AMERICAN THYROID ASSOCIATION
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Clinical Thyroidology® for the Public

VOLUME 12 | ISSUE 9 | SEPTEMBER 2019

Pregnant women who have positive TPO antibodies and even mild hypothyroidism are routinely treated with thyroid hormone replacement. The question is whether treatment with thyroid hormone helps women who have positive TPO antibodies only and normal thyroid hormone levels. This study looks at women who have a history of miscarriage and infertility to see if thyroid hormone replacement in TPO antibody positive women improves fertility.

DhillonSmith RK et al 2019 Levothyroxine in women with thyroid peroxidase antibodies before conception. N Engl J Med 380:1316–1325. Epub 2019 Mar 23. PMID: 30907987.

If the mother is severely deficient in iodine in early pregnancy, the child may also have low intelligence. The effects of mother's iodine levels during different periods of pregnancy have not been studied previously. The aim of this study was to assess the association between mother's iodine status in pregnancy and child IQ, and to investigate the association at different pregnancy periods.

Levie D et al Association of maternal iodine status with child IQ: a meta-analysis of individual-participant data. J Clin Endocrinol Metab. Epub Mar 28. PMID: 30920622

Routine thyroid testing often occurs in hospitalized patients with nonspecific symptoms during the evaluation of the cause of the illness that brought the patient into the hospital. Many studies have shown that routine thyroid testing in adults without a high likelihood for thyroid problems causing the acute reasons for hospitalization is rarely helpful. The goal of this study is to evaluate how often thyroid testing is done in children who are hospitalized, how often the results are abnormal, and the impact of thyroid testing on patient care.

Torky A et al Low Value of Thyroid Testing in Pediatric Inpatient Setting. Hosp Pediatr 9:24-29. PMID: 30559318.

The most common finding during a major illness is a low T_3 level caused by the illness and not by a thyroid problem. While most researchers and physicians believe that the thyroid hormone changes during a sickness are beneficial for recovery, there is debate on whether treatment with T_3 may be helpful when it declines to very low levels. In this study, the authors tried to evaluate the effect of treatment with T_3 on recovery from heart attack; specifically, to assess the potential benefits of T_3 on the extent of heart muscle damage and its function.

Pingitore A et al 2018 Usefulness of triiodothyronine replacement therapy in patients with ST elevation myocardial infarction and borderline/reduced triiodothyronine levels (from the THIRST study). Am J Cardiol. Epub 2018 Dec 18. PMID: 30638544.

Antithyroid medications, such as Methimazole, are used to treat a toxic nodular goiter short-term to get a patient ready for either surgery or radioactive iodine therapy. Long-term therapy with methimazole is not usually considered in treating patients with a toxic nodular goiter since this will never go into remission. This study was done to compare treatment of toxic nodular goiter with long-term methimazole as opposed to radioactive iodine therapy.

Azizi F, Takyar MA, Madreseh E, Amouzegar A. Treatment of toxic multinodular goiter: comparison of radioiodine and long-term methimazole treatment. Thyroid. Epub 2019

Up to 25% of thyroid biopsies result in an indeterminate biopsy result. While the use of molecular markers has greatly helped in the diagnosis of indeterminate nodules, these tests are expensive and may not be available everywhere. The purpose of this study was to compare the accuracy of fine needle vs core needle biopsies for the diagnosis of thyroid cancer in the evaluation of indeterminate nodules.

Yoon JH et al 2019 Ultrasonography-guided core needle biopsy did not reduce diagnostic lobectomy for thyroid nodules diagnosed as atypia of undetermined significance/follicular lesion of undetermined significance. Ultrasound Q. Epub 2019 Feb 4. PMID: 30724862.

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Clinical Thyroidology® for the Public

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EDITOR'S COMMENTS

Welcome to another issue of *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through Twitter at @thyroidfriends and on Facebook. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room. Also check out our friends in the **Alliance for Thyroid Patient Education**. The **Alliance** member groups consist of: the *American Thyroid Association, Bite Me Cancer, the Graves' Disease and Thyroid Foundation, the Light of Life Foundation, ThyCa: Thyroid Cancer Survivors' Association, Thyroid Cancer Canada, Thyroid Cancer Alliance* and *Thyroid Federation International*.

The American Thyroid Association (ATA) extends its appreciation to all of the patients and their families that are part of the ATA community — our **Friends of the ATA**. It is for you that the 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.

September is Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- Does levothyroxine therapy in TPO-positive women affect miscarriage rates?
- Does mild to moderate iodine deficiency in early pregnancy affect IQ in the children?
- Is routine thyroid testing in hospitalized children helpful?
- Does T_3 therapy help recover from heart attacks?
- Is long-term methimazole therapy effective in the treatment of toxic nodular goiters?
- Is a core needle biopsy helpful in the diagnosis of indeterminate thyroid biopsies?

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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Clinical Thyroidology® for the Public

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THYROID AND PREGNANCY

Does treatment with thyroid hormone improve fertility in women with normal thyroid function but positive thyroid peroxidase antibodies?

BACKGROUND

While miscarriage and preterm births occur in many pregnancies, the risks increase in women with thyroid problems due to both thyroid overactivity and thyroid underactivity. The presence of thyroid antibodies in patients with thyroid problems indicates autoimmune thyroid disease and is also associated with an increase in miscarriage rates and preterm birth. However, when woman have very mild thyroid abnormalities, the data is less clear, as studies do not show an increase in complications with mild thyroid underactivity or overactivity. Women who have positive thyroid peroxidase antibodies (TPO antibodies) and even mild hypothyroidism are routinely treated with thyroid hormone replacement. The question is whether treatment with thyroid hormone helps women who have positive TPO antibodies only and normal thyroid hormone levels. A previous study looked at thyroid hormone replacement in women undergoing assisted pregnancy and found no effect. This study looks at women who have a history of miscarriage and infertility to see if thyroid hormone replacement in TPO antibody positive women improves fertility.

THE FULL ARTICLE TITLE

DhillonSmith RK et al 2019 Levothyroxine in women with thyroid peroxidase antibodies before conception. N Engl J Med 380:1316–1325. Epub 2019 Mar 23. PMID: 30907987.

SUMMARY OF THE STUDY

Patients were recruited from almost 20,000 women in the UK from December 2011 through January 2016 who were 16-40 years of age with a history of prior miscarriage or infertility who were trying to get pregnant and were determined to have positive TPO antibody and normal thyroid hormone levels. They could not have a treated thyroid disorder, heart problems or be on medication know to effect thyroid function. A total of 952 women agreed to participate. Half of the women received a low dose of thyroid hormone (50 mcg levothyroxine) daily while the other half received a placebo pill. The study looked at live births after 34 weeks pf pregnancy, clinical pregnancy at 7 weeks and miscarriage before 24 weeks. The subjects were a good representation in that 44% were over age 35 yr, 65% had previous miscarriage and 45% were receiving infertility treatment. While all had normal thyroid function, 31% had a TSH in the high normal range (above 2.5 mIU).

There was no difference in any of the outcomes measured. Clinical pregnancy occurred in 57% of treated group and 58% of placebo group. Similarly, live births after 34 weeks was not different (37% in both groups). Neither age over 35, number of previous miscarriages or TSH above 2.5 made any difference in outcome analysis. There was no significant difference in in miscarriage rates (28% treated, 30% placebo), preterm birth before 34 weeks (4% both), birth weight or stillborn babies.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

It does not appear that treatment with thyroid hormone improves pregnancy outcome in women who have positive TPO antibodies and have normal thyroid function. Even though we know the presence of TPO antibodies does increase the risk for miscarriage and preterm birth, treatment with thyroid hormone does not seem to help when thyroid function is still normal. Since over-treatment with thyroid hormone also has potential risk for pregnancy outcomes, this suggests that women with normal thyroid function should not be given thyroid hormone in an attempt to improve pregnancy outcomes even when TPO antibodies are positive.

— Marjorie Safran, MD

ATA THYROID BROCHURE LINKS

Hyperthyroidism in Pregnancy: https://www.thyroid.org/hyperthyroidism-in-pregnancy/

THYROID AND PREGNANCY, continued

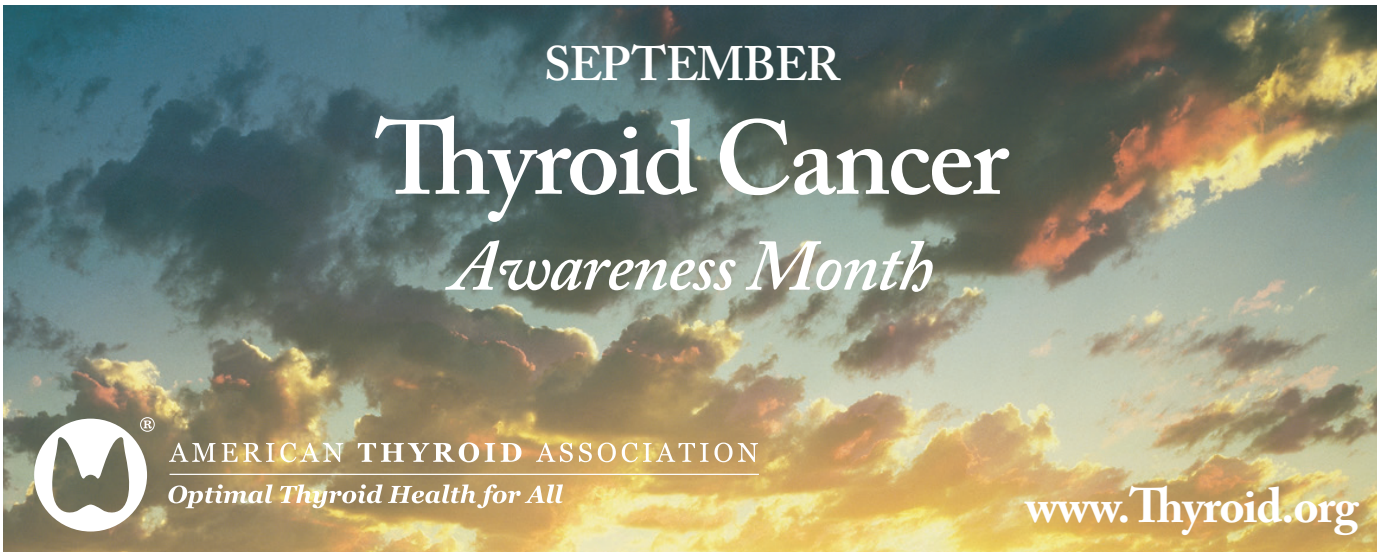
ABBREVIATIONS & DEFINITIONS

TPO antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

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, hypothyroidism).

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.



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IODINE AND PREGNANCY

Mild to moderately low levels of iodine in early pregnancy may be associated with lower verbal IQ in children

BACKGROUND

The thyroid gland uses iodine to make thyroid hormones. If there is not enough iodine in the diet, thyroid hormone levels fall and can cause hypothyroidism. Indeed, iodine deficiency is a common cause of hypothyroidism world-wide. Thyroid hormone is required for normal brain development in the baby during pregnancy. Severe hypothyroidism can cause abnormal brain development and low intelligence. Similarly, if the mother is severely deficient in iodine in early pregnancy, the child may also have low intelligence. On the other hand, the effects of mild or moderate iodine deficiency is not well known. The effects of mother's iodine levels during different periods of pregnancy have not been studied previously. The aim of this study was to assess the association between mother's iodine status in pregnancy and child IQ, and to investigate the association at different pregnancy periods.

THE FULL ARTICLE TITLE

Levie D et al Association of maternal iodine status with child IQ: a meta-analysis of individual-participant data. J Clin Endocrinol Metab. Epub Mar 28. PMID: 30920622

SUMMARY OF THE STUDY

The study was done using data from three European pregnancy groups from Netherlands, the United Kingdom, and Spain. They included mother-child pairs if mother's urinary iodine and creatinine levels were checked during pregnancy and if the child IQ test results were available. Two main types of intelligence were tested. Verbal IQ is the ability to solve problems using language. Non-verbal IQ is the ability to reason without using words. They excluded multiple pregnancies, use of fertility treatment, known thyroid disease, or use of medications that could affect the thyroid. Since the measurements were done by different methods researchers used techniques to standardize the values so they were able to compare 3 different groups.

The study included 6180 mother-child pairs. Urine samples were collected around 12-14 weeks of pregnancy. Urine iodine-to-creatinine ratios were used to assess mother's iodine status. Urine iodine-to-creatinine ratios were 159 mcg/L in the group from The Netherlands (iodine sufficient), 128 mcg/L in the group from Spain (mildly iodine deficient) and 96 mcg/L in the United Kingdom group (moderately iodine deficient). Associations between iodine status and child verbal IQ were seen during the first 12 weeks but not after 14 weeks of pregnancy. Urine iodine-to-creatinine ratios were not associated with the child's non-verbal IQ or mother's TSH or free T_4 levels.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that lower urinary iodine-to-creatinine ratios up to 14th week of pregnancy were associated with poorer child verbal IQ scores. This is important to patients because timing of iodine supplementation may be critical for the development of baby's language ability. The American Thyroid Association recommends women who are planning pregnancy, pregnant, or lactating should take 150 mcg of iodine. Ideally, iodine supplementation should start 3 months prior to pregnancy. We need future studies evaluating the effect of this strategy.

— Ebru Sulanc, MD

ATA THYROID BROCHURE LINKS

Iodine Deficiency: https://www.thyroid.org/iodine-deficiency/

Hyperthyroidism in Pregnancy: https://www.thyroid.org/hyperthyroidism-in-pregnancy/

IODINE AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

Iodine: an element found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. Common foods high in iodine include iodized salt, dairy products, seafood and some breads.

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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THYROID FUNCTION TESTS

The value of thyroid testing in hospitalized children is low

BACKGROUND

Routine thyroid testing often occurs in hospitalized patients with nonspecific symptoms during the evaluation of the cause of the illness that brought the patient into the hospital. Certain diagnoses in adults lead to thyroid testing, such as new onset atrial fibrillation or an acute presentation of a psychiatric illness. However, many studies have shown that routine thyroid testing in adults without a high likelihood for thyroid problems causing the acute reasons for hospitalization is rarely helpful.

For many reasons, routine thyroid testing in hospitalized children is at least as common as in adults. One reason for testing in children is in those who are at increased risk for thyroid disease or dysfunction, such as patients with new-onset type 1 diabetes or with the use of certain medications. The goal of this study is to evaluate how often thyroid testing is done in children who are hospitalized, how often the results are abnormal, and the impact of thyroid testing on patient care.

THE FULL ARTICLE TITLE

Torky A et al Low Value of Thyroid Testing in Pediatric Inpatient Setting. Hosp Pediatr 9:24-29. PMID: 30559318.

SUMMARY OF THE STUDY

This study examined hospital admissions at Children's National Medical Center between July 2015 and June 2016. Medical charts of hospitalized pediatric patients who underwent thyroid testing during this time period were reviewed. Thyroid testing was done in 5.7% of admitted patients. The majority (79.3%) had combined thyroid function tests (TFTs) with thyroid-stimulating hormone (TSH) and free thyroxine (FT_4). The psychiatry service ordered 41.6% of TFTs, followed by the endocrinology service (14.9%). A total of 205 tests (17.1% of patients) ordered were abnormal. The most common abnormalities included a normal FT_4 with an increased TSH, a normal FT_4 with a decreased TSH, and a high FT_4 with a normal TSH. Approximately 20% of children with new-onset type 1 diabetes had abnormal TFTs, but all abnormalities normalized when retested at outpatient follow up. Despite these abnormal results, only eight patients (0.66%) received treatment aimed at their thyroid and all of these were started on levothyroxine.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Thyroid testing is commonly performed in hospitalized children but rarely correlates to the cause of the hospitalization or impacts the immediate treatment. While abnormal thyroid results are common, they generally normalize without intervention. The authors encourage educating inpatient providers to only order thyroid testing based on strong clinical suspicion, as testing can be delayed in some patients until they are in the outpatient setting.

— Priya Mahajan, MD

ATA THYROID BROCHURE LINKS

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

THYROID FUNCTION TESTS, continued

ABBREVIATIONS & DEFINITIONS

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

Thyroxine (T4): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

Levothyroxine (T4): the major hormone produced by the thyroid gland

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THYROID HORMONE THERAPY

Triiodothyronine (T_3) treatment after mild heart attacks is safe but not associated with a clear benefit

BACKGROUND

During a major illness, the levels of thyroid hormones (T_4 and T_3) and thyroid stimulating hormone (TSH) change in most patients. These changes do not represent a problem in thyroid gland, but they are part of a larger hormonal reaction that happens at the time of a significant sickness. The most common finding is a low T_3 level, as the body shuts down the production of T_3 from T_4 during sickness. This may also occur after a heart attack. Indeed, 15-20% of patients have low levels of T_3 for several days after a heart attack. Patients with the lowest levels of T_3 are usually the sickest and have a higher chance of dying.

While most researchers and physicians believe that the hormonal changes during a sickness are helpful and beneficial for recovery, there is debate on whether treatment with T_3 may be helpful when it declines to very low levels. In the past, various animal and clinical investigations have been conducted to answer this question. In this study, the authors tried to evaluate the effect of treatment with T_3 on recovery from heart attack; specifically, to assess the potential benefits of T_3 on the extent of heart muscle damage and its function.

THE FULL ARTICLE TITLE

Pingitore A et al 2018 Usefulness of triiodothyronine replacement therapy in patients with ST elevation myocardial infarction and borderline/reduced triiodothyronine levels (from the THIRST study). Am J Cardiol. Epub 2018 Dec 18. PMID: 30638544.

SUMMARY OF THE STUDY

This study was done in Pisa, Italy. The authors recruited patients with heart attack who were admitted to cardiac intensive unit. The patients were eligible to enter the study if they had a low level of T_3 at the time of admission or a 20% drop in T_3 level within the first 72 hours after arrival to hospital. They also had to be treated with a heart procedure to open up the coronary arteries within 12 hours of the onset of their initial symptoms. Patients who were very sick, had history of previous thyroid disease or heart disease and took certain medications were not considered appropriate for the study. A total of 37 patients participated. Patients received either T_3 plus standard heart care (19) or just standard heart care (18). The 19 patients who received T_3 continued taking it for 6 months. The starting dose was based on patient's age (lower in older individuals), with later doses based on the results of blood tests for TSH, T_4 and T_3.

The average age of participants was 68 years and only 16% were female. TSH, T_4 and T_3 were measured at the time of admission, on daily basis during hospitalization and on regular basis after discharge. MRI was done to assess the extent of heart muscle damage after heart attack as well as its function (ability to pump blood). There was a minimum improvement in the function of heart muscle in patients who received T_3 but this was not statistically significant. No side effects were noted from T_3.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study confirmed that after a heart attack, patients who are sicker have a lower level of T_3. Although no harm was observed by treating patients with T_3 after a heart attack, this study showed that no significant improvement in the function or decrease in the extent of damaged heart muscle was noted from such treatment. At this point, T_3 treatment is not recommended after a heart attack based on this study and larger randomized clinical trials are needed.

— Shirin Haddady, MD

THYROID HORMONE THERAPY, continued

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

Thyroxine (T4): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

Triiodothyronine (T3): the active thyroid hormone, usually produced from thyroxine, available in pill form as Cytomel™.

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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HYPERTHYROIDISM

Long-term methimazole is an effective treatment for toxic nodular goiters

BACKGROUND

Hyperthyroidism is a condition where the thyroid gland is overactive and produces high levels of thyroid hormone in the blood. Graves' disease is the most common cause of hyperthyroidism in the United States. The entire gland is overactive in Graves' disease. Less common is a toxic nodular goiter, where one or more thyroid nodules are overactive and the rest of the gland is turned off. Antithyroid medications, such as Methimazole, are used to treat a toxic nodular goiter short-term to get a patient ready for either surgery or radioactive iodine therapy. The main results of either surgery or radioactive iodine therapy is the development of hypothyroidism, which will require life-long treatment with levothyroxine.

Long-term therapy with methimazole is not usually considered in treating patients with a toxic nodular goiter since this will never go into remission. However, methimazole has been shown to be safe for long term use in patients with Graves' disease. This study was done to compare treatment of toxic nodular goiter with long-term methimazole as opposed to radioactive iodine therapy.

THE FULL ARTICLE TITLE

Azizi F, Takyar MA, Madreseh E, Amouzegar A. Treatment of toxic multinodular goiter: comparison of radioiodine and long-term methimazole treatment. Thyroid. Epub 2019

SUMMARY OF THE STUDY

A total of 130 patients in Tehran, Iran were included in the clinical trial. They received methimazole therapy (for 5 to 8 years) or receive treatment with radioactive iodine therapy. Participants were less than 60 years old in age with an average age of about 50 years in both groups. Patients had a diagnosis of hyperthyroidism confirmed with thyroid function tests. Patients with Graves' disease were excluded. Patients either received a one-time dose of radioactive iodine therapy or were started on methimazole in a dose of 10 to 20 mg daily.

The patient in the methimazole-treated group were more likely to have normal thyroid function tests after 2 years (96 %) as compared to radioactive iodine therapy (54%). As expected, the size of the goiter was reduced more in the group treated with radioactive iodine therapy than methimazole. A few patients in both groups developed side effects from the treatments.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that long-term treatment with methimazole was safe and effective for normalizing the thyroid function in patients with a toxic nodular goiter with relatively few side effects. Methimazole therapy may be a viable and safe option for the treatment of toxic goiters over the long term. Further studies are needed to look at other outcomes such as impact on the quality of life and the cost of therapies.

—Vibhavasu Sharma, MD, FACE

ATA THYROID BROCHURE LINKS

Goiter: https://www.thyroid.org/goiter/

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

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

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

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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.

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.

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

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THYROID NODULES

Core needle biopsy does not prevent the need for thyroid surgery in indeterminate thyroid nodules

BACKGROUND

Thyroid nodules are very common, occurring in up to 50% of the population. The concern with thyroid nodules is whether they are cancerous, which is the case in 5-7% of nodules. Ultrasound is the common first step when a nodule is found on physical exam or identified by other imaging tests such as CT or MRI scans. Although ultrasound can identify thyroid nodule characteristics suggestive of thyroid cancer, most thyroid nodules are less clear. The most accurate way to determine if a thyroid cancer is present is to perform a fine needle aspiration biopsy, a minor procedure in which a fine needle is inserted into a thyroid nodule and cells from the nodule are removed through the needle. A pathologist, a doctor specializing in disease diagnosis through tissue sample analysis, then reviews these cells.

In up to 25% of biopsies, a diagnosis cannot be determined by looking at the cells alone. This is known as an indeterminate biopsy result. There are 3 categories for indeterminate nodules: 1) atypia of unknown significance or follicular lesion of unknown significance (AUS/FLUS), 2) follicular or hurtle cell lesion and 3) suspicious for papillary cancer. The likelihood for cancer is the lowest in the AUS/FLUS category. The use of molecular markers has greatly helped in the diagnosis of indeterminate nodules, as a negative result is consistent with a benign nodule. However, these tests are expensive and may not be available everywhere. Prior to the development of molecular markers, the recommendation was to repeat a biopsy and, if still indeterminate, proceed with surgery to remove the lobe containing the nodule. Some studies suggest repeating a biopsy with a core needle, which is a larger needle that will remove more cells for analysis than the usual fine needle, may be helpful in evaluating indeterminate nodules. The purpose of this study was to compare the accuracy of fine needle vs core needle biopsies for the diagnosis of thyroid cancer in the evaluation of the AUS/FLUS category of indeterminate nodules.

THE FULL ARTICLE TITLE

Yoon JH et al 2019 Ultrasonography-guided core needle biopsy did not reduce diagnostic lobectomy for thyroid nodules diagnosed as atypia of undetermined significance/follicular lesion of undetermined significance. Ultrasound Q. Epub 2019 Feb 4. PMID: 30724862.

SUMMARY OF THE STUDY

In this study, the authors evaluated every indeterminate biopsy result that fell into the ACUS/FLUS category from their institution that over a two-year period (2013-2015). They ultimately identified 149 ACUS/FLUS cases for which repeat biopsy was performed, either using fine needle (86 cases) or core needle (63 cases). In comparing the biopsy groups, the authors found the following: 1) The core needle technique was more likely to provide an adequate sample for analysis (98.4% vs. 88.4%), 2) A similar numbers of ACUS/FLUS cases were found to be benign for each group (55.6% core needle vs 50% fine needle), 3) 3.5% of repeat biopsies were identified as cancerous for the fine needle group as compared to 11.1% of the core needle group, 4) of the thyroid surgeries performed for each group, 73% in the fine needle group were confirmed cancers as compared to 65% of core needle cases and 5) core needle biopsies had a higher rate of minor complications as compared to fine needle biopsies (6.3% vs 0%).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Although this study is quite small, with relatively few patients ultimately undergoing surgery in each group, the authors found that core needle biopsy was somewhat better at identifying thyroid cancer in patients having had a previous ACUS/FLUS biopsy. However, because a significant number of biopsies in each group still showed indeterminate findings (not clearly cancerous or benign), the need for thyroid surgery was not reduced in the core needle group. In fact, the surgery rate for this group

THYROID NODULES, continued

was somewhat higher as compared to the fine needle group. In addition, the risk of complications from a core needle biopsy was significantly higher than in the fine needle biopsies, which is why the latter is the standard biopsy technique for thyroid nodules. Overall, this study therefore does not support use of core needle biopsies in the evaluation of thyroid nodules.

— Jason D. Prescott, MD PhD

ATA THYROID BROCHURE LINKS

Thyroid Nodules: https://www.thyroid.org/thyroid-nodules/
Fine Needle Aspiration Biopsy of Thyroid Nodules: https://www.thyroid.org/fna-thyroid-nodules/
Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/
Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

ABBREVIATIONS & DEFINITIONS

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

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 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.

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

Lobectomy: surgery to remove one lobe of the thyroid.

Molecular markers: genes and microRNAs that are expressed in benign or cancerous cells. Molecular markers can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign. The two most common molecular marker tests are the Afirma™ Gene Expression Classifier and Thyroseq™

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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:
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
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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
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Thyroid Cancer Canada
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Thyroid Federation International
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AMERICAN THYROID ASSOCIATION
ATA | Founded 1923

Friends of the ATA

FOUNDED 2005

Get the latest thyroid health information. You'll be among the first to know the latest cutting-edge thyroid research that is important to you and your family.

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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.

Thyroid Cancer
(Papillary and Follicular)

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.

CANCER OF THE THYROID

Thyroid cancer is relatively uncommon compared to other cancers. In the United States it is estimated that in 2016 approximately 64,000 new patients will be diagnosed with thyroid cancer, compared to over 240,000 patients with breast cancer and 135,000 patients with colon cancer. However, fewer than 2000 patients die of thyroid cancer each year. In 2013, the last year for which statistics are available, over 630,000 patients were living with thyroid cancer in the United States. Thyroid cancer is usually very treatable and is often cured with surgery (see *Thyroid Surgery brochure*) and, if indicated, radioactive iodine (see *Radioactive Iodine brochure*). Even when thyroid cancer is more advanced, effective treatment is available for the most common forms of thyroid cancer. Even though the diagnosis of cancer is terrifying, the prognosis for most patients with papillary and follicular thyroid cancer is usually excellent.

WHAT ARE THE TYPES OF THYROID CANCER?

Papillary thyroid cancer. Papillary thyroid cancer is the most common type, making up about 70% to 80% of all thyroid cancers. Papillary thyroid cancer can occur at any age. It tends to grow slowly and often spreads to lymph nodes in the neck. However, unlike many other cancers, papillary cancer has a generally excellent outlook, even if there is spread to the lymph nodes.

Follicular thyroid cancer. Follicular thyroid cancer makes up about 10% to 15% of all thyroid cancers in the United States. Follicular cancer can spread to lymph nodes in the neck, but this is much less common than with papillary cancer. Follicular cancer is also more likely than papillary cancer to spread to distant organs, particularly the lungs and bones.

Papillary and follicular thyroid cancers are also known as Well-Differentiated Thyroid Cancers (DTC). The information in this brochure refers to the differentiated thyroid cancers. The other types of thyroid cancer listed below will be covered in other brochures

Medullary thyroid cancer. Medullary thyroid cancer (MTC), accounts for approximately 2% of all thyroid cancers. Approximately 25% of all MTC runs in families and is associated with other endocrine tumors (see *Medullary Thyroid Cancer brochure*). In family members of an affected person, a test for a genetic mutation in the RET proto-oncogene can lead to an early diagnosis of medullary thyroid cancer and, as a result, to curative surgery.

Anaplastic thyroid cancer. Anaplastic thyroid cancer is the most advanced and aggressive thyroid cancer and the least likely to respond to treatment. Anaplastic thyroid cancer is very rare and is found in less than 2% of patients with thyroid cancer. (See *Anaplastic thyroid cancer brochure.*)

WHAT ARE THE SYMPTOMS OF THYROID CANCER?

Thyroid cancer often presents as a lump or nodule in the thyroid and usually does not cause any symptoms (see *Thyroid Nodule brochure*). Blood tests generally do not help to find thyroid cancer and thyroid blood tests such as TSH are usually normal, even when a cancer is present. Neck examination by your doctor is a common way in which thyroid nodules and thyroid cancer are found. Often, thyroid nodules are discovered incidentally on imaging tests like CT scans and neck ultrasound done for completely unrelated reasons. Occasionally, patients themselves find thyroid nodules by noticing a lump in their neck while looking in a mirror, buttoning their collar, or fastening a necklace. Rarely, thyroid cancers and nodules may cause symptoms. In these cases, patients may complain of pain in the neck, jaw, or ear. If a nodule is large enough to compress the windpipe or esophagus, it may cause difficulty with breathing, swallowing, or cause a "tickle in the throat". Even less commonly, hoarseness can be caused if a thyroid cancer invades the nerve that controls the vocal cords.

Thyroid Cancer
(Papillary and Follicular)

The important points to remember are that cancers arising in thyroid nodules generally do not cause symptoms, thyroid function tests are typically normal even when cancer is present, and the best way to find a thyroid nodule is to make sure that your doctor examines your neck as part of your periodic check-up.

WHAT CAUSES THYROID CANCER?

Thyroid cancer is more common in people who have a history of exposure to high doses of radiation, have a family history of thyroid cancer, and are older than 40 years of age. However, for most patients, we do not know the specific reason or reasons why thyroid cancer develops.

High dose radiation exposure, especially during childhood, increases the risk of developing thyroid cancer. Prior to the 1960s, X-ray treatments were often used for conditions such as acne, inflamed tonsils and adenoids, enlarged lymph nodes, or to treat enlargement of a gland in the chest called the thymus. All these treatments were later found to be associated with an increased risk of developing thyroid cancer later in life. Even X-ray therapy used to treat cancers such as Hodgkin's disease (cancer of the lymph nodes) or breast cancer has been associated with an increased risk for developing thyroid cancer if the treatment included exposure to the head, neck or chest. Routine X-ray exposure such as dental X-rays, chest X-rays and mammograms have not been shown to cause thyroid cancer.

Exposure to radioactivity released during nuclear disasters (1986 accident at the Chernobyl power plant in Russia or the 2011 nuclear disaster in Fukushima, Japan) has also been associated with an increased risk of developing thyroid cancer, particularly in exposed children, and thyroid cancers can be seen in exposed individuals as many as 40 years after exposure.

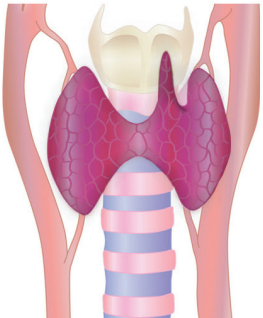
You can be protected from developing thyroid cancer in the event of a nuclear disaster by taking potassium iodide (see *Nuclear Radiation and the Thyroid brochure*). This prevents the absorption of radioactive iodine and has been shown to reduce the risk of thyroid cancer. The American Thyroid Association recommends that anyone living within 200 miles of a nuclear accident be given potassium iodide to take prophylactically in the event of a nuclear accident. If you live near a nuclear reactor and want more information about the role of potassium iodide, check the recommendations from your state at the following link: *www.thyroid.org/web-links-for-important-documents-about-potassium-iodide/*.

HOW IS THYROID CANCER DIAGNOSED?

A diagnosis of thyroid cancer can be suggested by the results of a fine needle aspiration biopsy of a thyroid nodule and can be definitively determined after a nodule is surgically excised (see *Thyroid Nodule brochure*). Although thyroid nodules are very common, less than 1 in 10 will be a thyroid cancer.

WHAT IS THE TREATMENT FOR THYROID CANCER?

Surgery. The primary therapy for all types of thyroid cancer is surgery (see *Thyroid Surgery brochure*). The extent of surgery for differentiated thyroid cancers (removing only the lobe involved with the cancer- called a lobectomy- or the entire thyroid – called a total thyroidectomy) will depend on the size of the tumor and on whether or not the tumor is confined to the thyroid. Sometimes findings either before surgery or at the time of surgery – such as spread of the tumor into surrounding areas or the presence of obviously involved lymph nodes – will indicate that a total thyroidectomy is a better option. Some patients will have thyroid cancer present in the lymph nodes of the neck (lymph node metastases). These lymph nodes can be removed at the time of the initial thyroid surgery or sometimes, as a later procedure if lymph node metastases become evident later on. For very small cancers (<1 cm) that are confined to the thyroid, involving only one lobe and without evidence of lymph node involvement a simple lobectomy (removal of only the involved lobe) is considered sufficient. Recent studies even suggest that small tumors – called micro papillary thyroid cancers – may be observed without surgery depending on their location in the thyroid. After surgery, most patients need to



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*

Thyroid Cancer
(Papillary and Follicular)

be on thyroid hormone for the rest of their life (see *Thyroid Hormone Treatment brochure*). Often, thyroid cancer is cured by surgery alone, especially if the cancer is small. If the cancer is larger, if it has spread to lymph nodes or if your doctor feels that you are at high risk for recurrent cancer, radioactive iodine may be used after the thyroid gland is removed.

Radioactive iodine therapy. (Also referred to as I-131 therapy). Thyroid cells and most differentiated thyroid cancers absorb and concentrate iodine. That is why radioactive iodine can be used to eliminate all remaining normal thyroid tissue and potentially destroy residual cancerous thyroid tissue after thyroidectomy (see *Radioactive Iodine brochure*). The procedure to eliminate residual thyroid tissue is called radioactive iodine ablation. This produces high concentrations of radioactive iodine in thyroid tissues, eventually causing the cells to die. Since most other tissues in the body do not efficiently absorb or concentrate iodine, radioactive iodine used during the ablation procedure usually has little or no effect on tissues outside of the thyroid. However, in some patients who receive larger doses of radioactive iodine for treatment of thyroid cancer metastases, radioactive iodine can affect the glands that produce saliva and result in dry mouth complications. If higher doses of radioactive iodine are necessary, there may also be a small risk of developing other cancers later in life. This risk is very small, and increases as the dose of radioactive iodine increases. The potential risks of treatment can be minimized by using the smallest dose possible. Balancing potential risks against the benefits of radioactive iodine therapy is an important discussion that you should have with your doctor if radioactive iodine therapy is recommended.

If your doctor recommends radioactive iodine therapy, your TSH will need to be elevated prior to the treatment. This can be done in one of two ways.

The first is by stopping thyroid hormone pills (levothyroxine) for 3-6 weeks. This causes high levels of TSH to be produced by your body naturally. This results in hypothyroidism, which may involve symptoms such as fatigue, cold intolerance and others, that can be significant. To minimize the symptoms of hypothyroidism your doctor may prescribe T3 (Cytomel®, liothyronine) which is a short acting form of thyroid hormone that is usually taken after the levothyroxine is stopped until the final 2 weeks before the radioactive iodine treatment.

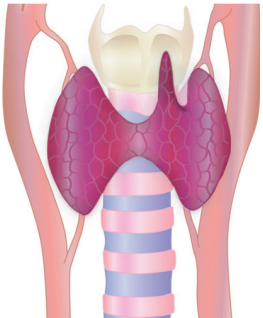
Alternatively, TSH can be increased sufficiently without stopping thyroid hormone medication by injecting TSH into your body. Recombinant human TSH (rhTSH, Thyrogen®) can be given as two injections in the days prior to radioactive iodine treatment. The benefit of this approach is that you can stay on thyroid hormone and avoid possible symptoms related to hypothyroidism.

Regardless of whether you go hypothyroid (stop thyroid hormone) or use recombinant TSH therapy, you may also be asked to go on a low iodine diet for 1 to 2 weeks prior to treatment (see *Low Iodine Diet FAQ*), which will result in improved absorption of radioactive iodine, maximizing the treatment effect.

TREATMENT OF ADVANCED THYROID CANCER.

Thyroid cancer that spreads (metastasizes) outside the neck area is rare, but can be a serious problem. Surgery and radioactive iodine remain the best way to treat such cancers as long as these treatments continue to work. However, for more advanced cancers, or when radioactive iodine therapy is no longer effective, other forms of treatment are needed. External beam radiation directs precisely focused X-rays to areas that need to be treated—often tumor that has recurred locally or spread to bones or other organs. This can kill or slow the growth of those tumors. Cancer that has spread more widely requires additional treatment.

New chemotherapy agents that have shown promise treating other advanced cancers are becoming more widely available for treatment of thyroid cancer. These drugs rarely cure advanced cancers that have spread widely throughout the body but they can slow down or partially reverse the growth of the cancer. These treatments are usually given by an oncologist (cancer specialist) and often require care at a regional or university medical center.



FURTHER INFORMATION

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Thyroid Cancer
(Papillary and Follicular)

WHAT IS THE FOLLOW-UP FOR PATIENTS WITH THYROID CANCER?

Periodic follow-up examinations are essential for all patients with thyroid cancer because the thyroid cancer can return—sometimes several years after successful initial treatment. These follow-up visits include a careful history and physical examination, with particular attention to the neck area. Neck ultrasound is an important tool to view the neck and look for nodules, lumps or cancerous lymph nodes that might indicate the cancer has returned. Blood tests are also important for thyroid cancer patients. Most patients who have had a thyroidectomy for cancer require thyroid hormone replacement with levothyroxine once the thyroid is removed (see *Thyroid Hormone Treatment brochure*). The dose of levothyroxine prescribed by your doctor will in part be determined by the initial extent of your thyroid cancer. More advanced cancers usually require higher doses of levothyroxine to suppress TSH (lower the TSH below the low end of the normal range). In cases of minimal or very low risk cancers, it's typically safe to keep TSH in the normal range. The TSH level is a good indicator of whether the levothyroxine dose is correctly adjusted and should be followed periodically by your doctor.

Another important blood test is measurement of thyroglobulin (Tg). Thyroglobulin is a protein produced by normal thyroid tissue and thyroid cancer cells, and is usually checked at least once a year. Following thyroidectomy and radioactive iodine ablation, thyroglobulin levels usually become very low or undetectable when all tumor cells are gone. Therefore, a rising thyroglobulin level should raise concern for possible cancer recurrence. Some patients will have thyroglobulin antibodies (TgAb) which can make it difficult to rely on the Tg result, as this may be inaccurate.

In addition to routine blood tests, your doctor may want to repeat a whole-body iodine scan to determine if any thyroid cells remain. Increasingly, these scans are only done for high risk patients and have been largely replaced by routine neck ultrasound and thyroglobulin measurements that are more accurate to detect cancer recurrence, especially when done together.

WHAT IS THE PROGNOSIS OF THYROID CANCER?

Overall, the prognosis of differentiated thyroid cancer is excellent, especially for patients younger than 45 years of age and those with small cancers. Patients with papillary thyroid cancer who have a primary tumor that is limited to the thyroid gland have an excellent outlook. Ten year survival for such patients is 100% and death from thyroid cancer anytime thereafter is extremely rare. For patients older than 45 years of age, or those with larger or more aggressive tumors, the prognosis remains very good, but the risk of cancer recurrence is higher. The prognosis may not be quite as good in patients whose cancer is more advanced and cannot be completely removed with surgery or destroyed with radioactive iodine treatment. Nonetheless, these patients often are able to live a long time and feel well, despite the fact that they continue to live with cancer. It is important to talk to your doctor about your individual profile of cancer and expected prognosis. It will be necessary to have lifelong monitoring, even after successful treatment.

FURTHER INFORMATION

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