medullary thyroid cancer at some point in their life.

We have come to understand not all RET mutations are the same - that only some mutations correspond to risk of early development of medullary thyroid cancer and that others correlate with more aggressive medullary thyroid cancer. The 2015 American Thyroid Association guidelines for management of medullary thyroid cancer categorize MEN2A mutations into 3 categories – low, moderate, and high risk. This study examined the association of these mutations with the aggressiveness of the cancer.

THE FULL ARTICLE TITLE

Voss RK et al Medullary thyroid carcinoma in MEN2A: ATA moderate- or high-risk RET mutations do not predict disease aggressiveness. J Clin Endocrinol Metab 2017;102:2807-13.

SUMMARY OF THE STUDY

At MD Anderson, 262 MEN2A patients with a moderate or high-risk medullary thyroid cancer mutation and medullary thyroid cancer were examined. They looked at overall survival and time to development of spread of the medullary thyroid cancer outside of the neck between patients with a moderate-risk RET mutation (127 patients) and a high-risk RET mutation (135 mutation). There was no difference in percentage of patients that developed spread of the medullary thyroid cancer outside of the neck or the time to development of spread of the medullary thyroid cancer outside of the neck between the groups. Overall survival was also not statistically significant between the two groups. Medullary thyroid cancer did develop at a younger age in patients with high-risk RET mutations.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The current study challenges the implications of being diagnosed with a high- vs moderate-risk MEN2A RET mutation. The high-risk mutation group did develop medullary thyroid cancer at a significantly younger age, which would confirm the ATA recommendation to perform surgery to remove the thyroid (thyroidectomy) at a younger age in these patients. However, the moderate- and high-risk group had similar outcomes, and therefore, renaming the groups "early" and "late" onset (rather than 'risk') may be more appropriate.

— Melanie Goldfarb MD, MSc, FACS, FACE

ATA THYROID BROCHURE LINKS"

Thyroid Cancer (Medullary): - https://www.thyroid.org/medullary-thyroid-cancer/

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

ABBREVIATIONS & DEFINITIONS

Medullary thyroid cancer: a relatively rare type of thyroid cancer that often runs in families. Medullary cancer arises from the C-cells in the thyroid and is associated with mutations in the RET oncogene

THYROID CANCER, continued

MEN2A: Multiple endocrine neoplasia, type 2A. A hereditary syndrome in which medullary thyroid cancer is often seen in association with other endocrine tumors such as pheochromocytoma (a tumor of the adrenal glands) and hyperparathyroidism (elevated parathyroid hormone levels usually caused by tumors of the parathyroid glands).

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

Mutation: A permanent change in one of the genes.

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THYROID CANCER

The merits of ultrasound screening for familial non-medullary thyroid cancer are strongly dependent on the number of affected family members

BACKGROUND

Thyroid cancer is the fastest growing cancer in the United States. There are 3 different types of thyroid cancer: papillary thyroid cancer, follicular thyroid cancer and medullary thyroid cancer. Medullary thyroid cancer has a clear genetic, familial form that runs in families. When a patient is diagnosed with medullary cancer, quite often other members of their family are screened for the same cancer. Most patients with non-medullary thyroid cancer (ie papillary and follicular thyroid cancer) do not have any family members with the same cancer but some do have a familial form. For non-medullary thyroid cancer, an individual is considered to have a familial form of the cancer if he or she and two first-degree relatives have this diagnosis.

While having a family history of thyroid cancer is a risk factor for developing non-medullary thyroid cancer, the benefit of screening family members after an individual gets diagnosed with thyroid cancer is not known. The objective of this study was to identify criteria that would predict benefit of screening family members of patients with non-medullary thyroid cancer.

THE FULL ARTICLE TITLE

Klubo-Gwiezdzinska J Results of screening in familial non-medullary thyroid cancer. Thyroid 2017 Aug;27(8):1017-1024.

SUMMARY OF THE STUDY

Study patients were selected from patients who enrolled at the National Institutes of Health Clinical Center between 2010 and 2015. Patients with non-medullary thyroid cancer with at least two first-degree relatives affected with non-medullary thyroid cancer, and who were older than 7 years-old, were included. This was the index group which consisted of 56 patients with familial non-medullary thyroid cancer. Information was collected from patient records, family history questionnaires and patient interviews. All at-risk family members who agreed to participate in the study were screened yearly by physical examination and thyroid ultrasound. The screened group consisted of 183 "at risk" family members of these patients in the index group. When thyroid nodules were found on ultrasound in the "at risk" family members that were larger than 5 mm, they underwent fine-needle aspiration biopsy. If non-medullary thyroid cancer was diagnosed, these patients were treated.

Overall, the study identified 25 families with familial non-medullary thyroid cancer. Thyroid cancer was detected by screening in 4.6% (2/43) of at-risk individuals from families with 2 members affected, and in 22.7% (15/66) of at-risk members from families with 3 or more patients affected. The cancers detected in the family members were smaller, had a lower rate of spreading to the neck lymph nodes, required less extensive surgery and had a lower rate of radioactive iodine therapy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study showed that screening of first-degree family members that include 2 patients with familial non-medullary thyroid cancer identifies a percentage of patients that may be similar to that in the general population. However, screening of first-degree family members that include 3 or more patients with familial non-medullary thyroid cancer is far more likely to uncover a greater number of other family members with the cancer. Additionally, screening of at-risk family members resulted in finding low-risk familial non-medullary thyroid cancer earlier and was associated with a less aggressive initial treatment. Therefore, screening with thyroid ultrasound should be considered in families with three or more family members affected by familial non-medullary thyroid cancer. However, physicians should be careful especially in older adults, as active screening may increase risk of overtreatment.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

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

Thyroid Cancer (Medullary): https://www.thyroid.org/medullary-thyroid-cancer/

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Familial non-medullary thyroid cancer: type of thyroid cancer that runs in families that is not medullary thyroid cancer. This is usually papillary thyroid cancer and occurs in about 10% of thyroid cancers.

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

Medullary thyroid cancer: a relatively rare type of thyroid cancer that often runs in families. Medullary cancer arises from the C-cells in the thyroid.

Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

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.

Thyroid fine needle aspiration biopsy (FNAB): a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

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

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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.

WHO WE ARE (in alphabetical order)

AMERICAN THYROID ASSOCIATION
www.thyroid.org
ATA Patient Resources:
http://www.thyroid.org/thyroid-information/
Find a Thyroid Specialist: www.thyroid.org
(Toll-free): 1-800-THYROID
thyroid@thyroid.org

BITE ME CANCER
http://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

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.
www.thyca.org
(Toll-free): 877-588-7904
thyca@thyca.org

THYROID CANCER CANADA
www.thyroidcancercanada.org
416-487-8267
info@thyroidcancercanada.org

THYROID FEDERATION INTERNATIONAL
www.thyroid-fed.org
tfi@thyroid-fed.org

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JOIN US

"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.

Hyperthyroidism

WHAT IS THE THYROID GLAND?

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

WHAT IS HYPERTHYROIDISM?

The term *hyperthyroidism* refers to any condition in which there is too much thyroid hormone produced in the body. In other words, the thyroid gland is overactive. Another term that you might hear for this problem is thyrotoxicosis, which refers to high thyroid hormone levels in the blood stream, irrespective of their source.

WHAT ARE THE SYMPTOMS OF HYPERTHYROIDISM?

Thyroid hormone plays a significant role in the pace of many processes in the body. These processes are called your *metabolism*. If there is too much thyroid hormone, every function of the body tends to speed up. It is not surprising then that some of the symptoms of hyperthyroidism are nervousness, irritability, increased perspiration, heart racing, hand tremors, anxiety, difficulty sleeping, thinning of your skin, fine brittle hair and weakness in your muscles—especially in the upper arms and thighs. You may have more frequent bowel movements, but diarrhea is uncommon. You may lose weight despite a good appetite and, for women, menstrual flow may lighten and menstrual periods may occur less often. Since hyperthyroidism increases your metabolism, many individuals initially have a lot of energy. However, as the hyperthyroidism continues, the body tends to break down, so being tired is very common.

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

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

WHAT CAUSES HYPERTHYROIDISM?

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

Hyperthyroidism

HOW IS HYPERTHYROIDISM DIAGNOSED?

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

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

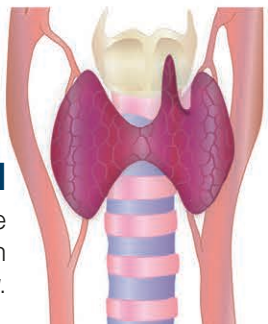
HOW IS HYPERTHYROIDISM TREATED?

No single treatment is best for all patients with hyperthyroidism. The appropriate choice of treatment will be influenced by your age, the type of hyperthyroidism that you have, the severity of your hyperthyroidism, other medical conditions that may be affecting your health, and your own preference. It may be a good idea to consult with an endocrinologist who is experienced in the treatment of hyperthyroid patients. If you are unconvinced or unclear about any thyroid treatment plan, a second opinion is a good idea.

ANTITHYROID DRUGS

Drugs known as *antithyroid agents*—methimazole (Tapazole®) or in rare instances propylthiouracil (PTU)—may be prescribed if your doctor chooses to treat the hyperthyroidism by blocking the thyroid gland's ability to make new thyroid hormone. Methimazole is presently the preferred one due to less severe side-effects. These drugs work well to control the overactive thyroid, bring quick control of hyperthyroidism and do not cause permanent damage to the thyroid gland. In about 20% to 30% of patients with Graves' disease, treatment with antithyroid drugs for a period of 12 to 18 months will result in prolonged remission of the disease. For patients with toxic nodular or multinodular goiter, antithyroid drugs are sometimes used in preparation for either radioiodine treatment or surgery.

Antithyroid drugs cause allergic reactions in about 5% of patients who take them. Common minor reactions are red skin rashes, hives, and occasionally fever and joint pains. A rarer (occurring in 1 of 500 patients), but more serious side effect is a decrease in the number of white blood cells. Such a decrease can lower your resistance to infection. Very rarely, these white blood cells disappear completely, producing a condition known as *agranulocytosis*, a potentially fatal problem if a serious infection occurs. If you are taking one of these drugs and get an infection such as a fever or sore throat, you should stop the drug immediately and have a white blood cell count that day. Even if the drug has lowered your white blood cell count, the count will return to normal if the drug is stopped immediately. But if you continue to take one of these drugs in spite of a low white blood cell count, there is a risk of a more serious, even life-threatening infection. Liver damage is another very rare side effect. A very serious liver problem can occur with PTU use which is why this medication should not generally be prescribed. You should stop either methimazole or PTU and call your doctor if you develop yellow eyes, dark urine, severe fatigue, or abdominal pain.



FURTHER INFORMATION

Further details on this and other thyroid-related topics are available in the patient information section on the American Thyroid Association® website at ***www.thyroid.org***.

Hyperthyroidism

RADIOACTIVE IODINE

Another way to treat hyperthyroidism is to damage or destroy the thyroid cells that make thyroid hormone. Because these cells need iodine to make thyroid hormone, they will take up any form of iodine in your blood stream, whether it is radioactive or not. The radioactive iodine used in this treatment is administered by mouth, usually in a small capsule that is taken just once. Once swallowed, the radioactive iodine gets into your blood stream and quickly is taken up by the overactive thyroid cells. The radioactive iodine that is not taken up by the thyroid cells disappears from the body within days. Over a period of several weeks to several months (during which time drug treatment may be used to control hyperthyroid symptoms), radioactive iodine destroys the cells that have taken it up. The result is that the thyroid or thyroid nodules shrink in size, and the level of thyroid hormone in the blood returns to normal. Sometimes patients will remain hyperthyroid, but usually to a lesser degree than before. For them, a second radioiodine treatment can be given if needed. More often, *hypothyroidism* (an underactive thyroid) occurs after a few months and lasts lifelong, requiring treatment. In fact, when patients have Graves' disease, a dose of radioactive iodine is chosen with the goal of making the patient hypothyroid so that the hyperthyroidism does not return in the future. Hypothyroidism can easily be treated with a thyroid hormone supplement taken once a day (see *Hypothyroidism* brochure).

Radioactive iodine has been used to treat patients for hyperthyroidism for over 60 years and has been shown to be generally safe. Importantly, there has been no clear increase in cancer in hyperthyroid patients that have been treated with radioactive iodine. As a result, in the United States more than 70% of adults who develop hyperthyroidism are treated with radioactive iodine. More and more children over the age of 5 are also being safely treated with radioiodine.

SURGERY

Your hyperthyroidism can be permanently cured by surgical removal of most of your thyroid gland. This procedure is best performed by a surgeon who has much experience in thyroid surgery. An operation could be risky unless your hyperthyroidism is first controlled by an antithyroid drug (see above) or a beta-blocking drug (see below). Usually for some days before surgery, your surgeon may want you to take drops of nonradioactive iodine—either Lugol's iodine or supersaturated potassium iodide (SSKI). This extra iodine reduces the blood supply to the thyroid gland and thus makes the surgery easier and safer. Although any surgery is risky, major complications of thyroid surgery occur in less than 1% of patients operated on by an experienced thyroid surgeon. These complications include damage to the parathyroid glands that surround the thyroid and control your body's calcium levels (causing problems with low calcium levels) and damage to the nerves that control your vocal cords (causing you to have a hoarse voice).

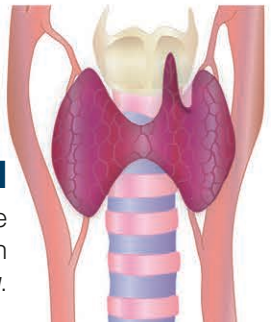
After your thyroid gland is removed, the source of your hyperthyroidism is gone and you will likely become hypothyroid. As with hypothyroidism that develops after radioiodine treatment, your thyroid hormone levels can be restored to normal by treatment once a day with a thyroid hormone supplement.

BETA-BLOCKERS

No matter which of these three methods of treatment are used for your hyperthyroidism, your physician may prescribe a class of drugs known as the *beta adrenergic blocking agents* that block the action of thyroid hormone on your body. They usually make you feel better within hours to days, even though they do not change the high levels of thyroid hormone in your blood. These drugs may be extremely helpful in slowing down your heart rate and reducing the symptoms of palpitations, shakes, and nervousness until one of the other forms of treatment has a chance to take effect. Propranolol (Inderal®) was the first of these drugs to be developed. Some physicians now prefer related, but longer-acting beta-blocking drugs such as atenolol (Tenormin®), metoprolol (Lopressor®), nadolol (Corgard®), and Inderal-LA® because of their more convenient once- or twice-a-day dosage.

OTHER FAMILY MEMBERS AT RISK

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



FURTHER INFORMATION

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