AMERICAN THYROID ASSOCIATION
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Clinical Thyroidology® for the Public

VOLUME 12 | ISSUE 5 | MAY 2019

IODINE DEFICIENCY

Iodine content is low or absent in some US multivitamin and prenatal vitamin brands

Iodine is essential for the production of thyroid hormone and for normal development of the baby during pregnancy. It has been reported that only 60% of the different types of prenatal multivitamin supplements marketed in the US list iodine among the ingredients. This study aimed to assess whether multivitamins are a significant source of iodine by looking at the iodine content reported in the most frequently purchased US adult and prenatal multivitamin preparations.

Patel A et al 2018 Iodine content of the best-selling United States adult and prenatal multivitamin preparations. Thyroid. Epub 2018 Oct 30. PMID: 30266075.

THYROID AND PREGNANCY

Pregnancy and perinatal outcome among hypothyroid mothers

Hypothyroidism is common in women of reproductive age and has known adverse effects on pregnancy. This study took advantage of national registries in Finland where nearly all women receive free maternity care and deliver at national hospitals and data is collected. The goal of the study was to look at pregnancy complications in a large group of patients and evaluate whether consistent use of thyroid hormone in hypothyroid mothers affected the outcomes.

Turunen S et al Pregnancy and perinatal outcome among hypothyroid mothers: a population-based cohort study. Thyroid 2019 29:135–141

HYPERTHYROIDISM

Treatment of hyperthyroidism resulting in hypothyroidism decreases the risk of heart disease related hospitalization and death risk

Thyroid hormone has major effects on the heart and hyperthyroidism can cause major problems and symptoms such as irregular heart rhythms and palpitations. Despite treatment, the negative effects related to hyperthyroidism may persist. This study examined the effect of radioactive iodine therapy and surgery on heart disease related problems, hospitalizations and mortality.

Essi et al 2018 Cardiovascular morbidity and mortality after treatment of hyperthyroidism with either radioactive iodine or thyroidectomy. Thyroid 28:1111–1120. Epub 2018 Jul 23.

HYPOTHYROIDISM

Levothyroxine treatment increases mortality in patients with heart failure

It is well known that overt hypothyroidism has negative effects on the heart function that improve with levothyroxine treatment. While levothyroxine replacement may improve heart failure, it is possible that in this group it could have harmful effects, especially if the levothyroxine dose is too high. This study evaluated the long-term effects of levothyroxine therapy in patients with heart failure.

Einfeldt MN 2018 Long-term outcome in heart failure patients treated with levothyroxine: an observational nationwide cohort study. J Clin Endocrinol Metab. Epub 2018 Dec 4. PMID: 30517746.

THYROID CANCER

Active surveillance for low risk papillary thyroid cancer can be considered in select patients

Active surveillance involves closely monitoring the thyroid cancer over time, instead of treating it with immediate surgery. Prior studies have shown that active surveillance is safe in papillary thyroid cancers measuring 1 cm or smaller and confined to the thyroid without any lymph node involvement or spread outside of the neck. This study compared outcomes of active surveillance for patients with cancers <1 cm to those with larger cancers (1-2 cm).

Sakai T et al 2019 Active surveillance for T1bN0M0 papillary thyroid carcinoma. Thyroid 29:59–63. Epub 2019 Jan 8. PMID: 30560718.

THYROID CANCER

The TIRADS ultrasound system can decrease unnecessary biopsies of PET-positive thyroid nodules

Occasionally, PET scanning will identify unexpected/previously undetected thyroid nodules. Since ~1/3 of PET-positive thyroid nodules will end up being thyroid cancer, most experts recommend biopsy of these nodules. The purpose of this study is to determine if the TIRADS ultrasound system can predict the absence of thyroid cancer in previously undetected thyroid nodules identified during PET scanning and, thus, avoid thyroid biopsy.

Trimboli P et al 2018 Fine-needle aspiration in all thyroid incidentalomas at 18F-FDG PET/CT: can EU-TIRADS revise the dogma? Clin Endocrinol (Oxf) 89:642–648. Epub 2018 Aug 6. PMID: 30019402.

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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.

May is International Thyroid Awareness Month. Celebrate World Thyroid Day is on May 25!

In this issue, the studies ask the following questions:

- Is iodine content in prenatal vitamins adequate?
- Does adequate levothyroxine therapy in hypothyroid mothers improve pregnancy outcomes?
- Does treatment of hyperthyroidism affect the risk for cardiac problems?
- Does levothyroxine therapy affect the death rate in patients with heart failure?
- Can low risk thyroid cancers be safely watched without surgery?
- Can a new radiology grading system decrease the need for biopsy of thyroid nodules discovered on PET scans?

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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IODINE DEFICIENCY

Iodine content is low or absent in some US multivitamin and prenatal vitamin brands

BACKGROUND

Iodine is essential for the production of thyroid hormone and for normal development of the baby during pregnancy. During pregnancy and breastfeeding there is an increased requirement for iodine both because of a need for higher thyroid hormone production and for secretion of iodine into breast milk. Many studies have shown that iodine deficiency has been associated with adverse effects in babies and infants that range from severe mental retardation to mild brain deficits. Therefore, organizations such as the American Thyroid Association and the American Academy of Pediatrics have recommended that women who are planning a pregnancy, are pregnant or are breastfeeding should ingest a daily supplement that contains 150 mcgs of iodine.

In the US, it has been challenging to identify the sources of dietary iodine, because most food packaging does not detail their contents for this element. Dairy products and seafood are two important sources, but the consumption of these two types of foods is highly variable across the US population. Although in many regions of the world, universal salt iodization has been successful in preventing iodine deficiency, iodization of salt has never been mandated in the US. Currently, only 53% of salt sold for use in homes contains iodine and salt used in processed foods typically is not iodized.

Due to the variable intake of iodine content in food sources and different types of diets followed by the US population, there is concern that some groups of people are at risk for iodine deficiency. Specifically, mild iodine deficiency has been recently documented to be present among pregnant US women. The importance of multivitamin supplements as a source of iodine for pregnant and non-pregnant US adults is not well understood. A study reviewing the use of multivitamin supplements in the US and Canada reported that supplement use ranged from 7% to 85%, showing how difficult it is to accurately determine the extent of multivitamin use. In addition, it has been reported that only 60% of the different types of prenatal multivitamin supplements marketed in the US list iodine among the ingredients. It also has been shown that iodine content is the most variable and least accurately labeled nutrient contained in US adult multivitamins.

This study aimed to assess whether multivitamins are a significant source of iodine in nonpregnant and pregnant adults by looking at the iodine content reported in the most frequently purchased US adult and prenatal multivitamin preparations, knowing how many purchases for these supplements were made over the course of one year.

THE FULL ARTICLE TITLE

Patel A et al 2018 Iodine content of the best-selling United States adult and prenatal multivitamin preparations. Thyroid. Epub 2018 Oct 30. PMID: 30266075.

SUMMARY OF THE STUDY

Data for this study was obtained from Information Resources, Inc. (Chicago, IL), a market research firm. It provided information about the 99 US adult and 60 prenatal multivitamins with the largest market share from July 2016 to July 2017. Supplements sold at food, drug, value chains, mass merchandise and military stores were included. However, not included were sales made over the Internet, direct selling and specialty stores. The iodine content and its source was determined using the product labels. Ten products from the adult multivitamin group and one from the prenatal group were excluded because their label was either unavailable or the iodine content could not be determined.

Nearly 74% of the adult multivitamin brands contained iodine, and approximately 75% of these contained 150 mcg per daily dose. The source of the iodine was potassium iodide in all these products. Although some products contained as little as 38 mcgs, none exceeded 150 mcgs per daily dose. Of the prenatal multivitamins, almost 58% of products contained iodine, and 91% contained 150 mcgs per daily dose. The iodine source

IODINE DEFICIENCY, continued

was potassium iodide in about 75% of the brands, and the sources for the rest was kelp and one brand used inactivated yeast. These last two sources have previously been shown to be variable in their iodine content. Overall, the price of prenatal vitamins is higher than the general adult multivitamin.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Although the majority of the best-selling US brands of adult multivitamins contain iodine, a relatively high proportion (25%) do not. Among the prenatal multivitamins, 40% do not contain iodine. Even though most products contain the recommended amount, there is a wide range in iodine content going from as little as 25 mcgs to 93% higher than the recommended daily dose.

The limitations of this study include the fact that it relied on the manufacturers' listed iodine content, which may not match the actual content. Also, although using consumer data it was possible to determine how many doses were purchased, it was unclear how many doses were actually consumed, and data from products purchased for example, on the internet was not included.

In summary, multivitamin products appear to be a significant source of iodine nutrition for many US adults. However, in spite of recommendations regarding iodine content in prenatal vitamins, about 40% of the evaluated products do not contain iodine. Therefore, it is extremely important that women, especially when pregnant, breast-feeding or planning a pregnancy, read the labels of their multivitamin supplements to ensure that they are receiving an adequate amount of iodine.

ATA THYROID BROCHURE LINKS

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

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.

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THYROID AND PREGNANCY

Pregnancy and perinatal outcome among hypothyroid mothers

BACKGROUND

Hypothyroidism is common in women of reproductive age. About 1% of women will have known hypothyroidism before getting pregnant and another 0.5% of women will be diagnosed with hypothyroidism during pregnancy. Overt hypothyroidism (low T_4 and high TSH) has known adverse effects on pregnancy outcome including a higher risk of miscarriage and lower IQ in offspring. The effect of less severe hypothyroidism (high TSH but normal T_4, subclinical hypothyroidism) varies with some studies, but not all, showing increased rates of caesarean section, labor induction and ICU admission of the babies. This study took advantage of national registries in Finland where nearly all women receive free maternity care and deliver at national hospitals and data is collected. The goal of the study was to look at pregnancy complications in a large group of patients and evaluate whether consistent use of thyroid hormone in hypothyroid mothers effected the outcomes.

THE FULL ARTICLE TITLE

Turunen S et al Pregnancy and perinatal outcome among hypothyroid mothers: a population-based cohort study. Thyroid 2019 29:135–141

SUMMARY OF THE STUDY

The investigators studied all pregnancies with a single baby in Finland from 2004-2013. There were 16,364 mothers with a diagnosis of hypothyroidism and 550,860 mothers who were not hypothyroid. They used the extensive Finnish Medical Birth Registry that collects data on mothers and newborns within 7 days of delivery, the Finnish Malformation Registry to identify congenital malformations and the Prescription Register to track thyroid hormone use. Women were considered to be hypothyroid if they had a diagnosis of hypothyroidism or if they purchased thyroid medication within 3 mo prior to pregnancy or during pregnancy.

For the whole group, about 3% of the mothers had hypothyroidism complicating pregnancy. Among these women, 95.8% purchased levothyroxine at some time during the pregnancy, but only 37.5% purchased medication consistently throughout pregnancy. There was higher risk of adverse outcomes in all the hypothyroid mothers, including high blood pressure during pregnancy, severe pre-eclampsia (high blood pressure and kidney disease), gestational diabetes and caesarian section. The mothers who filled levothyroxine prescriptions regularly throughout pregnancy did not have an increased risk for high blood pressure or severe pre-eclampsia. There were more babies born early in the mothers with hypothyroidism, but not in those hypothyroid mothers who filled their levothyroxine prescription consistently. There was a slight increase in congenital malformations in babies born of hypothyroid mothers.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study confirms many previous studies documenting the adverse effect of hypothyroidism on pregnancy and perinatal outcomes, most of which, but not all are reversed by regular thyroid hormone administration. This study supports the importance of taking thyroid medication during pregnancy when indicated.

— Marjorie Safran, MD

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/
Pregnancy and Thyroid Disease: https://www.thyroid.org/thyroid-disease-pregnancy/
Thyroid Hormone Treatment: https://www.thyroid.org/thyroid-hormone-treatment/

THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

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

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

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

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

Congenital: Condition that exists at birth.

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal.

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HYPERTHYROIDISM

Treatment of hyperthyroidism resulting in hypothyroidism decreases the risk of heart disease related hospitalization and death risk

BACKGROUND

Hyperthyroidism is a state when the thyroid is overactive and there is too much thyroid hormone in the body. The main cause of hyperthyroidism in the United States is Graves' disease. This is an autoimmune disease where the body makes an antibody that attacks and turns on the thyroid. There are 3 major options for treatment of hyperthyroidism: 1) antithyroid drugs, such as methimazole or PTU, that decrease the thyroid hormone production; 2) surgery to remove the overactive thyroid and 3) radioactive iodine that is taken up by the thyroid and destroys the gland. The most common result of surgery and radioactive iodine therapy is hypothyroidism. Hypothyroidism can also develop if the dose of antithyroid drug is too high.

Thyroid hormone has major effects on the heart. Hyperthyroidism can cause major problems and symptoms such as irregular heart rhythms and palpitations. Rarely, these problems can lead to death. Despite treatment, the negative effects related to hyperthyroidism may persist. This study examined the effect of radioactive iodine therapy and surgery on heart disease related problems, hospitalizations and mortality.

THE FULL ARTICLE TITLE

Essi et al 2018 Cardiovascular morbidity and mortality after treatment of hyperthyroidism with either radioactive iodine or thyroidectomy. Thyroid 28:1111–1120. Epub 2018 Jul 23.

SUMMARY OF THE STUDY

Two groups of patients who had been treated for hyperthyroidism in Finland from 1986 to 2007 were identified from a registry. Patients were treated either with surgery or with radioactive iodine therapy. A control group of Finnish residents was formed by randomly selecting 3 age and sex-matched subjects for each patient from a national population registry. A nationwide database system was used to identify causes of all heart related hospitalizations and death.

A total of 4334 patients were in the surgery group (615 men and 3719 women) and 1814 in the radioactive iodine therapy group (329 men and 1489 women). About half of the patients had Graves' disease, one third toxic nodular goiter and the cause was unspecified in the rest. Patients in the surgery group were younger than those who received radioactive iodine therapy. Hospitalization rates before treatment were higher in the hyperthyroidism patients as compared to control group. The most common reasons for hospitalization were high blood pressure and abnormal heart rhythms. The risk of hospitalization decreased after treatment of hyperthyroidism. When the radioactive iodine treatment resulted in hypothyroidism (requiring thyroid hormone treatment), hospitalization rates were similar in the surgery and radioactive iodine therapy groups. However, if radioactive iodine therapy did not result in hypothyroidism there was a greater risk of hospitalization, most often due to abnormal rhythms. Death due to heart disease was similar between hyperthyroid patients and the control group. Death risk was similar in patients treated with surgery and in patients who became hypothyroid after radioactive iodine therapy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this study, patients with hyperthyroidism had increased risk of hospitalization for heart disease. The risk was decreased after surgery or radioactive iodine therapy when it resulted in hypothyroidism but remained higher in patients who did not develop hypothyroidism after treatment. Heart disease related death was also higher in patients treated with radioactive iodine therapy who did not develop hypothyroidism while it was similar between control group and patients treated with surgery or radioactive iodine therapy that resulted in hypothyroidism. The results suggest that the goal of treatment for hyperthyroidism should be to achieve hypothyroidism.

— Ebru Sulanc, MD, FACE

HYPERTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/
Radioactive Iodine: https://www.thyroid.org/radioactive-iodine/
Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/
Thyroid Hormone Treatment: https://www.thyroid.org/thyroid-hormone-treatment/

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.

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

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

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

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HYPOTHYROIDISM

Levothyroxine treatment increases mortality in patients with heart failure

BACKGROUND

Hypothyroidism is a common condition that can affect the entire body and is treated with levothyroxine. It is clear that patients with overt hypothyroidism (high TSH and a low T_4) should be treated with levothyroxine. It is less clear if patients with mild hypothyroidism (high TSH, normal T_4) benefit from treatment. Finally, patients with thyroid abnormalities due to medical illnesses and not due to problems with the thyroid itself should not be treated.

In terms of heart function, it is well known that overt hypothyroidism has negative effects on the heart function that improve with levothyroxine treatment. However, studies of treating patients with subclinical (mild) hypothyroidism with heart problems have shown controversial results, with some studies suggesting that treating does not provide any benefit to the patient. This is especially true in patients with heart failure. While levothyroxine replacement may improve heart failure, it is possible that in this group it could have harmful effects, especially if the levothyroxine dose is too high. This Danish nationwide study evaluated the long-term effects of levothyroxine therapy in patients with heart failure.

THE FULL ARTICLE TITLE

Einfeldt MN 2018 Long-term outcome in heart failure patients treated with levothyroxine: an observational nationwide cohort study. J Clin Endocrinol Metab. Epub 2018 Dec 4. PMID: 30517746.

SUMMARY OF THE STUDY

This study used the Danish national registers to identify and collect clinical information for all Danish citizens >18 years of age who were diagnosed with heart failure during a hospital admission between 1997 and 2012. The patients who received levothyroxine treatment were identified from a nationwide database of all claimed prescriptions. The patients were divided in three groups: (1) patients already receiving levothyroxine at the time of the heart failure diagnosis, (2) patients who started levothyroxine treatment after being diagnosed with heart failure and (3) patients with heart failure not treated with levothyroxine. The study compared the overall death rate, the heart-specific death rate, the number of heart attacks and the combination of major adverse cardiovascular events (including death, heart attack, and stroke) between these patient groups.

A total of 224,670 patients with an average age of 71 years were diagnosed with heart failure; 209,103 of these patients did not receive levothyroxine, 6560 were already being treated with levothyroxine, and 9007 started levothyroxine treatment after the diagnosis of heart failure. Levothyroxine treatment started either before or after the diagnosis of heart failure was associated with an increased risk of death, both overall and due to heart problems, and major adverse cardiac events. The risk of having a heart attack was higher in patients who were already taking levothyroxine at the time of heart failure and lower in patients who started levothyroxine treatment after this diagnosis.

Information regarding the severity of the patients' heart disease before starting thyroid treatment, the severity of the hypothyroidism and whether the levothyroxine dose was adequate based on thyroid function test results measured on treatment was not available and was not included in the analysis.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that levothyroxine treatment in patients with heart failure results in an increase risk of death and adverse events. However, the results are severely limited by the lack of information of the presence of hypothyroidism as the reason for levothyroxine and by the lack of thyroid test results that would determine if the levothyroxine dose was appropriate. Certainly, until more definitive data is available, physicians need to use caution when prescribing levothyroxine for patients with heart failure. The reasons for treating must be clear and the patients need to be monitored closely to make sure that they take an adequate thyroid hormone dose.

— Alina Gavrila, MD, MMSC

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

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

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

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

Levothyroxine (T4): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tyrosint™ and generic preparations.

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.

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.

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THYROID CANCER

Active surveillance for low risk papillary thyroid cancer can be considered in select patients

BACKGROUND

The number of new thyroid cancer cases has increased over recent years, especially the number of small, low-risk papillary thyroid cancers. It is clear now that treating these small cancers aggressively with surgery results in more potential harm to patients than if the small cancer was simply watched. Because of this, simply watching, known as active surveillance, became a promising alternative to surgery for these low-risk cancers in select patients. Active surveillance involves closely monitoring the thyroid cancer over time, instead of treating it with immediate surgery. Prior studies have shown that active surveillance is safe in papillary thyroid cancers measuring 1 cm or smaller and confined to the thyroid without any lymph node involvement or spread outside of the neck. However, little is known about outcomes of active surveillance for patients with larger cancers measuring 1-2 cm and confined to the thyroid. This study compared outcomes of active surveillance for these patients to this with cancers <1 cm. The authors also examined outcomes of patients who had surgery for these small cancers.

THE FULL ARTICLE TITLE

Sakai T et al 2019 Active surveillance for T1bN0M0 papillary thyroid carcinoma. Thyroid 29:59–63. Epub 2019 Jan 8. PMID: 30560718.

SUMMARY OF THE STUDY

The study included patients who were followed at the Cancer Institute Hospital in Tokyo, Japan, since 1995. Among 406 patients with papillary thyroid cancer < 1 cm, 360 (89%) underwent active surveillance and 46 (11%) underwent surgery. Among 392 patients with papillary thyroid cancer 1-2 cm, 331 (84%) underwent active surveillance and 61 (16%) underwent surgery. The patients in the active surveillance program were followed with physical exam, neck ultrasound and chest X-rays every 6 to 12 months after diagnosis. These patients were evaluated for increase in cancer size, development of spread to the lymph nodes and spread to other parts of the body. The follow-up was 7.3 - 7.9 years. If progression of the cancer was seen or the patient changed their mind, surgery was performed.

The authors found that the 5- and 10-year rates of progression were similar in patients with papillary thyroid cancer < 1cm compared with those with 1-2 cm cancers during active surveillance. A total of 11 patients with 1-2 cm cancers had surgery after active surveillance and none had the cancer come back. Of the patients with 1-2 cm cancers who had immediate surgery, 8 had the cancer come back. The rate of cancer coming back was significantly higher for cancers ≥1.5 cm than <1.5 cm in this group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that patients with 1-2 cm papillary thyroid cancers had similar progression rates to patients with <1 cm cancers during active surveillance. Additionally, delayed surgery was not associated with any harm in these patients. These findings are important as they show that active surveillance of small thyroid cancers, especially those <15 mm in size, is safe. Expanding active surveillance to larger cancers would decrease the number of thyroid surgeries and subsequent complications. However, more research is still needed to determine exactly which thyroid cancer patients are ideal for active surveillance, considering age, other health issues and the expertise of treatment team.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

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

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

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).

Active surveillance: Involves closely monitoring the thyroid cancer over time, instead of treating it with immediate surgery.

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.

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

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THYROID CANCER

The TIRADS ultrasound system can decrease unnecessary biopsies of PET-positive thyroid nodules

BACKGROUND

PET scanning is a type of imaging commonly used to locate areas of cancer in the human body. This is done in patients with a diagnosed cancer to see if it has spread to other parts if the body. This works because cancer cells are more active than normal cells and will take up more of the tracer (18F-FDG) and will light up positive on the PET scan. However, not all areas that are PET-positive are cancer. Some thyroid nodules are PET-positive and occasionally, PET scanning will identify unexpected/previously undetected thyroid nodules. Up to 1/3 of PET-positive thyroid nodules will end up being thyroid cancer. For this reason, most experts recommend biopsy of these nodules, especially when they are >1 cm in diameter, in order to determine whether or not a thyroid cancer is present. Unfortunately, thyroid biopsy results do not always rule out cancer and, in such cases, thyroid surgery is often needed. This means that some surgically removed thyroid nodules will ultimately be found to be benign (noncancerous).

An important area of research is the development of new technologies that might allow doctors to avoid thyroid surgery (and even thyroid biopsy) for patients having PET-positive thyroid nodules, but for whom these nodules are benign. One such technology is thyroid ultrasound, which can identify thyroid nodule features that may predict the presence of thyroid cancer. Several different systems have been developed for predicting, on the basis of ultrasound findings, whether or not a thyroid cancer is present in a thyroid nodule. One of these systems is called TIRADS. The TIRADS system places thyroid nodules into one of four different categories (2 thorough 5), depending on how many ultrasound features suspicious for thyroid cancer are identified. The greater number of suspicious ultrasound features identified, the higher the probability of thyroid cancer and the higher the TIRADS category (with TIRADS category 5 having the highest risk of cancer and category 2 having the lowest risk). It is important to note that, although thyroid cancer risk does increase as the TIRADS category number increases, the TIRADS system is by no means perfect. A TIRADS 5 category, for example, does not mean a 100% probability of thyroid cancer.

The purpose of this study is to determine if the TIRADS ultrasound system can predict the absence of thyroid cancer in previously undetected thyroid nodules identified during PET scanning and, thus, avoid thyroid biopsy.

THE FULL ARTICLE TITLE

Trimboli P et al 2018 Fine-needle aspiration in all thyroid incidentalomas at 18F-FDG PET/CT: can EU-TIRADS revise the dogma? Clin Endocrinol (Oxf) 89:642–648. Epub 2018 Aug 6. PMID: 30019402.

SUMMARY OF THE STUDY

The authors looked at every PET scan done at their institution over a four-year period (between 2014 and 2017). They ultimately identified 66 cases for which PET scanning identified an unexpected thyroid nodule and for which thyroid surgery was performed. For this group, 13 thyroid nodules were found to be cancerous, while the remaining 53 nodules were benign. In evaluating the TIRADS category for each of the 13 cancerous nodules, the authors found that none of these cancers were classified in the TIRADS 2 category, while the number of cancers increased with each increase in TIRADS category number (11 of the 13 cancers were classified as TIRADS 5).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that the TIRADS system for estimating thyroid cancer risk among thyroid nodules identified unexpectedly by PET scanning may be useful for further determining the risk of thyroid cancer in these cases. Since no thyroid cancers were present for any TIRADS category <3, this study suggests that biopsy, and potentially surgery, is not be needed for PET-positive nodules classified into these TIRADS categories. It is important to note that this

THYROID CANCER, continued

study is quite small, with relatively few patients included for assessment, so the results need to be validated in a larger study. Nonetheless, the results of this study certainly do justify larger studies examining the role of ultrasound in improving diagnosis of thyroid cancer for nodules identified by PET scanning.

— 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

Positron-Emission-Tomography (PET) scans: a nuclear medicine imaging test that uses a small amount of radio-labeled glucose (18F-FDG) to identify cancer. Since cancer cells are more active than normal cells, the cancer cells take up more of the radiolabeled glucose and show up on the PET scan. PET scans are frequently combined with CT scans to accurately identify where the cancer is located.

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

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

Thyroid biopsy: 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.

AMERICAN THYROID ASSOCIATION
ATA | Founded 1923

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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
info@checkyourneck.com

Thyca: Thyroid Cancer Survivors' Association, Inc.
www.thyca.org
(Toll-free): 877-588-7904
thyca@thyca.org

Thyroid Cancer Alliance
www.thyroidcanceralliance.org
www.thyroidcancerpatientinfo.org
Rotterdam, The Netherlands

Thyroid Cancer Canada
www.thyroidcancercanada.org
416-487-8267
info@thyroidcancercanada.org

Thyroid Federation International
www.thyroid-fed.org
tfi@thyroid-fed.org

AMERICAN THYROID ASSOCIATION
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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.

Become a Friend of the ATA!
Subscribe to *Friends of the ATA e-news*

By subscribing to *Friends of the ATA Newsletter*, you will receive:

- *Friends of the ATA e-news*, providing up-to-date information on thyroid issues, summaries of recently published articles from the medical literature that covers the broad spectrum of thyroid disorders., and invitations to upcoming patient events
- 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

AMERICAN THYROID ASSOCIATION
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Donate Now!

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.

Iodine Deficiency

WHAT IS THE THYROID GLAND?

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

WHAT IS IODINE DEFICIENCY?

Iodine is an element that is needed for the production of thyroid hormone. The body does not make iodine, so it is an essential part of your diet. Iodine is found in various foods *(see Table 1)*. If you do not have enough iodine in your body, you cannot make enough thyroid hormone. Thus, iodine deficiency can lead to enlargement of the thyroid (goiter – see *Goiter brochure*), hypothyroidism (see *Hypothyroidism brochure*) and to intellectual disabilities in infants and children whose mothers were iodine deficient during pregnancy.

Before the 1920s, iodine deficiency was common in the Great Lakes, Appalachian, and Northwestern U.S. regions and in most of Canada. Prevention of iodine deficiency by the introduction of iodized salt has virtually eliminated iodine deficiency and the so-called "goiter belt" in these areas. However, many other parts of the world do not have enough iodine available through their diet and iodine deficiency continues to be an important public health problem globally. Approximately 30% of the world's population remains at risk for iodine deficiency.

HOW DO YOU DIAGNOSE IODINE DEFICIENCY?

Iodine deficiency is diagnosed across populations and not specifically in individuals. Since iodine is released from the body through the urine, the best way to determine iodine deficiency across a large population is to measure the amounts of iodine in urine samples. Iodine deficiency is defined as a median urinary iodine concentration less than 100µg/L in a nonpregnant population, or <150 µg/L in a population of pregnant women.

In the United States, iodine status has remained generally adequate in since the 1940s although studies have shown that urinary iodine levels dropped by about half between the early 1970s and the early 1990s, and most recently mild iodine deficiency has re-emerged in pregnant women.

Iodine deficiency remains a major issue in other parts of the world, including parts of Europe, Africa and Asia.

WHAT ARE THE SOURCES OF IODINE?

Iodine is present naturally in soil and seawater. The availability of iodine in foods differs in various regions of the world. Individuals in the United States can maintain adequate iodine in their diet by using iodized table salt, by eating foods high in iodine, particularly dairy products, seafood, meat, some breads, and eggs, and by taking a multivitamin containing iodine *(see below)*. However, the amount of iodine in foods is not listed on food packaging in the U.S., and it can be difficult to identify sources of iodine in foods.

WHAT ARE THE SYMPTOMS OF IODINE DEFICIENCY?

All of the symptoms of iodine deficiency are related to its effect on the thyroid:

GOITER – Without adequate iodine, the thyroid progressively enlarges (develops a goiter) as it tries to keep up with demand for thyroid hormone production. Worldwide, iodine deficiency is the most common cause of thyroid enlargement and goiter (see *goiter brochure*). Within a goiter, nodules can develop. Patients with a large goiter may experience symptoms of choking, especially when lying down, and difficulty swallowing and breathing.

TABLE 1:
COMMON SOURCES OF DIETARY IODINE

Cheese
Cows milk
Eggs
Frozen Yogurt
Ice Cream
Iodine-containing multivitamins
Iodized table salt
Saltwater fish
Seaweed (including kelp, dulce, nori)
Shellfish
Soy milk
Soy sauce
Yogurt

HYPOTHYROIDISM – As the body's iodine levels fall, hypothyroidism may develop, since iodine is essential for making thyroid hormone. While this is uncommon in the United States, iodine deficiency is the most common cause of hypothyroidism worldwide (see *Hypothyroidism brochure*).

Iodine Deficiency

PREGNANCY-RELATED PROBLEMS – Iodine deficiency is especially important in women who are pregnant or nursing their infants. Severe iodine deficiency in the mother has been associated with miscarriages, stillbirth, preterm delivery, and congenital abnormalities in their babies. Children of mothers with severe iodine deficiency during pregnancy can have intellectual disabilities and problems with growth, hearing, and speech. In the most severe form, an underactive thyroid can result in cretinism (a syndrome characterized by permanent brain damage, deaf mutism, spasticity, and short stature), although this has become rare worldwide. Iodine deficiency is the most common preventable cause of intellectual disabilities in the world. Even mild iodine deficiency during pregnancy, which may be present in some women in the United States, may be associated with low intelligence in children.

HOW IS IODINE DEFICIENCY TREATED?

There are no tests to confirm if you have enough iodine in your body. When iodine deficiency is seen in an entire population, it is best managed by ensuring that common foods that people eat contain sufficient levels of iodine. Since even mild deficiency during pregnancy can have effects on a pregnancy and the developing baby, all U.S. women who are planning pregnancy, pregnant, or breastfeeding should take a multivitamin containing 150 µg iodine per day.

HOW IS IODINE DEFICIENCY PREVENTED?

As with many diseases, it is better to prevent the problem rather than have to treat it. Over the last 80 years, world-wide efforts have been made to eliminate iodine deficiency. Elimination of iodine deficiency has been a major goal of the Iodine Global Network, UNICEF, and the World Health Organization. Iodized salt has been the mainstay of the prevention of iodine deficiency worldwide. In regions where iodized salt is not widely available, or where pregnant women are known to have inadequate iodine intakes, use of a daily iodine-containing supplement may be recommended for pregnant and breastfeeding women. Injections of iodized oil are occasionally used in severely iodine deficient regions of the world where widespread iodized salt use is not possible.

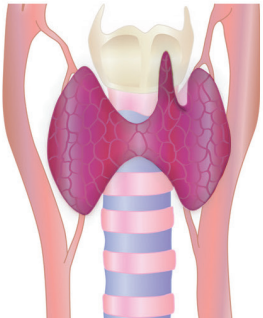
UNITED STATES RECOMMENDATIONS – The Institute of Medicine has set the Recommended Dietary Allowance (RDA) for iodine in adult men and women at 150 µg per day. Individuals who add salt to their food regularly during cooking or at the table should use iodized salt. In the US and Canada, one teaspoon of iodized salt contains approximately 250 µg iodine. Most U.S. iodine-containing multivitamins marketed for non-pregnant adults have at least 150 µg iodine, but only about 60% of the types of prenatal multivitamins in the U.S. contain iodine.

RECOMMENDATIONS FOR IODINE INTAKE DURING PREGNANCY AND BREAST FEEDING – Recommended iodine intakes are higher for women who are pregnant or breastfeeding than for other adults. The RDA is 220 µg iodine per day for pregnant women and 290 µg iodine per day for breastfeeding women. Because the effects of iodine deficiency are most severe in pregnant women and their babies, the American Thyroid Association® has recommended that all U.S. women who are planning pregnancy, pregnant, or breastfeeding take a prenatal multivitamin containing 150 µg iodine per day.

ARE THERE PROBLEMS WITH TAKING TOO MUCH IODINE?

Taking too much iodine can also cause problems. This is especially true in individuals that already have thyroid problems, such as nodules, hyperthyroidism and autoimmune thyroid disease. Administration of large amounts of iodine through medications (i.e.: Amiodarone), radiology procedures (iodinated intravenous dye) and dietary excess (Dulce, kelp) can cause or worsen hyperthyroidism and hypothyroidism.

In addition, individuals who move from an iodine-deficient region (for example, parts of Europe) to a region with adequate iodine intake (for example, the United States) may also develop thyroid problems since their thyroids have become very good at taking up and using small amounts of iodine. In particular, these patients may develop iodine-induced hyperthyroidism (see *Hyperthyroidism brochure*).



FURTHER INFORMATION

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

For information on thyroid patient support organizations, please visit the *Patient Support Links* section on the ATA website at *www.thyroid.org*