american thyroid association

Clinical Thyroidology for the Public

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Does subclinical thyroid dysfunction contribute to the frailty syndrome in men over 65 years of age?

Frailty is a condition seen in older adults and is defined when three or more of the following components are present: loss of muscle mass and strength, weakness, exhaustion, slowness and low activity. Subclinical thyroid dysfunction, which represents mild thyroid abnormalities, also increases with age and can cause similar problems. This study evaluated the potential association between subclinical thyroid dysfunction and frailty.

Virgini VS et al; Osteoporotic Fractures in Men (MrOS) Research Group. Subclinical thyroid dysfunction and frailty among older men. J Clin Endocrinol Metab. October 23, 2015:jc20153191 [Epub ahead of print].

Both hypothyroidism and hyperthyroidism in the mother during early pregnancy may increase the risk of their children having difficulty with mathematics.

Thyroid hormone is essential for normal brain development in the baby during pregnancy. Experimental studies on mild hypothyroidism suggest that either undertreatment or overtreatment can affect brain development in the baby. This study used a Finnish database to assess some possible clinical associations between first-trimester maternal thyroid-function tests and scholastic performance in children at ages 8 and 16 years.

Päkkilä FM et al. Maternal and child's thyroid function and child's intellect and scholastic performance. Thyroid. November 13, 2015 [Epub ahead of print].

Hypothyroidism is associated with a faulty increase in Hemoglobin A1C levels

It has been noted that patients with diabetes who also have hypothyroidism may have higher levels of HBA1C. This study was done to look at the effect of thyroid hormone treatment on HBA1c levels in patients with hypothyroidism and well as the effects on the diagnoses of pre diabetes and the control of diabetes after treatment.

Anantarapu S et al Effects of thyroid hormone replacement on glycated he n non-diabetic subjects with overt hypothyroidism. Arch Endocrinol Metab. September 25 2015 [Epub ahead of print].

Hyperthyroidism and hypothyroidism are uncommon causes of anemia

Abnormal thyroid hormone levels, such as hyperthyroidism and hypothyroidism, can be potential causes of anemia (low blood count). This study was done to see if there is a relationship between abnormal thyroid hormone levels and anemia using a large population of adults in the United Kingdom.

M'Rabet-Bensalah K et al Thyroid dysfunction and anemia in a large population-based study. Clin Endocrinol (Oxf). 2015 Dec 10. doi: 10.1111/cen.12994. [Epub ahead of print]

The ThyroSeq V2.1 multi-gene next-generation sequencing panel is effective at predicting a diagnosis of thyroid cancer in nodules with indeterminate cytology.

Up to 10-20% of thyroid biopsies are indeterminate, meaning that a diagnosis of cancer vs benign cannot be made on the basis of examining the cells alone. This usually leads to surgery despite the fact that most indeterminate nodules are benign. In recent years, the use of molecular marker testing on thyroid biopsy specimens has helped identify benign indeterminate nodules and avoid surgery. The goal of this study was to determine how good the ThyroseqV2.1 molecular marker test is at predicting whether a nodule with indeterminate cytology is benign or cancerous.

Nikiforov YE et al. Impact of the multi-gene ThyroSeq next-generation sequencing assay on cancer diagnosis in thyroid nodules with atypia of undetermined significance/follicular lesion of undetermined significance cytology. Thyroid. Nov;25(11):1217-23.

Detecting recurrence of papillary thyroid cancer costs much more in those with low-risk than high risk cancer.

While the overall survival rate of papillary thyroid cancer is excellent (over 90%), patients must be monitored for recurrence of the cancer for several years after initial treatment. This cancer surveillance has important financial implications both for patients and the overall health system. The aim of the current study was to analyze the financial cost of monitoring for recurrence of papillary thyroid cancer in the first 3 years after surgery for low risk patients versus intermediate- and high- risk patients.

Wang LY1 et al. Cost-effectiveness analysis of papillary thyroid cancer surveillance. Cancer 2015;121(23):4132-40.

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EDITOR'S COMMENTS

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

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

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

February is Hypothyroidism Awareness Month.

In this issue, the studies ask the following questions:

1. Does subclinical hypothyroidism contribute to the frailty syndrome in elderly men?
2. Does maternal thyroid dysfunction increase the risk of their children having difficulty with math?
3. Does hypothyroidism affect Hemaglobin A1C levels?
4. Is anemia associated with thyroid dysfunction?
5. Can the Thyroseq gene mutation analysis help predict thyroid cancer in indeterminate nodules?
6. Is there a difference in the cost of monitoring high-risk vs low-risk thyroid cancer patients?

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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SUBCLINICAL THYROID DYSFUNCTION

Does subclinical thyroid dysfunction contribute to the frailty syndrome in men over 65 years of age?

BACKGROUND

Frailty is a condition seen in older adults and is defined when three or more of the following components are present: loss of muscle mass and strength, weakness, exhaustion, slowness and low activity. Subclinical thyroid dysfunction, which represents mild thyroid abnormalities, also increases with age and can cause similar problems. This study evaluated the potential association between subclinical thyroid dysfunction and frailty.

THE FULL ARTICLE TITLE

Virgini VS et al; Osteoporotic Fractures in Men (MrOS) Research Group. Subclinical thyroid dysfunction and frailty among older men. J Clin Endocrinol Metab. October 23, 2015:jc20153191 [Epub ahead of print].

SUMMARY OF THE STUDY

A total of 1455 men ≥65 years of age from the Osteoporotic Fractures in Men Study (MrOS) were included in the study. TSH and free T_4 levels were measured. A frailty assessment was based on the following five components: loss of muscle mass and strength, weakness, exhaustion, slowness and low activity. Participants with three components were classified as "frail," those with 1 to 2 components as "intermediate," and those with no component as "robust." After 5 years, the participants who were still alive were reassessed.

The mean age of the study population was 73.6 years. A total of 1327 (91.2%) participants had normal thyroid function, 26 (1.8%) had subclinical hyperthyroidism (a mildly overactive thyroid) and 102 (7.0%) had subclinical hypothyroidism (a mildly underactive thyroid). The study found that more patients with normal thyroid function were robust (45.5%), as compared with those with subclinical hyperthyroidism (15.4%) or hypothyroidism (37.3%). Patients aged 64-75 years old with subclinical hyperthyroidism were more likely to be frail when compared with participants who had normal thyroid function. There was no difference between thyroid groups in the five individual frailty components. The follow-up analysis revealed similar results.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that subclinical hyperthyroidism was associated with increased odds of frailty. The association between subclinical hyperthyroidism and frailty at baseline was particularly strong among individuals who were between 65 and 74 years of age. In contrast, subclinical hypothyroidism was not associated with an increased risk of frailty. Even though further confirmatory studies are needed, the results of this study are important for both physicians and patients. There may be a need for closer follow-up of men aged 65-74 in terms of thyroid function and frailty assessment.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

Thyroid Disease in the Older Patient: http://www.thyroid.org/thyroid-disease-older-patient/

ABBREVIATIONS & DEFINITIONS

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.

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

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

Frailty: a term used to determine the degree of function in elderly individuals. A frailty assessment is based on the following five components: loss of muscle mass and strength, weakness, exhaustion, slowness and low activity.

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HYPOTHYROIDISM

Both hypothyroidism and hyperthyroidism in the mother during early pregnancy may increase the risk of their children having difficulty with mathematics.

BACKGROUND

Thyroid hormone is essential for normal brain development in the baby during pregnancy. The baby depends on thyroid hormone from the mother during the first trimester. Hypothyroidism and/or positive TPO antibody in the mother is associated with increased risk of early miscarriage and fetal disorders. Experimental studies on mild hypothyroidism suggest that either undertreatment or overtreatment can affect brain development in the baby.

Between 1985 and 1986, the Northern Finland Birth Cohort (NFBC) study began compiling data on a group of 9362 mothers and 9479 children. The current article used the NFBC to assess some possible clinical associations between first-trimester maternal thyroid-function tests and scholastic performance in children at ages 8 and 16 years.

THE FULL ARTICLE TITLE

Päkkilä FM et al. Maternal and child's thyroid function and child's intellect and scholastic performance. Thyroid. November 13, 2015 [Epub ahead of print].

SUMMARY OF THE STUDY

Between 1985 and 1986, the NFBC study began compiling demographic, maternal health, pregnancy, delivery and neonatal outcome data on a cohort of 9362 mothers and 9479 children. Blood samples were drawn in women who were 6 to 20 weeks pregnant (average 10.7 weeks; dates confirmed by ultrasound in 70%) In 2006, 5805 samples had thyroid-function tests performed. Normal values were found in 4747 mothers; 40 had overt hypothyroidism and another 318 had a normal free T_4 but an elevated TSH (subclinical hypothyroidism); 45 had overt hyperthyroidism and another 79 had a normal free T_4 but a low TSH (subclinical hyperthyroidism), while 67 had a normal TSH but a low free T_4 (hypothyroxinemia). The 5% of mothers whose TPO antibody level was above 167.7 IU/ml were deemed TPOAb-positive. Dietary iodine intake at the time was more than adequate: about 300 µg/day.

Data on the health of the cohort children were acquired from routine child welfare clinic visits, national registers, questionnaires, and clinical examinations. Parents completed a questionnaire on health, development, school, and social situations of the children at 7 to 8 years of age (90% response rate). The children's main teachers completed a questionnaire on impairments in learning reading, writing, or mathematics (92% response rate). At age 16, the adolescents were asked to self-evaluate their school performance in Finnish language and mathematics, using a data-collection tool previously shown to reflect school grades accurately (80% response rate). About 5070 individuals had teacher-estimated performance at 8 years and about 4360 had scholastic self-evaluations at 16 years.

Mothers with hypothyroidism (overt plus subclinical) were more obese, smoked less, and had significantly higher median TPO-antibody levels. Obesity was also significantly higher in mothers with hypothyroxinemia, and maternal obesity is associated with reduced offspring IQ. Mothers who had hyperthyroidism had a significantly smaller percentage of offspring who were male (36%, vs. 51% female).

No differences were found between the 8-year-old offspring of the mothers who were euthyroid and those who had hypothyroidism, hypothyroxinemia, or hyperthyroidism. Overall, 16-year-old offspring of the 358 mothers who had hypothyroidism showed no overall difference in scholastic performance as compared with the offspring of euthyroid mothers, but when the 318 cases of subclinical hypothyroidism were analyzed separately, the risk of having difficulty in mathematics was increased as compared with the 4747 adolescents from euthyroid mothers. The 16-year-old offspring of the 124 mothers with hyperthyroidism (overt plus subclinical) also had an increased risk of difficulty with mathematics.

HYPOTHYROIDISM, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this Northern Finnish cohort, 16-year-old offspring of mothers with first-trimester tests that indicated subclinical hypothyroidism were at increased risk of having difficulty in mathematics. The 16-year-old offspring of mothers with tests indicating hyperthyroidism (overt plus subclinical) were also found to be at increased risk of having difficulty in mathematics. These data suggest another reason to consider screening for thyroid disease in the mother early in pregnancy.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

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

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

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

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.

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

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

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

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HYPOTHYROIDISM

Hypothyroidism is associated with a faulty increase in Hemoglobin A1C levels

BACKGROUND

Hypothyroidism causes many metabolic abnormalities as well as multiple clinical symptoms. Some studies suggest that blood sugar may be affected in hypothyroidism and levels may increase. Indeed, it has been noted that patients with diabetes who also have hypothyroidism may have higher levels of Hemoglobin A1C (HBA1C). This test is done to diagnose and monitor control of blood sugar by patients with diabetes. An elevated HBA1C usually indicates worse control of diabetes.

This study was done to look at the effect of thyroid hormone treatment on HBA1c levels in patients with hypothyroidism. This study was also done to look at the effect thyroid hormone treatment has on the diagnoses of pre diabetes and the control of diabetes after treatment.

THE FULL ARTICLE TITLE

Anantarapu S et al Effects of thyroid hormone replacement on glycated he n non-diabetic subjects with overt hypothyroidism. Arch Endocrinol Metab. September 25 2015 [Epub ahead of print].

SUMMARY OF THE STUDY

This study was done at a large hospital in India. Patients who were newly diagnosed with hypothyroidism were studied. They were at least 20 years old. Blood tests were done before starting the thyroid hormone and 3 months after the tests showed normal thyroid hormone levels. An HBA1C test and an oral glucose tolerance test were done on all patients. The results showed a significant drop in the HBA1c levels for patients diagnosed as having pre diabetes (HBA1C between 5.7 to 6.5 %) and diabetes (HBA1C above 6.5%) after starting thyroid hormone therapy. There was no change in the number of patients with elevated fasting glucose levels or impaired glucose tolerance after treatment with thyroid hormone. The body weight did not change to a great extent.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that hypothyroidism may be falsely increasing the levels of the HBA1C test. While thyroid hormone therapy decreases the HBA1C test results, suggesting an improvement of blood sugar control, actual measurements of fasting blood sugars and overall glucose tolerance were unchanged on thyroid hormone therapy. This may lead to errors in diagnosing pre diabetes and diabetes in patients with hypothyroidism. This is important for both physicians and patients to know.

—Vibhavasu Sharma, MD

ATA THYROID BROCHURE LINKS

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

Thyroid Hormone Treatment: http://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.

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

HBA1c: Hemoglobin A1c is a blood test done to diagnose diabetes and monitor control in patients with diabetes. The higher the number, the worse control of the diabetes.

Oral Glucose Tolerance Test: This is a blood test done after giving the patients a certain amount of sugar by mouth. It may also be used to diagnose diabetes.

Diabetes: A chronic condition caused by higher than normal blood sugar levels due to the inability of the body to process the sugars.

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HYPERTHYROIDISM AND HYPOTHYROIDISM

Hyperthyroidism and hypothyroidism are uncommon causes of anemia

BACKGROUND

Abnormal thyroid hormone levels, such as hyperthyroidism and hypothyroidism, can be potential causes of anemia (low blood count). All three of these are common medical problems. They also all can produce symptoms of fatigue. This study was done to see if there is a relationship between abnormal thyroid hormone levels and anemia using a large population of adults in the United Kingdom.

THE FULL ARTICLE TITLE

M'Rabet-Bensalah K et al Thyroid dysfunction and anemia in a large population-based study. Clin Endocrinol (Oxf). 2015 Dec 10. doi: 10.1111/cen.12994. [Epub ahead of print]

SUMMARY OF THE STUDY

This was a study of nearly 9,000 adults in the United Kingdom who had blood tests for hyperthyroidism, hypothyroidism, and anemia. Approximately 10% of the group had either hyperthyroidism or hypothyroidism, and nearly 6% of the group had anemia. Some common causes of anemia were also tested for, and 121 individuals in the group were identified as having either iron deficiency, inflammation, or chronic kidney disease that caused their anemia. Those who had hyperthyroidism more frequently also had anemia, compared to those who had normal thyroid hormone levels. The authors concluded that in adults with anemia that is not easily explainable, abnormal thyroid hormone levels are found only 5% of the time. Thus, testing for hyperthyroidism or hypothyroidism in adults with anemia may not be particularly useful.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that abnormal thyroid hormone levels is a rather infrequent finding among adults with anemia. However, the authors did not study whether medications or other diseases that can affect thyroid hormone levels might have been present in the subjects. Future research that studies if having risk factors for abnormal thyroid hormone levels are present in anemic individuals can help us understand how these two common disorders might be related.

— Angela M. Leung, MD, MSc

ATA THYROID BROCHURE LINKS

Hyperthyroidism: http://www.thyroid.org/hyperthyroidism/

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

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.

Anemia: low blood count, specifically low levels of red blood cells which carry oxygen around to all of the cells in the body. Fatigue is a common symptom of anemia.

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THYROID NODULES

The ThyroSeq V2.1 multi-gene next-generation sequencing panel is effective at predicting a diagnosis of thyroid cancer in nodules with indeterminate cytology.

BACKGROUND

Thyroid nodules are very common and raise the possibility of thyroid cancer. The general recommendation is that nodules larger than 1 cm should be evaluated with a thyroid biopsy. While a thyroid biopsy gives a diagnosis in most cases, up to 10-20% of biopsies are indeterminate, meaning that a diagnosis of cancer vs benign cannot be made on the basis of examining the cells alone. This usually leads to surgery despite the fact that most indeterminate nodules are benign. In recent years, the use of molecular marker testing on thyroid biopsy specimens has helped identify benign indeterminate nodules and avoid surgery. The molecular marker test discussed in this study called ThyroseqV2.1 detects gene mutations in the DNA and RNA of the nodule that might increase the risk for cancer in the nodule. If certain cancer-associated gene mutations such as BRAF, RAS, RET/PTC, p53, etc. are found to be present in the thyroid nodule, there is a high risk that the nodule is cancerous. Conversely, if these gene mutations are absent, the nodule is most likely benign. The goal of this study was to determine how good the ThyroseqV2.1 test is at predicting whether a nodule with indeterminate cytology is benign or cancerous.

THE FULL ARTICLE TITLE

Nikiforov YE et al. Impact of the multi-gene ThyroSeq next-generation sequencing assay on cancer diagnosis in thyroid nodules with atypia of undetermined significance/follicular lesion of undetermined significance cytology. Thyroid. Nov;25(11):1217-23.

SUMMARY OF THE STUDY

From March 2014 to March 2015, 465 thyroid biopsy samples in 441 patients were diagnosed as indeterminate (AUS/FLUS) at the University of Pittsburgh Medical Center and all had the ThyroseqV2.1 test performed on biopsy specimen. The test found 3 parathyroid nodules and 462 thyroid lesions. ThyroseqV2.1 did not show a gene mutation in 431 (93%) of AUS/FLUS nodules. ThyroseqV2.1 did detect a gene mutation in 31(7%) nodules and 26 patients had thyroidectomy revealing 20 (77%) thyroid cancers. The majority (18) of these cancers were follicular variant of papillary thyroid cancer. Of the 431 patients with a negative ThyroseqV2.1, 69 patients still had surgery and 2 nodules (3%) were cancer. The most common gene mutations were NRAS and HRAS.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The important finding of this study is that the Thyroseq2.1 molecular test can be valuable in the evaluation of indeterminate nodules with AUS/FLUS cytology. The data suggest that if the Thyroseq2.1 molecular test is negative (no gene mutations), there is 97% likelihood that the nodule is benign and surgery can be avoided. If the Thyroseq2.1 molecular test is positive for a gene mutation, there is a 77% change that the nodule is cancerous, so surgery is indicated. The results of this study are important to patients with indeterminate thyroid nodules to help determine which patients have a high or low risk for cancer, and thereby tailor management of either surgery or continued monitoring accordingly.

—Wendy Sacks, MD

ATA THYROID BROCHURE LINKS

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

Thyroid cancer: http://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

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.

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THYROID NODULES, continued

Indeterminate Thyroid Biopsy: this happens when a diagnosis of benign or cancerous cannot be made with certainty by looking at the cells. This results in cytology readings of atypia of unknown significance (AUS), follicular lesion of unknown significance (FLUS) and follicular or hurtle cell lesions. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

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

Mutation: A permanent change in one of the genes that can lead to cancer.

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.

Cancer-associated genes: these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC and RAS.

Thyroid Awareness Monthly Campaigns

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

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THYROID CANCER

Detecting recurrence of papillary thyroid cancer costs much more in those with low-risk than high risk cancer.

BACKGROUND

In the United States the incidence of thyroid cancer has nearly tripled in the last 30 years, mainly due to increase in the diagnosis of papillary thyroid cancers. While the overall survival rate of papillary thyroid cancer is excellent (over 90%), patients must be monitored for recurrence of the cancer for several years after initial treatment. This cancer surveillance involves periodic physician visits, blood samples to measure thyroid stimulating hormone (TSH) and thyroglobulin levels, periodic neck ultrasounds and, depending upon the case, even CT, MRI or PET scans.

The American Thyroid Association (ATA) has developed a three tiered risk stratification system which uses the cellular features and extent of spread of each cancer to classify patients as being at low, intermediate, or high risk of having a recurrence after their initial treatment. The type and frequency of tests required to effectively monitor for recurrence depends upon one's risk category. Patients in a high risk category often receive more frequent and extensive investigations then those in a low risk category and this has important financial implications both for patients and the overall health system. However, at a time of growing national interest in providing cost-effective health care, there have been no studies examining the financial cost for surveillance of patients with papillary thyroid cancer to detect recurrences. The aim of the current study was to analyze the financial cost of monitoring for recurrence of papillary thyroid cancer in the first 3 years after surgery for low risk patients versus intermediate- and high- risk patients.

THE FULL ARTICLE TITLE

Wang LY1 et al. Cost-effectiveness analysis of papillary thyroid cancer surveillance. Cancer 2015;121(23):4132-40.

SUMMARY OF THE STUDY

The authors studied the records of 1,087 patients who had surgery for thyroid cancer at Memorial Sloan-Kettering Cancer Centre between January 2000 and December 2010. Only patients who had a) papillary thyroid cancer treated with a total thyroidectomy, and b) had not had surgery for another type of cancer and c) had been followed for 36 months or more after surgery were included in the analysis. Patients were divided into each of the three ATA risk categories of low risk (362 patients, 33%), intermediate risk (561 patients, 52%) and high risk (164 patients,15%) and then the total cost for all the surveillance tests and procedures (i.e. blood tests, neck ultrasounds, radioiodine scans, doctors' visits etc) within each group was calculated.

During the study period there were only 3 recurrences in the low risk group (0.8%), 44 in the intermediate risk group (7.8%) and 22 in the high risk group (13.4%). The cost per patient in the low, intermediate and high risk groups were $1,225, $1,760 and $2,774 respectively. However, it cost $149,619 to detect one recurrence in the low risk group compared to $22,434 in the intermediate risk group and $20,680 in the high risk group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that the cost per patient to monitor for recurrence is higher in those with high risk papillary thyroid cancer vs low risk cases. This is to be expected because this group of patients has a much higher risk of cancer recurrence and so they require more frequent (and costly) laboratory testing, imaging and physician appointments following their initial cancer treatment. However, because very few patients in the low risk group actually had a recurrence of their cancer, the cost to detect each one was more than 6 times higher than the cost for intermediate and high-risk patients. Consequently, the authors suggest that current surveillance of low risk papillary thyroid cancer is not cost-effective and that hopefully these finding will promote more discussion and research into the appropriate way to monitor low risk papillary thyroid cancer patients for recurrences.

It should be noted however that this study was from a single, high volume thyroid cancer center and may not reflect the cost of thyroid cancer surveillance nationally. As well, the authors did not consider the

THYROID CANCER, continued

patient experience in their calculations and the need to balance the costs of thyroid cancer surveillance with the profound value to the patient that comes with knowing that he/she is free from cancer.

— Philip Segal, MD

ATA THYROID BROCHURE LINKS

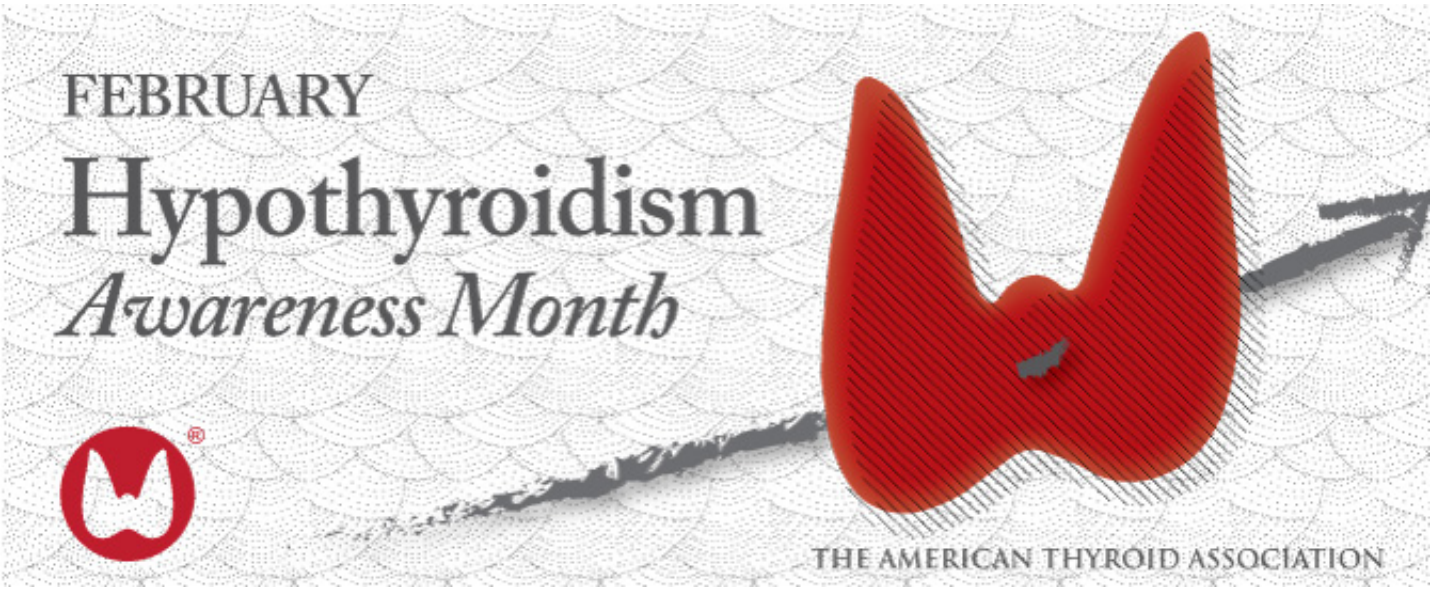
Thyroid cancer: http://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

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

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

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



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FOUNDED 1923
www.thyroid.org

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 towards the improvement of thyroid education and resources for patients.

WHO WE ARE (in alphabetical order)

- **American Thyroid Association**
- **Bite Me Cancer**
- **Graves' Disease and Thyroid Foundation**
- **Light of Life Foundation**
- **ThyCa: Thyroid Cancer Survivors' Association, Inc.**
- **Thyroid Cancer Canada**
- **Thyroid Federation International**

AMERICAN THYROID ASSOCIATION

www.thyroid.org
ATA Patient Resources: http://www.thyroid.org/patients/
Find a Thyroid Specialist: www.thyroid.org
Phone (toll-free): 1-800-THYROID
e-mail: thyroid@thyroid.org

ATA Mission: The ATA leads in promoting thyroid health and understanding thyroid biology.
ATA Vision: The ATA is the leading organization focused on thyroid biology and the prevention and treatment of thyroid disorders through excellence and innovation in research, clinical care, education, and public health.
ATA Values: The ATA values scientific inquiry, clinical excellence, public service, education, collaboration, and collegiality.

To further our mission, vision and values the ATA sponsors "Friends of the ATA" online to advance the information provided to patients and the public such as this publication, *Clinical Thyroidology for the Public*. We welcome your support.

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AMERICAN THYROID ASSOCIATION
FOUNDED 1923

Light of Life Foundation
checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

Thyroid Federation International

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

Thyroid Cancer Canada
Cancer de la thyroïde Canada

BITE ME cancer
attitude is everything

ATA Alliance for Thyroid Patient Education

Continued...

BITE ME CANCER

http://www.bitemecancer.org

Bite Me Cancer was formed as a nonprofit foundation in September, 2010, by Nikki Ferraro, who was 17-years old at the time. Nikki was diagnosed with a rare form of thyroid cancer in April 2010 when she was a junior at Chantilly HS in Virginia. Nikki was determined to lead a Relay for Life team just two weeks after her diagnosis. She named the team Bite Me Cancer and experienced immediate success. When Nikki decided to create a foundation a few months later, she wanted to continue the legacy of her team name and thus her foundation became the Bite Me Cancer Foundation.

e-mail: info@bitemecancer.org

GRAVES' DISEASE AND THYROID FOUNDATION

www.gdatf.org

Phone (toll-free): 1-877-NGDF-123 or 643-3123

e-mail: Gravesdiseasefd@gmail.com

Founded in 1990, the Graves' Disease Foundation offers support and resources to Graves' disease patients, their families, and health care professionals. Their mission is to find the cause of and the cure for Graves' thyroid disease through research, to improve the quality of life for persons with Graves' disease and their caregivers and to educate persons with Graves' disease, their caregivers, healthcare professionals, and the general public about Graves' disease and its treatment. The web site features a monitored bulletin board.

LIGHT OF LIFE FOUNDATION

www.checkyourneck.com

email: info@checkyourneck.com

The Light of Life Foundation, founded in 1997, is a nonprofit organization that strives to improve the quality of life for thyroid cancer patients, educate the public and professionals about thyroid cancer, and promote research and development to improve thyroid cancer care.

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Cancer de la thyroïde Canada

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ATA Alliance for Thyroid Patient Education

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THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

www.thyca.org
Phone (toll-free): 877 588-7904
e-mail: thyca@thyca.org

ThyCa: Thyroid Cancer Survivors' Association, Inc., founded in 1995, is an international nonprofit organization, guided by a medical advisory council of renowned thyroid cancer specialists, offering support and information to thyroid cancer survivors, families, and health care professionals worldwide.

THYROID CANCER CANADA

www.thyroidcancercanada.org
Phone: 416-487-8267
Fax: 416-487-0601
e-mail: info@thyroidcancercanada.org

Thyroid Cancer Canada is a non-profit organization founded in 2000. The organization works towards creating an environment in which people who are dealing with thyroid cancer, especially the newly diagnosed, are met with support and information. Their goals & objectives include facilitating communication among thyroid cancer patients, providing credible information about the disease, providing emotional support, and assisting thyroid cancer patients with voicing their needs to health care professionals and those who are responsible for health care policy.

THYROID FEDERATION INTERNATIONAL

http://www.thyroid-fed.org/
e-mail: tfi@thyroid-fed.org

Thyroid Federation International (TFI) was established in Toronto in 1995. Thyroid Federation International aims to work for the benefit of those affected by thyroid disorders throughout the world by providing a network of patient support organizations.

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Thyroid Federation International

Thyroid Cancer Canada
Cancer de la thyroïde Canada

BITE ME cancer
attitude is everything

Hypothyroidism

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 HYPOTHYROIDISM?

Hypothyroidism is an underactive thyroid gland. Hypothyroidism means that the thyroid gland can't make enough thyroid hormone to keep the body running normally. People are hypothyroid if they have too little thyroid hormone in the blood. Common causes are autoimmune disease, surgical removal of the thyroid, and radiation treatment.

WHAT ARE THE SYMPTOMS?

When thyroid hormone levels are too low, the body's cells can't get enough thyroid hormone and the body's processes start slowing down. As the body slows, you may notice that you feel colder, you tire more easily, your skin is getting drier, you're becoming forgetful and depressed, and you've started getting constipated. Because the symptoms are so variable and non-specific, the only way to know for sure whether you have hypothyroidism is with a simple blood test for TSH.

KEEPING OTHER PEOPLE INFORMED

Tell your family members. Because thyroid disease runs in families, you should explain your hypothyroidism to your relatives and encourage them to get regular TSH tests. Tell your other doctors and your pharmacist about your hypothyroidism and the drug and dose with which it is being treated. If you start seeing a new doctor, tell the doctor that you have hypothyroidism and you need your TSH tested every year. If you are seeing an endocrinologist, ask that copies of your reports be sent to your primary care doctor.

WHAT CAN YOU EXPECT OVER THE LONG TERM?

There is no cure for hypothyroidism, and most patients have it for life. There are exceptions: many patients with viral thyroiditis have their thyroid function return to normal, as do some patients with thyroiditis after pregnancy.

Hypothyroidism may become more or less severe, and your dose of thyroxine may need to change over time. You have to make a lifetime commitment to treatment. But if you take your pills every day and work with your doctor to get and keep your thyroxine dose right, you should be able to keep your hypothyroidism completely controlled throughout your life. Your symptoms should disappear and the serious effects of low thyroid hormone should stop getting worse and should actually improve. If you keep your hypothyroidism well-controlled, it will not shorten your life span.

WHAT CAUSES HYPOTHYROIDISM?

There can be many reasons why the cells in the thyroid gland can't make enough thyroid hormone. Here are the major causes, from the most to the least common.

- *Autoimmune disease.* In some people's bodies, the immune system that protects the body from invading infections can mistake thyroid gland cells and their enzymes for invaders and can attack them. Then there aren't enough thyroid cells and enzymes left to make enough thyroid hormone. This is more common in women than men. Autoimmune thyroiditis can begin suddenly or it can develop slowly over years. The most common forms are Hashimoto's thyroiditis and atrophic thyroiditis.
- *Surgical removal of part or all of the thyroid gland.* Some people with thyroid nodules, thyroid cancer, or Graves' disease need to have part or all of their thyroid removed. If the whole thyroid is removed, people will definitely become hypothyroid. If part of the gland is left, it may be able to make enough thyroid hormone to keep blood levels normal.
- *Radiation treatment.* Some people with Graves' disease, nodular goiter, or thyroid cancer are treated with radioactive iodine (I-131) for the purpose of destroying their thyroid gland. Patients with Hodgkin's disease, lymphoma, or cancers of the head or neck are treated with radiation. All these patients can lose part or all of their thyroid function.

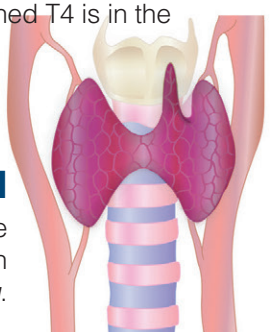
Hypothyroidism

- *Congenital hypothyroidism (hypothyroidism that a baby is born with).* A few babies are born without a thyroid or with only a partly formed one. A few have part or all of their thyroid in the wrong place (ectopic thyroid). In some babies, the thyroid cells or their enzymes don't work right.
- *Thyroiditis.* Thyroiditis is an inflammation of the thyroid gland, usually caused by an autoimmune attack or by a viral infection. Thyroiditis can make the thyroid dump its whole supply of stored thyroid hormone into the blood at once, causing brief hyperthyroidism (too much thyroid activity); then the thyroid becomes underactive.
- *Medicines.* Medicines such as amiodarone, lithium, interferon alpha, and interleukin-2 can prevent the thyroid gland from being able to make hormone normally. These drugs are most likely to trigger hypothyroidism in patients who have a genetic tendency to autoimmune thyroid disease.
- *Too much or too little iodine.* The thyroid gland must have iodine to make thyroid hormone. Iodine comes into the body in food and travels through the blood to the thyroid. Keeping thyroid hormone production in balance requires the right amount of iodine. Taking in too much iodine can cause or worsen hypothyroidism.
- *Damage to the pituitary gland.* The pituitary, the "master gland," tells the thyroid how much hormone to make. When the pituitary is damaged by a tumor, radiation, or surgery, it may no longer be able to give the thyroid instructions, and the thyroid may stop making enough hormone.
- *Rare disorders that infiltrate the thyroid.* In a few people, diseases deposit abnormal substances in the thyroid and impair its ability to function. For example, amyloidosis can deposit amyloid protein, sarcoidosis can deposit granulomas, and hemochromatosis can deposit iron.

HOW IS HYPOTHYROIDISM DIAGNOSED?

The correct diagnosis of hypothyroidism depends on the following:

- *Symptoms.* Hypothyroidism doesn't have any characteristic symptoms. There are no symptoms that people with hypothyroidism always have and many symptoms of hypothyroidism can occur in people with other diseases. One way to help figure out whether your symptoms are due to hypothyroidism is to think about whether you've always had the symptom (hypothyroidism is less likely) or whether the symptom is a change from the way you used to feel (hypothyroidism is more likely).
- *Medical and family history.* You should tell your doctor:
  - about changes in your health that suggest that your body is slowing down;
  - if you've ever had thyroid surgery;
  - if you've ever had radiation to your neck to treat cancer;
  - if you're taking any of the medicines that can cause hypothyroidism— amiodarone, lithium, interferon alpha, interleukin-2, and maybe thalidomide;
  - whether any of your family members have thyroid disease.
- *Physical exam.* The doctor will check your thyroid gland and look for changes such as dry skin, swelling, slower reflexes, and a slower heart rate.
- *Blood tests.* There are two blood tests that are used in the diagnosis of hypothyroidism.
- *TSH (thyroid-stimulating hormone) test.* This is the most important and sensitive test for hypothyroidism. It measures how much of the thyroid hormone thyroxine (T4) the thyroid gland is being asked to make. An abnormally high TSH means hypothyroidism: the thyroid gland is being asked to make more T4 because there isn't enough T4 in the blood.
- *T4 tests.* Most of the T4 in the blood is attached to a protein called thyroxine-binding globulin. The "bound" T4 can't get into body cells. Only about 1%–2% of T4 in the blood is unattached ("free") and can get into cells. The free T4 and the free T4 index are both simple blood tests that measure how much unattached T4 is in the blood and available to get into cells.



FURTHER INFORMATION

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

Hypothyroidism

HOW IS HYPOTHYROIDISM TREATED?

THYROXINE (T4) REPLACEMENT.

Hypothyroidism can't be cured. But in almost every patient, hypothyroidism can be completely controlled. It is treated by replacing the amount of hormone that your own thyroid can no longer make, to bring your T4 and TSH back to normal levels. So even if your thyroid gland can't work right, T4 replacement can restore your body's thyroid hormone levels and your body's function. Synthetic thyroxine pills contain hormone exactly like the T4 that the thyroid gland itself makes. All hypothyroid patients except those with severe myxedema (life-threatening hypothyroidism) can be treated as outpatients, not having to be admitted to the hospital.

SIDE EFFECTS AND COMPLICATIONS.

The only dangers of thyroxine are caused by taking too little or too much. If you take too little, your hypothyroidism will continue. If you take too much, you'll develop the symptoms of hyperthyroidism—an overactive thyroid gland. The most common symptoms of too much thyroid hormone are fatigue but inability to sleep, greater appetite, nervousness, shakiness, feeling hot when other people are cold, and trouble exercising because of weak muscles, shortness of breath , and a racing, skipping heart. Patients who have hyperthyroid symptoms at any time during thyroxine replacement therapy should have their TSH tested. If it is low, indicating too much thyroid hormone, their dose needs to be lowered.

FOLLOW-UP

You'll need to have your TSH checked about every 6 to 10 weeks after a thyroxine dose change. You may need tests more often if you're pregnant or you're taking a medicine that interferes with your body's ability to use thyroxine. The goal of treatment is to get and keep your TSH in the normal range. Babies with hypothyroidism must get all their daily treatments and have their TSH levels checked as they grow, to prevent mental retardation and stunted growth. Once you've settled into a thyroxine dose, you can return for TSH tests about once a year.

YOU NEED TO RETURN SOONER IF ANY OF THE FOLLOWING APPLY TO YOU:

- Your symptoms return or get worse.
- You want to change your thyroxine dose or brand, or change taking your pills with or without food.
- You gain or lose a lot of weight (as little as a 10-pound difference for those who weren't overweight to begin with).
- You start or stop taking a drug that can interfere with absorbing thyroxine (such as certain antacids, calcium supplements and iron tablets), or you change your dose of such a drug. Medications containing estrogen also impact thyroxine doses, so any change in such a medication should prompt a re-evaluation of your thyroxine dose.
- You're not taking all your thyroxine pills. Tell your doctor honestly how many pills you've missed.
- You want to try stopping thyroxine treatment. If ever you think you're doing well enough not to need thyroxine treatment any longer, try it only under your doctor's close supervision. Rather than stopping your pills completely, you might ask your doctor to try lowering your dose. If your TSH goes up, you'll know that you need to continue treatment.

FURTHER INFORMATION

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