Volume 14 | Issue 1 | January 2021

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Over the years, providing medical decisions and recommendations in clinical practice has evolved into a more patient-centered approach. In the current model of shared decision making, information and opinions are exchanged between patients and providers to develop a treatment plan that works best for each individual patient. These studies: 1) describe a survey tool to improve communication from patients to their physicians and 2) examine physician–patient interactions as perceived by physicians.

- Bellastella G et al 2019 EMPATHY: a new tool for identifying the most suitable thyroxine formulation in hypothyroid patients. Thyroid **29:**928–933. PMID: 30963820.
- Esfandiari NH et al 2019 Patient requests for tests and treatments impact physician management of hypothyroidism. Thyroid. Epub 2019 Oct 10. PMID: 31436135.

Postpartum thyroiditis is estimated to happen after 8% of pregnancies. While it usually occurs in women with previously normal thyroid function during pregnancy, it may also occur in mothers who suffer from hypothyroidism before pregnancy. The goal of this study was to evaluate the frequency of postpartum thyroiditis in women with Hashimoto's thyroiditis with and without hypothyroidism before pregnancy.

Moleti M et al 2020; Postpartum thyroiditis in women with euthyroid and hypothyroid Hashimoto's thyroiditis antedating pregnancy. J Clin Endocrinol Metab. Epub 2020 Apr 17. PMID: 32301483.

The need to treat subclinical hyperthyroidism is not clear, partly due to the risks of the treatment options. Some studies suggest that subclinical hyperthyroidism increases the risk of osteoporosis, irregular heart beat (atrial fibrillation) and heart failure. The goal of this study was to determine the effectiveness of treating subclinical hyperthyroidism with either radioactive iodine therapy or the antithyroid medication methimazole .

Azizi F et al. 2020 Treatment of subclinical hyperthyroidism in the elderly: Comparison of radioiodine and long-term methimazole treatment. Thyroid. Epub 2020 Aug 18. PMID: 32811342.

Specialists, such as endocrinologists, often treat thyroid cancer patients initially. Long-term care may be then be transitioned to the primary care provider (PCP). Little is known how confident PCPs are in caring for and managing people who have survived thyroid cancer. The purpose of this study is to understand PCP involvement and confidence in caring for thyroid cancer survivors.

Radhakrishnan A et al 2020 Primary care provider involvement in thyroid cancer survivorship care. J Clin Endocrinol Metab 105(9):dgaa437. PMID: 32639557.

Papillary thyroid microcarcinoma is generally managed with less extensive surgery, often only a thyroid lobectomy. However, despite the excellent prognosis, some patients still have a prophylactic central neck dissection. This study investigated the benefit of prophylactic central neck dissection to decrease recurrence of thyroid cancer in the neck in patients with papillary thyroid microcarcinoma who underwent thyroid lobectomy.

Ryu YJ and Yoon JH 2020 Impact of prophylactic unilateral central neck dissection needed for patients with papillary thyroid microcarcinoma. Gland Surg **9:**352–361. PMID: 32420259.

The management of thyroid cancer has undergone a lot of changes over the last 10+ years. In particular, there has been a marked decrease in the use of radioactive iodine therapy after surgery for thyroid cancer. This paper summarizes an agreement between the major medical societies to reach more collaborative and consistent, evidence-based guiding principles for the best management of thyroid cancer.

Tuttle RM, et al 2019 Controversies, consensus, and collaboration in the use of ^{131}I therapy in differentiated thyroid cancer: a joint statement from the American Thyroid Association, the European Association of Nuclear Medicine, the Society of Nuclear Medicine and Molecular Imaging, and the European Thyroid Association. Thyroid **29:**461–470. PMID: 30900516.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 14 | Issue 1 | January 2021

Clinical Thyroidology® for the Public

EDITOR'S COMMENTS

Happy New Year and 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/)

January is Thyroid Awareness month.

In this issue, the studies ask the following questions:

- Does physician perception and patient input affect the treatment of hypothyroidism?
- How often does postpartum thyroiditis occur in women with Hashimoto's thyroiditis?
- What is the best option for treating mild hyperthyroidism in the elderly?
- What is the role of primary care providers in caring for thyroid cancer survivors?
- Is there any role for central neck dissection in the management of small papillary thyroid cancers?
- What is the current role of radioactive iodine therapy in 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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 14 | Issue 1 | January 2021

Clinical Thyroidology® for the Public

HYPOTHYROIDISM

Physician perception and patient input are important influences in the treatment of hypothyroidism

BACKGROUND

Over the years, the traditional, paternalistic approach to providing medical decisions and recommendations in clinical practice has, appropriately, evolved into a more patient-centered approach. In the current model of shared decision making, information and opinions are exchanged between patients and providers to develop a treatment plan that works best for each individual patient. There are many studies published in primary care journals about these two-way patient–physician interactions but there seems to be less attention paid to this within the specialties, including endocrinology. This may be changing, as demonstrated by the two publications summarized here.

The first of these, by Bellastella et al., describes a survey tool to improve communication from patients to their physicians. The second, by Esfandiari et al., examines physician–patient interactions as perceived by physicians.

THE FULL ARTICLE TITLE

- Bellastella G et al 2019 EMPATHY: a new tool for identifying the most suitable thyroxine formulation in hypothyroid patients. Thyroid **29:**928–933. PMID: 30963820.
- Esfandiari NH et al 2019 Patient requests for tests and treatments impact physician management of hypothyroidism. Thyroid. Epub 2019 Oct 10. PMID: 31436135.

SUMMARY OF THE STUDY

BELLASTELLA G ET AL

The aim of this study was to describe a patient survey tool that would help physicians choose the formulation of synthetic levothyroxine that would provide the best option for thyroid hormone replacement in their patients with autoimmune hypothyroidism. A total of 300 patients with mild-moderate untreated hypothyroidism secondary to autoimmune thyroiditis were recruited for the study. Inclusion criteria for the study were age <60 years, TSH >10 mIU/L, and "low/normal" serum free T_3 and free T_4 levels. Patients were assigned to two groups, each containing 50 men and 100 women. One of the groups, referred to here as **E**$^+$, was assigned to answer a survey entitled EMPATHY (Evaluation of Malabsorption in Patients with Hypothyroidism.). The other group, referred to here as **E**$^-$, did not take the survey. EMPATHY consisted of seven questions. The first six were designed to uncover a history of drug allergies or intolerance, stomach issues including inflammatory and irritable bowel disease, dietary restrictions, soy intake, or alcohol abuse. The final question presented a check-off panel of foods and food types in various categories, including nickel allergy, lactose intolerance, histamine intolerance, citric acid intolerance, gluten intolerance, and cornstarch allergy.

At baseline, age and serum thyroid-function tests (free T_4, free T_3, TSH) were similar in **E**$^+$ and **E**$^-$ patients. A drug/food allergy or intolerance was suspected in 30 **E**$^+$ patients based on answers to the questions. Levothyroxine treatment was started at a dose of 1.6 µg/kg/day in both groups in the form of tablets, soft gel capsules, or liquid. During the next 6 months, the levothyroxine dose was adjusted to achieve a target TSH of 0.4 to 2.5 mIU/L. During this period, the percentage of tablets and liquid preparations taken by the **E**$^+$ group was less, but not significantly less, than comparable formulations taken by the **E**$^-$ group. In contrast, approximately 20 percent of patients in the **E**$^+$ group were taking soft-gel T_4 preparations, as compared with less than half that number in the **E**$^-$ group. During the periods 2 months and 6 months after starting levothyroxine therapy, there were significantly more dose adjustments in the **E**$^-$ group than in the **E**$^+$ group. Also, 95% of patients in the **E**$^+$ group had reached the target TSH after 6 months while 89% were in range in the **E**$^-$ group.

The authors concluded that screening for drug and food allergies or intolerances in patients with autoimmune hypothyroidism may be useful in selecting the best levothyroxine formulation for thyroid hormone replacement.

HYPOTHYROIDISM, continued

ESFANDIARI NH ET AL

The focus of this study was to determine physicians' perception of the barriers to managing thyroid hormone replacement in patients with hypothyroidism. The authors conducted a survey among randomly chosen physician members of the Endocrine Society (ES), American Academy of Family Practice (AAFP), and American Geriatrics Society (AGS) with regard to their decision-making in treating their patients with hypothyroidism. The goal of the study was to determine whether physician and patient behaviors influence choices for thyroid hormone replacement therapy. The survey asked physicians about their practice patterns and interactions with their patients and what they believed were barriers. In addition, there were several sets of questions about the confidence that physicians had in interventions using decision support tools for managing thyroid hormone replacement. The survey was mailed to 600 physician addresses; the response rate among the remaining 566 physicians was 63%. Among these, 36% were primary care physicians, 32% endocrinologists, and 32% geriatricians. The majority of physicians (64%) had not read guidelines for the treatment of hypothyroidism. The makeup of the clinical practice of these physicians varied widely, as expected when comparing primary care physicians and specialists. In 70% of the physicians, they were treating fewer than 25% of their patients with levothyroxine for hypothyroidism. The remaining 30% prescribed levothyroxine to >26% of their patients.

A total of 70% of physicians considered it "somewhat likely" to "very likely" that patient compliance was a barrier for them in managing thyroid hormone replacement in their patients with hypothyroidism while 41% rated patient requests for tests and treatments as being a barrier. This perception was mainly associated with endocrinologists and less likely in physicians who had been practicing medicine for more than 20 years. Concern about patient dissatisfaction was noted in 32% of physicians, and this response was correlated with patient requests for tests and treatments as a barrier to managing thyroid hormone replacement. Physicians stated that they were "very likely" or "likely" to receive the following requests from patients: 1) to adjust their dose of thyroid hormone even when the thyroid-function tests were normal (50%); 2) to use thyroid hormone preparations other than levothyroxine (50%); 3) to maintain serum T_4 concentrations below normal (30%) and 4) to adjust thyroid hormone doses based on serum free T_3 concentrations (20%). Further, 21% indicated they sometimes or almost always adjusted the dose of thyroid hormone based on symptoms when thyroid function tests were normal, 12% indicated they would use thyroid hormone preparations other than levothyroxine, 15% indicated they sometimes or almost always maintained serum TSH concentrations below normal, and about 8 % indicated they sometimes or almost always adjusted the dose of thyroid hormone based on serum free T_3 concentrations.

Surprisingly, this study suggests that patient requests for tests and treatments outranks other more traditionally perceived barriers to patient compliance, including multiple providers managing thyroid medication, patients taking multiple other medications, clinic-visit time constraints and lack of clinical decision support tools.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Both of these studies indicate that a patient-centered approach to the management of hypothyroidism, along with shared decision making between physicians and patients, leads to increased patient satisfaction and better compliance by patients. Tools that can increase the communication between patients and physicians, as well as engaging patients in their own care, are likely to also lead to better patient outcomes.

— Alan P. Farwell, MD

HYPOTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/

Thyroid Hormone Treatment: https://www.thyroid.org/thyroid-hormone-treatment/

ABBREVIATIONS & DEFINITIONS

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis/Autoimmune thyroiditis, hypothyroidism).

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

Primary hypothyroidism: the most common cause of hypothyroidism cause by failure of the thyroid grand.

Thyroxine (T_4): the major hormone produced by the thyroid gland. T4 gets converted to the active hormone T3 in various tissues in the body.

Triiodothyronine (T_3): the active thyroid hormone, usually produced from thyroxine.

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

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

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

Desiccated thyroid extract: thyroid hormone pill made from animal thyroid glands. Currently desiccated thyroid extract is made from pig thyroids and is available as Armour Thyroid™ and Nature-Throid™.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 14 | Issue 1 | January 2021

Clinical Thyroidology® for the Public

THYROID AND PREGNANCY

Postpartum thyroiditis in women with euthyroid and hypothyroid Hashimoto's thyroiditis prior to pregnancy

BACKGROUND

Postpartum thyroiditis is a short lived inflammation in thyroid gland that occurs in the first year after pregnancy. It is estimated to happen after 8% of pregnancies. In this condition, a course of hyperthyroidism (1 – 3 months after delivery) is followed by 6-12 months of hypothyroidism, then thyroid function returns to normal. Women may have just the hyperthyroid phase, just the hypothyroid phase, or both phases.

While postpartum thyroiditis usually occurs in women with previously normal thyroid function during pregnancy, it may also occur in mothers who suffer from hypothyroidism before pregnancy. In the United States, Hashimoto's thyroiditis is the most common cause of hypothyroidism. This diagnosis is made with positive thyroid peroxidase (TPO) antibodies in the setting of hypothyroidism. However, not all patients with Hashimoto's thyroiditis are hypothyroid; some have normal thyroid function despite positive TPO antibodies and do not need yet need to take thyroid hormone.

The goal of this study was to evaluate the frequency of postpartum thyroiditis in women with Hashimoto's thyroiditis with and without hypothyroidism before pregnancy.

THE FULL ARTICLE TITLE

Moleti M et al 2020; Postpartum thyroiditis in women with euthyroid and hypothyroid Hashimoto's thyroiditis antedating pregnancy. J Clin Endocrinol Metab. Epub 2020 Apr 17. PMID: 32301483.

SUMMARY OF THE STUDY

This study was done in Italy. The medical records of 1378 women from 2008 to 2017 visits in a university hospital were reviewed. A total of 167 women with Hashimoto's thyroiditis who became pregnant during the study time were included; 98 were on thyroid hormone before pregnancy and 69 had normal thyroid hormone level before pregnancy.

Overall, 65 women (38.9%) developed postpartum thyroiditis; this occurred more commonly in women with Hashimoto thyroiditis who did not need to take thyroid hormone before pregnancy than in hypothyroid women.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Women with Hashimoto thyroiditis who are not hypothyroid before pregnancy are at increased risk of developing postpartum thyroiditis after childbirth. This study suggests that physicians and patients should be aware of this increased risk in the postpartum period. However, the number of cases reviewed in this study was relatively small and conclusion should be confirmed by subsequent studies.

— Shirin Haddady, MD MPH

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/
Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/
Thyroid Hormone Treatment: https://www.thyroid.org/thyroid-hormone-treatment/
Thyroid Disease in Pregnancy: https://www.thyroid.org/thyroid-disease-pregnancy/
Postpartum Thyroiditis: https://www.thyroid.org/postpartum-thyroiditis/

THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

Postpartum thyroiditis: an inflammation of the thyroid in women who have just delivered a baby. The inflammation first causes mild hyperthyroidism for 1-3 months after delivery. This is followed by hypothyroidism starting 4-6 months after delivery. The hypothyroidism resolves and normal thyroid function returns 12-18 months after delivery in most women. While many women have both the hyperthyroid and the hypothyroid phase, some women may only have one or the other.

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

Hashimotos thyroiditis: the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy it.

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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 14 | Issue 1 | January 2021

Clinical Thyroidology® for the Public

HYPERTHYROIDISM

Treatment of subclinical hyperthyroidism in the elderly

BACKGROUND

Subclinical hyperthyroidism refers to a mildly overactive thyroid and is defined as a low TSH (thyroid stimulating hormone) and a normal free thyroxine (FT_4). The two most common causes of subclinical hyperthyroidism are Graves' disease and one or more overactive nodules in the thyroid (toxic nodular goiter). As in overt hyperthyroidism, treatment options include radioactive iodine therapy, antithyroid medications and surgery. Unlike overt hyperthyroidism, the need to treat subclinical hyperthyroidism is less clear. This is partly due to the risks of the treatment options.

Subclinical hyperthyroidism can be broken down into Grade 1, when the TSH is slightly decreased (0.1-0.39 mU/L) and Grade 2 in which the TSH level is below 0.1mU/L. Most discussion about treating subclinical hyperthyroidism is focused on Grade 2. Some studies suggest that Grade 2 subclinical hyperthyroidism increases the risk of osteoporosis (weakening of the bones), irregular heart beat (atrial fibrillation) and heart failure.

The goal of this study was to determine the effectiveness of treating Grade 2 subclinical hyperthyroidism with either radioactive iodine therapy or the antithyroid medication methimazole (MMI). The results that were looked at included: return to normal thyroid function, as well as onset of an underactive thyroid, heart disease and death.

THE FULL ARTICLE TITLE

Azizi F et al. 2020 Treatment of subclinical hyperthyroidism in the elderly: Comparison of radioiodine and long-term methimazole treatment. Thyroid. Epub 2020 Aug 18. PMID: 32811342.

SUMMARY OF THE STUDY

Between 2006 and 2017, 83 patients with Grade 2 subclinical hyperthyroidism were enrolled in the study. Their average age was between 65 and 74 years old. Of these, 41 patients were treated with radioactive iodine and 42 patients were treated with MMI long term.

The results show that 5 years after receiving the radioactive iodine therapy, 66% of the patients developed an underactive thyroid and 34% had normal thyroid hormone levels. Among the patients who received MMI, 94% of them remained with normal thyroid hormone level and only 6% developed an underactive thyroid. No serious effects occurred in either group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Over a study period of 5 years, both a one-time dose of radioactive iodine or daily MMI medication were effective and safe for treating Grade 2 subclinical hyperthyroidism in elderly patients. Hypothyroidism (underactive thyroid) developed in a greater proportion of patients who received radioactive iodine than in those who received MMI. This is important for patients to understand that the current treatment option for treating this condition work well and are safe.

— Maria Brito, MD

ATA THYROID BROCHURE LINKS

Hyperthyroidism in Pregnancy: https://www.thyroid.org/hyperthyroidism-in-pregnancy/
Graves' Disease: https://www.thyroid.org/graves-disease/
Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/

HYPERTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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

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

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

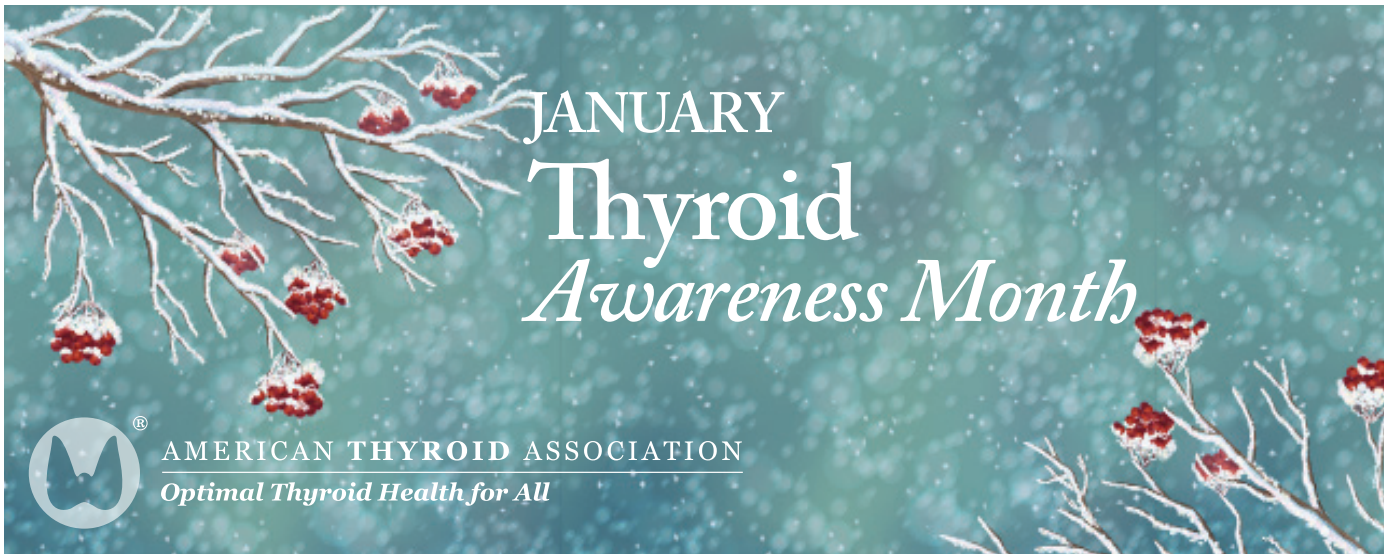
Toxic nodular goiter: characterized by one or more nodules or lumps in the thyroid that may gradually grow and increase their activity so that the total output of thyroid hormone in the blood is greater than normal.

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.

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

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

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



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Volume 14 | Issue 1 | January 2021

Clinical Thyroidology® for the Public

THYROID CANCER

Primary care provider involvement in caring for thyroid cancer survivors

BACKGROUND

The number of patients diagnosed with thyroid cancer has increased in recent years. A majority of patients with thyroid cancer are diagnosed with papillary or follicular thyroid cancer. While the long-term outcomes of patients with thyroid cancer are excellent, these patients need long-term follow up and surveillance (close observation to make sure their cancer does not come back). Specialists, such as endocrinologists (doctors who specialize in the endocrine system including thyroid diseases), often treat these patients initially. Long-term care may be then be transitioned to the primary care provider (PCP). However, studies have shown that PCPs are often not comfortable in caring for people who have survived cancer. Little is known how confident PCPs are in caring for and managing people who have survived thyroid cancer. The purpose of this study is to understand PCP involvement and confidence in caring for thyroid cancer survivors.

THE FULL ARTICLE TITLE

Radhakrishnan A et al 2020 Primary care provider involvement in thyroid cancer survivorship care. J Clin Endocrinol Metab 105(9):dgaa437. PMID: 32639557.

SUMMARY OF THE STUDY

Patients diagnosed with thyroid cancer from 2014 to 2015 were identified from the Georgia and Los Angeles Surveillance, Epidemiology, and End Results (SEER) registries and were asked to identify the doctor most involved in their thyroid cancer care (other than their surgeon or endocrinologist). A total of 289 PCPs were identified and surveyed through mail surveys and follow-up phone calls. PCPs were asked if they were involved in long-term care of thyroid cancer survivors. PCPs were also were asked to report their confidence in caring for thyroid cancer survivors including discussing the role of thyroglobulin levels and neck ultrasounds, and knowing when to refer a patient back to the thyroid specialist. PCP involvement was reported as involved versus not involved, and confidence was reported as high versus low. PCPs were asked if they were familiar with the established guidelines for managing patients with thyroid cancer: the 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer and the 2017 National Comprehensive Cancer Network's Clinical Practice Guidelines in Oncology: Thyroid Carcinoma.

Of the 289 PCPs surveyed 162 responded (56% response rate). A total of 76% of PCPs reported being involved in the care and long-term surveillance of thyroid cancer survivors. PCPs who felt that the clinical guidelines most guided their treatment decisions were found to have the most involvement in caring for thyroid cancer survivors. PCPs reported their confidence in handling the following: referring a patient to a specialist (39%), role of a neck ultrasound (36%) and thyroglobulin levels (27%), and ending long-term surveillance (14%). PCPs who noted they were involved in the care of thyroid cancer survivors were more likely to report high confidence in discussing the role of thyroglobulin levels.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While many PCPs report being involved in thyroid cancer survivors care, there are gaps in their confidence in handling various aspects of care. One option to improve primary care confidence in caring for thyroid cancer survivors includes having thyroid survivorship clinical guidelines that clarify the specific role and responsibility of the PCP.

— Priya Mahajan, MD

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).

Follicular Thyroid Cancer: the second most common type of thyroid cancer.

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/

Thyroglobulin: a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker in patients that do not have thyroglobulin antibodies.

Neck ultrasound: a common imaging test used to evaluate the structure of the thyroid gland and neck. Ultrasound uses sound waves to create a picture of the structure of the thyroid gland and surrounding neck.

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Volume 14 | Issue 1 | January 2021

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THYROID CANCER

Can central neck dissection for papillary thyroid microcarcinoma be avoided to decrease thyroid cancer overtreatment?

BACKGROUND

The diagnosis of papillary thyroid microcarcinoma (thyroid cancer smaller than 1cm in size) has increased because of increased detection by medical imaging (often for non-thyroid related reasons). Papillary thyroid microcarcinoma is generally managed with less extensive surgery than larger thyroid cancers since it rarely spreads to the lymph nodes outside the neck. This means that often only the lobe containing the thyroid cancer is removed (thyroid lobectomy). Overall, patients with papillary thyroid microcarcinoma are considered to be at low risk for cancer recurrence after surgery.

However, despite the excellent prognosis, some patients still have lymph nodes under and behind the thyroid removed routinely even if they do not look abnormal on visual inspection at the time of surgery (a prophylactic central neck dissection). This study investigated the benefit of prophylactic central neck dissection to decrease recurrence of thyroid cancer in the neck in patients with papillary thyroid microcarcinoma who underwent thyroid lobectomy.

THE FULL ARTICLE TITLE

Ryu YJ and Yoon JH 2020 Impact of prophylactic unilateral central neck dissection needed for patients with papillary thyroid microcarcinoma. Gland Surg **9:**352–361. PMID: 32420259.

SUMMARY OF THE STUDY

This was a medical chart review of > 5000 patients who underwent a thyroid lobectomy for papillary thyroid microcarcinoma from 2004-2012 at hospital with extensive thyroid cancer management experience. Of those charts reviewed, 1071 patients were studied who did not have evidence of cancer spread to the lymph nodes prior to surgery. Patients were excluded if they were followed up for <1 year, had experienced thyroid cancer recurrence within 6 months, had thyroid pathology other than classical papillary thyroid carcinoma, had known nodules in the remaining thyroid lobe, or had abnormal serum thyroid function test results. Cancer recurrence was defined as the presence of abnormal lymph nodes on neck ultrasound. All recurrences were confirmed by fine needle biopsy that showed papillary thyroid cancer. Case follow up was for an average of almost 7 years.

In total, 613 patients had a lobectomy alone and 458 patients had a lobectomy plus prophylactic central neck dissection. In the central neck dissection group, 363 (79.3%) did not show thyroid cancer in lymph nodes and 95 (20.7%) did have thyroid cancer in lymph nodes. Only 27 total patients had detectable recurrences of thyroid cancer. Most were in the thyroid lobe that was not operated on. A total of 18 recurrences occurred in patients who did not have a central neck dissection and 9 occurred in those with a central neck dissection. Most were detected within 5 years of the initial surgery. The main factor that predicted recurrent thyroid cancer was cancer size > 6 mm and the presence of Hashimoto's thyroiditis. The central neck dissection did not prevent recurrence in a significant way. Risks of complications including nerve damage to the recurrent laryngeal nerve and bleeding were low and no different between patients that had central neck dissection and those that did not.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Prophylactic central neck dissection in patients with papillary thyroid microcarcinoma did not decrease the risk of recurrent thyroid cancer and removal of central lymph nodes should not be a standard part of surgery for papillary thyroid microcarcinoma when a lobectomy is the operation of choice. This is important for patients because it shows more extensive surgery for papillary thyroid microcarcinoma does not appear helpful in general. Even shorter operative time and less time under general

THYROID CANCER, continued

anesthesia is a significant benefit. Additionally, this study (and these studies in general) was performed where the thyroid cancer surgeons have extensive experience. For surgeons who have less experience (<25 thyroid surgeries per year), a lobectomy alone is simpler and generally has less risk of complication than a surgery that involves lymph node dissection.

— Joshua Klopper, MD

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

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.

Lobectomy: surgery to remove one lobe of the thyroid.

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

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

Central neck compartment: the central portion of the neck between the hyoid bone above, and the sternum and collar bones below and laterally limited by the carotid arteries.

Prophylactic central neck dissection: careful removal of all lymphoid tissue in the central compartment of the neck, even if no obvious cancer is apparent in these lymph nodes.

Hashimotos thyroiditis: the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy it.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 14 | Issue 1 | January 2021

Clinical Thyroidology® for the Public

THYROID CANCER

Controversies, consensus, and collaboration in the use of radioactive iodine therapy in thyroid cancer

BACKGROUND

The management of thyroid cancer has undergone a lot of changes over the last 10+ years. The 2015 American Thyroid Association (ATA) management guidelines for thyroid nodules and thyroid cancer recommend a patient-centered approach to evaluating the risk of thyroid cancer recurrence and overall prognosis for each individual patient. This has led to a decrease in total thyroidectomies (removal of the entire thyroid) and an increase in the removal only of the lobe containing the cancer (lobectomy), keeping the other lobe intact. Partially due to this change in surgical approach, there has been a marked decrease in the use of radioactive iodine therapy after surgery for thyroid cancer.

There has been discussion in the greater nuclear medicine community regarding some of these recommendations and two prominent nuclear medicine organizations, the European Association of Nuclear Medicine (EANM) and the Society of Nuclear Medicine and Molecular Imaging (SNMMI), declined to endorse the guidelines.

In order to promote better understanding of differences in perspective and to reach a more collaborative and consistent, evidence-based set of recommendations, or at least of guiding principles, representatives from the ATA and the European Thyroid Association (ETA) met with representatives from the EANM and the SNMMI to draft a consensus paper. This paper aims to support cooperation among medical societies, to define the goals radioactive iodine therapy, to acknowledge that the published literature is lacking with regard to the best dose of radioactive iodine therapy to use and to better improve the definition of thyroid cancer that is no longer responding to radioactive iodine therapy

THE FULL ARTICLE TITLE

Tuttle RM, et al 2019 Controversies, consensus, and collaboration in the use of ^{131}I therapy in differentiated thyroid cancer: a joint statement from the American Thyroid Association, the European Association of Nuclear Medicine, the Society of Nuclear Medicine and Molecular Imaging, and the European Thyroid Association. Thyroid **29:**461–470. PMID: 30900516.

SUMMARY OF THE STUDY

A 2-day meeting was held in Martinique in January 2018. A panel of 18 senior leaders and subject-matter experts from 8 countries and 4 organizations (the ATA, EANM, SNMMI, and ETA) convened to consider, debate, and exchange ideas regarding the use of ^{131}I in the management of thyroid cancer. After much discussion and a review of 60 publications, in addition to expert opinion, the conference participants agreed on a set of principles, which are summarized as follows:

1. The best thyroid cancer management requires cooperation between endocrinologists, surgeons and nuclear medicine physicians.

2. The goal of radioactive iodine therapy should be specifically defined as (a) destroying remaining normal thyroid tissue, (b) treatment of suspected microscopic cancer remaining after surgery or (c) treatment of known visible cancer.

3. Proper patient selection for radioactive iodine therapy requires assessment of postoperative cancer status and not simply preoperative staging.

4. Evaluation of postoperative cancer status should be standardized in terms of blood tests and imaging tests.

5. Proper patient selection for radioactive iodine therapy also requires evaluation of multiple factors, including patient preference, potential side effects, and availability and quality of medical resources.

6. The best administered radioactive iodine therapy cannot be determined from the available literature, favoring more individualized dosing decisions.

THYROID CANCER, continued

7. Identification of cancers that are unlikely to respond to radioactive iodine therapy should not to exclude them from consideration of radioactive iodine therapy.

8. Criteria used to identify cancers that are unlikely to respond to radioactive iodine therapy will continue to evolve, especially with progress in evidence-based studies and better imaging.

9. Prospective studies are needed to address knowledge and evidence gaps with regard to radioactive iodine therapy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Defining the best use of radioactive iodine therapy in thyroid cancer remains controversial, is subject to interpretation of evidence, and is influenced by many patient and health care delivery variables. Collaboration between endocrinologists, surgeons and nuclear medicine physicians will help refine the use of radioactive iodine therapy in the patient-centered care of thyroid cancer.

— Alan P. Farwell, MD

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

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

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).

Follicular thyroid cancer: the second most common type of thyroid cancer.

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ATA Alliance for Thyroid Patient Education

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

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Graves' Disease & Thyroid Foundation

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

Light of Life Foundation
checkyourneck.com

Bite Me Cancer

MCT8 - AHDS Foundation

Thyroid Cancer Alliance

Thyroid Cancer Canada
Cancer de la thyroïde Canada

Thyroid Federation International

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

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

Thyroid Federation International
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tfi@thyroid-fed.org

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- Updates on the latest patient resources through the ATA website and elsewhere on the world wide web
- Special e-mail alerts about thyroid topics of special interest to you and your family

We will use your email address to send you *Friends of the ATA e-news* and occasional email updates. We won't share your email address with anyone, and you can unsubscribe at any time.

www.thyroid.org

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ATA | *Founded 1923*

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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.

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?

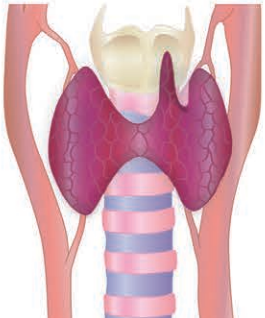
Women found to have a TSH level greater than 10 mIU/L in the first trimester of pregnancy should be treated for hypothyroidism. Conversely, women with a TSH of 2.5 or less, do not need levothyroxine treatment. For women with TSH measured between these (2.5-10), ATA recommendations for treatment vary 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*