Clinical THYROIDOLOGY FOR THE PUBLIC

AMERICAN THYROID ASSOCIATION
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Normal thyroid function in both the mother and the baby is important during pregnancy to prevent complications during delivery and the postpartum period. Hypothyroidism is a common medical condition that occurs more often in women. This study was done to assess how much thyroid hormone, in the form of levothyroxine, should be given to women who are diagnosed with hypothyroidism during pregnancy.

Abalovich M et al Adequate levothyroxine doses for the treatment of hypothyroidism newly discovered during pregnancy. Thyroid 2013;23:1479-83. Epub September 20, 2013.

The most common cause of hyperthyroidism is Graves' disease, the autoimmune disorder caused by TSH receptor antibodies. In some patients who appear to have typical Graves' disease do not have measurable TSH receptor antibodies. The present study was designed to look at a large number of such patients to see if the cause of the hyperthyroidism could be determined.

Nishihara E et al, The prevalence of TSH receptor germline mutations and clinical courses in 89 hyperthyroid patients with diffuse goiter and negative anti-TSH receptor antibodies. Thyroid. November 26, 2013 [Epub ahead of print].

Chang C-C et al 10-year analysis of thyrotoxic periodic paralysis in 135 patients: focus on symptomatology and precipitants. Eur J Endocrinol 2013;169:529-36.

Thyroglobulin is a protein produced by both normal and cancerous thyroid cells. This is used as a thyroid cancer marker after initial therapy since, if any thyroid cancer cells are present, levels of thyroglobulin are often detectable. This study is an analysis of many other studies as to the usefulness of measuring serum thyroglobulin levels in managing patients with thyroid cancer.

Giovanella L et al, Unstimulated high-sensitive thyroglobulin in follow-up of differentiated thyroid cancer patients: a meta-analysis. J Clin Endocrinol Metab. 2013 Nov 27.

Dettmer M et al. Comprehensive microRNA expression profiling identifies novel markers in follicular variant of papillary thyroid carcinoma. Thyroid 2013 Nov;23(11):1383-9.

Cancer-associated gene mutations are present in over half of thyroid cancers. RAS is the second most common gene mutation. The aim of this study was to examine the role of screening for RAS expression in thyroid biopsy specimens in patients with thyroid cancer.

Gupta N et al. RAS mutations in thyroid FNA specimens are highly predictive of predominantly low-risk follicular-pattern cancers. J Clin Endocrinol Metab 2013;98:E914-22. Epub March 28, 2013; doi: 10.1210/jc.2012-3396.

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EDITOR'S COMMENTS

Welcome to *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 are also planning additional content, possibly some topic reviews, in future issues. 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*, the *Graves' Disease and Thyroid Foundation*, the *Light of Life Foundation*, *ThyCa: Thyroid Cancer Survivors Association*, *Thyroid Cancer Canada and Thyroid Federation International*.

In this issue, the studies ask the following questions:

1. How much Levothyroxine should be started for hypothyroidism during pregnancy?
2. Is Graves' disease always an autoimmune disorder?
3. What causes thyrotoxic periodic paralysis?
4. When thyroglobulin is undetectable, is any further testing needed in following patients with thyroid cancer?
5. Are microRNAs a useful molecular marker for cancer in thyroid nodule biopsies?
6. What is the significance the molecular marker RAS in papillary cancer?

We welcome your feedback and suggestions. Let us know what you want to see in this publication. I hope you find these summaries interesting and informative.

— Alan P. Farwell, MD

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THYROID AND PREGNANCY

How much levothyroxine should be started for hypothyroidism diagnosed during pregnancy?

BACKGROUND

Thyroid hormone in the baby is essential during pregnancy for normal brain development. Normal thyroid function in the mother is important during pregnancy to prevent complications during delivery and the postpartum period. In the first trimester, the baby gets its' thyroid hormone from the mother. Hypothyroidism, or an underactive thyroid, is a common medical condition that occurs more often in women. During pregnancy, hypothyroidism in generally treated aggressively, with the idea to normalize thyroid levels as soon as possible. This study was done to assess how much thyroid hormone, in the form of levothyroxine, should be given to women who are diagnosed with hypothyroidism during pregnancy.

THE FULL ARTICLE TITLE

Abalovich M et al Adequate levothyroxine doses for the treatment of hypothyroidism newly discovered during pregnancy. Thyroid 2013;23:1479-83. Epub September 20, 2013.

SUMMARY OF THE STUDY

This was a study of 77 women in Argentina with hypothyroidism diagnosed during pregnancy. All women were started on levothyroxine treatment immediately after hypothyroidism was diagnosed. Women were followed by thyroid stimulating hormone (TSH) blood tests to confirm the effectiveness of levothyroxine treatment. The TSH goals were less than 2.5 mIU/L in the first trimester and less than 3 mI/L in the second and third trimesters. The authors show that women with milder forms of hypothyroidism require less levothyroxine. Overall, the dose of levothyroxine is weight-based, and women required starting doses ranging from 1.20-2.33 mcg/kg/day during pregnancy, depending on the severity of hypothyroidism.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is an important study as it provides recommendations for the selection of an initial levothyroxine dose in women with hypothyroidism diagnosed during pregnancy. This guidance is important in decreasing the risks of untreated hypothyroidism, which during pregnancy can result in poor outcomes to the mother and baby. It is suggested that levothyroxine be monitored with a TSH blood test 2-4 weeks after starting the medication.

— Angela M. Leung, MD

ATA THYROID BROCHURE LINKS

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

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. Replacement therapy means the goal is a TSH in the normal range and is the usual therapy. Suppressive therapy means that the goal is a TSH below the normal range and is used in thyroid cancer patients to prevent growth of any remaining cancer cells.

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

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HYPERTHYROIDISM

Some patients with apparent Graves' disease do not have an autoimmune thyroid disorder

BACKGROUND

One of the most common causes of hyperthyroidism is Graves' disease, an autoimmune process in which the patient's immune cells make antibodies against the thyroid stimulating hormone (TSH) receptor on the thyroid gland cells. These autoantibodies stimulate the thyroid to grow, resulting in a diffuse enlargement (goiter), and to produce excessive amounts of thyroid hormone, resulting in hyperthyroidism. Graves' disease with hyperthyroidism is characterized by the presence of diffuse thyroid enlargement, suppression of pituitary TSH, elevations of thyroxine (T_4) and/or triiodothyronine (T_3), the presence of TSH receptor antibodies in the blood, an elevated radioactive iodine uptake by the thyroid gland and clinical symptoms such as weight loss, increased perspiration, anxiety, tremor, rapid heart rate and frequent bowel movements. Some patients with Graves' disease may have subclinical (mild) hyperthyroidism without symptoms but with a goiter, suppressed TSH, TSH receptor antibodies, but with normal T_4 and T_3. Although TSH receptor antibodies are detected in the majority of patients with Graves' disease, there are some patients in whom such antibodies cannot be detected, but yet appear to have typical Graves' disease. Some of the antibody negative patients may actually have Graves' disease but the antibody levels are too low to detect initially. A small number of the patients may have a mutation of the TSH receptor resulting in the receptor being chronically turned on causing diffuse enlargement of the thyroid and clinical or subclinical hyperthyroidism. This would resemble the clinical and biochemical findings with Graves' disease but without the antibodies.

The present study was designed to look at a large number of patients with hyperthyroidism, diffuse goiters, but no measurable TSH receptor antibodies to see if the cause of the hyperthyroidism could be determined.

THE FULL ARTICLE TITLE

Nishihara E et al, The prevalence of TSH receptor germline mutations and clinical courses in 89 hyperthyroid patients with diffuse goiter and negative anti-TSH receptor antibodies. Thyroid. November 26, 2013 [Epub ahead of print].

SUMMARY OF THE STUDY

Over a 10 year period, close to 25,000 patients with hyperthyroidism were evaluated at Kuma Hospital in Japan. From this group, 89 patients had diffuse goiters with negative TSH receptor antibodies. About 10% of the 68 patients who were followed for more than a year developed TSH receptor antibodies and another 6% had weakly positive antibody levels, suggesting that they actually had mild Graves' disease when first seen and then evolved into more typical Graves' disease. A total of 4 of the 89 patients were found to have mutations in the thyroid TSH receptor that was responsible for the goiter and hyperthyroidism. Screening of family members of these patients identified an additional 7 patients with the mutations and all had subclinical or overt hyperthyroidism, while the other family members without the mutation had normal thyroid function. Patients with the mutations did not have a spontaneous remission of the hyperthyroidism with or without antithyroid drugs, unlike some patients with Graves' disease who may go into remission either spontaneously or after a course of antithyroid drug treatment.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this series of patients, about 5% of the 89 adult patients who clinically appeared to have Graves' disease but did not have TSH-receptor antibodies in their blood had activating mutations of the TSH receptor causing the hyperthyroidism and some of these mutations were found in other family members indicating that the disorder runs in families. Approximately 10-15% of the 89 patients actually had Graves' disease that became apparent over time. Thus, the cause of the hyperthyroidism in the majority of the patients remained undefined. Nevertheless, the standard therapies of antithyroid drugs, radioactive iodine, or surgery can be used in these patients irrespective of the cause. Importantly, the antithyroid drugs will not bring about a remission for those with TSH receptor mutations.

— Glenn D. Braunstein, M.D.

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HYPERTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Hyperthyroidism: http://www.thyroid.org/what-is-hyperthyroidism

Graves' disease: http://www.thyroid.org/what-is-graves-disease

ABBREVIATIONS & DEFINITIONS

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

Goiter: a thyroid gland that is enlarged for any reason is called a goiter. A goiter can be seen when the thyroid is overactive, underactive or functioning normally. If there are nodules in the goiter it is called a nodular goiter; if there is more than one nodule it is called a multinodular goiter.

TSH receptor: A molecule (protein) located on the thyroid cell surface that binds TSH and stimulates the production of the thyroid hormones within the thyroid cell.

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

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

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

Genetic hyperthyroidism: A rare form of hyperthyroidism caused by genetic mutations in the TSH receptor that cause it to be permanently in the "on" position (activating mutations).

Mutation: a permanent change in one of the genes.

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.

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

Triiodothyronine (T_3): the active thyroid hormone, usually produced from thyroxine, available in pill form as Cytomel™.

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

Radioactive iodine uptake (RAIU): this is a measurement of activity of the thyroid gland and is reported as the percent of a dose of radioactive iodine that is retained in the thyroid gland 24 h after the dose is given. An increase in RAIU usually indicates hyperthyroidism.

Antibodies: proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses that cause infections. Occasionally the antibodies get confused and attack the body's own tissues, causing autoimmune disease.

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HYPERTHYROIDISM

A 10-year analysis of thyrotoxic periodic paralysis

BACKGROUND

Some people who make too much thyroid hormone, a disease state called hyperthyroidism or thyrotoxicosis, can have attacks of weakness or even whole body paralysis (inability to move). The weakness is associated with very low levels of potassium in the blood and therefore this condition is called thyrotoxic periodic paralysis (TPP). Graves' disease, an autoimmune thyroid disease that causes high thyroid hormone levels in the blood is most often associated with TPP. Asian men are the most common group to get TPP, but it can affect other groups of people. The cause of low potassium levels and paralysis in patients with hyperthyroidism is not altogether clear, although high sugar diets and increased exercise are thought to be triggers. This study was done in Taiwan where they were able to follow a large number of people with TPP over 10 years. Their goal was to gain an understanding of the factors that trigger TPP and to identify the degree of hyperthyroidism by patient symptoms and by blood levels of thyroid hormone that are associated with the attack of paralysis.

THE FULL ARTICLE TITLE

Chang C-C et al 10-year analysis of thyrotoxic periodic paralysis in 135 patients: focus on symptomatology and precipitants. Eur J Endocrinol 2013;169:529-36.

SUMMARY OF THE STUDY

Over a period of 10 years (2002 to 2012), 135 patients with TPP (130 men, 5 women) were studied, the largest group of patients followed over time in one hospital.

The majority of cases of TPP (96%) were due to Graves' disease, an autoimmune thyroid disease that causes high thyroid hormone levels in the blood. They found that TPP more frequently occurred in the mornings and in the summer and fall. Additionally, the extent of hyperthyroidism on the blood test did not correlate with the onset of TPP. In other words, even people with mild hyperthyroidism could develop TPP. Most people in the study (about 75%) found out for the first time about their thyroid abnormality when they presented to the doctor with paralysis. The best factor they found to trigger TPP was a high sugar load in the diet. It is important to correct the hyperthyroidism to prevent future attacks of low potassium and paralysis.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that any degree hyperthyroidism, whether it is mild, moderate or severe by blood tests or by patient symptoms, can cause low potassium and paralysis.. High sugar diets and increased exercise can trigger TPP, but these are not the only factors. Quickly treating the low potassium and the thyroid problem is very important for patients. It is important for patients with hyperthyroidism to be aware of TPP.

—Wendy Sacks, MD

ATA THYROID BROCHURE LINKS

Graves' disease: http://www.thyroid.org/what-is-graves-disease

ABBREVIATIONS & DEFINITIONS

Thyrotoxic periodic paralysis (TPP): attacks of weakness or even whole body paralysis (inability to move) associated with very low levels of potassium in the blood. TPP is most commonly associated with Graves' disease.

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.

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

Antibodies: proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses that cause infections. Occasionally the antibodies get confused and attack the body's own tissues, causing autoimmune disease.

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THYROID CANCER

When thyroglobulin is undetectable, is any further testing needed in following patients with thyroid cancer?

BACKGROUND

Thyroglobulin is a protein produced by both normal and cancerous thyroid cells. Treatment of thyroid cancer frequently involves total thyroidectomy and radioiodine therapy followed by thyroid hormone therapy to suppress serum TSH and turn off any residual normal thyroid cells. In this situation, the serum thyroglobulin level can be used as a thyroid cancer marker. Indeed, if any thyroid cancer cells are present, levels of thyroglobulin are often detectable, either on TSH suppression therapy or after stimulation with rhTSH (stimulated thyroglobulin testing). Measurement of thyroglobulin under these conditions has become standard practice in the follow up of patients with thyroid cancer. This study is an analysis of many other studies as to the usefulness of measuring serum thyroglobulin levels in managing patients with thyroid cancer.

THE FULL ARTICLE TITLE

Giovanella L et al, Unstimulated high-sensitive thyroglobulin in follow-up of differentiated thyroid cancer patients: a meta-analysis. J Clin Endocrinol Metab. 2013 Nov 27.

SUMMARY OF THE STUDY

This study is an analysis of many other studies evaluating the utility of measuring thyroglobulin levels under thyroid hormone suppression therapy and after stimulation with rhTSH in patients with thyroid cancer. The authors identified 9 studies that used the newer, more sensitive thyroglobulin assay. These studies included a total of 3178 patients. The investigators found that when the basal thyroglobulin level under thyroid hormone suppression therapy is <0.1 ng/ml, it accurately predicts that the stimulated thyroglobulin level will be <1, which indicates absence of residual cancer cells.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study is helpful because it indicates that for most patients with thyroglobulin values of <0.1 ng/ml while on thyroid hormone suppression, stimulated thyroglobulin testing is unnecessary since the likelihood of identifying residual cancer is very small. These findings will cut down on the need to perform stimulated thyroglobulin testing, which is both inconvenient for patients and expensive. Long term follow up of patients with thyroid cancer, however, still requires periodic measurement of thyroglobulin, since other studies indicate that ~4% of patients with initially undetectable basal thyroglobulin levels eventually had recurrent cancer.

— M. Regina Castro, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://www.thyroid.org/cancer-of-the-thyroid-gland

Radioactive Iodine Therapy: http://www.thyroid.org/radioactive-iodine

ABBREVIATIONS & DEFINITIONS

Total thyroidectomy: surgery to remove the entire thyroid gland.

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

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.

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

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THYROID CANCER, continued

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).

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

Stimulated thyroglobulin testing: this test is used to measure whether there is any cancer present in a patient that has previously been treated with surgery and radioactive iodine. TSH levels are increased, either by withdrawing the patient from thyroid hormone or treating the patient with rhTSH (Thyrogen™), then levels of thyroglobulin are measured. Sometimes this test is combined with a whole body iodine scan.

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THYROID CANCER

Analysis of microRNAs in papillary thyroid cancer

BACKGROUND

Many cancers are thought to arise from genetic mutations in cancer-associated genes. Mutations in several of these cancer-associated genes have been shown to be present in certain types of thyroid cancer. Molecular markers based on these genes can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign. MicroRNAs are small molecules that have specific actions within a cell to affect the expression of certain genes. Some microRNAs are associated with some cancers. The main goal of this study was to examine microRNA expression in tissue samples of papillary thyroid cancer to determine if this could be used as a molecular marker. A second goal of this study was to examine for relationships between microRNA expression and clinical outcomes of thyroid cancer patients.

THE FULL ARTICLE TITLE

Dettmer M et al. Comprehensive microRNA expression profiling identifies novel markers in follicular variant of papillary thyroid carcinoma. Thyroid 2013 Nov;23(11):1383-9.

SUMMARY OF THE STUDY

The authors of this study examined microRNA expression in 17 tissue samples of follicular variant of papillary thyroid cancer and compared the results to those of 27 samples of classic variant of papillary thyroid cancer and 8 samples of normal thyroid tissue. The clinical outcomes of thyroid cancer patients in the study were determined a review of patient records and by review of cancer registry data. The tissue in the study was obtained from the University Hospital in Zurich, Switzerland and surrounding institutions performing pathology reviews. The molecular analyses were performed at the study University of Pittsburgh.

The authors reported that the levels of some microRNAs were similar between samples of follicular variant and classic variant papillary thyroid cancer, but some of the microRNAs expressed were different between the two tumor subtypes. Two newly discovered microRNAs (miR-375 and MiR-551b) were more highly expressed in follicular variant and classic variant papillary thyroid cancer than in normal tissue. The increased expression of two separate microRNAs (miR-181a-2-3p, miR-99b-3p) was associated with a decreased risk of thyroid cancer recurrence for follicular variant of papillary cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that there are differences in microRNA expression between normal thyroid tissue and papillary cancer and between follicular and classic variants of papillary thyroid cancer. Further, the expression of some microRNAs appear to be associated with a better outcome in papillary thyroid cancer. Further studies are required to confirm these findings and to determine if microRNAs will be an important molecular marker to help diagnose and manage the treatment of thyroid cancer in the future.

— Anna Sawka, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://www.thyroid.org/cancer-of-the-thyroid-gland

ABBREVIATIONS & DEFINITIONS

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.

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 CANCER, continued

microRNA: a short RNA molecule that has specific actions within a cell to affect the expression of certain genes.

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.

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

Follicular variant of papillary thyroid cancer: a subtype of papillary cancer that may have a worse prognosis as compared to the classic variant.

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

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THYROID CANCER

Mutations of the RAS oncogene are found in follicular variant papillary thyroid carcinoma

BACKGROUND

Cancer-associated gene mutations are present in over half of thyroid cancers. Molecular markers based on certain cancer-associated genes in thyroid biopsy specimens can be used to either diagnose cancer or to determine that the nodule is benign. The 2 most common gene mutations are BRAF and RAS. These mutations are associated with a high risk of cancer when detected on thyroid nodule biopsy specimens. The aim of this study was to examine the role of screening for RAS expression in thyroid biopsy specimens in patients with thyroid cancer.

THE FULL ARTICLE TITLE

Gupta N et al. RAS mutations in thyroid FNA specimens are highly predictive of predominantly low-risk follicular-pattern cancers. J Clin Endocrinol Metab 2013;98:E914-22. Epub March 28, 2013; doi: 10.1210/jc.2012-3396.

SUMMARY OF THE STUDY

The study included 921 patients who underwent a thyroid nodule biopsy between April 2007 and April 2009. All samples were evaluated with a panel of molecular markers. RAS mutations were found in 7.2% of the biopsies. The thyroid cytology results of these biopsies with positive RAS mutations were read as indeterminate in 93% , cancer in 4% and negative for cancer in 3%.

Of the 63 RAS-positive nodules resected, cancer was confirmed in 83%. These included 46 follicular variant papillary cancers, 4 follicular cancers, one medullary thyroid cancer and one anaplastic thyroid cancer. Only 1/3 of the RAS-positive cancerous nodules had findings on ultrasound that were suspicious of cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study confirms that RAS mutations in thyroid biopsy specimens are strongly suggestive of thyroid cancer, with the vast majority being follicular variant papillary cancers. Further, initial cytology in thyroid biopsies from RAS-positive nodules is mostly indeterminate. Since an ultrasound is frequently not suggestive of cancer in RAS-positive nodules, screening for this mutation in nodules with indeterminate cytology can be helpful to determine whether surgery is indicated. Total thyroidectomy should be considered for initial surgical management of most patients with RAS-positive thyroid biopsy results.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

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

Thyroid Cancer: http://www.thyroid.org/cancer-of-the-thyroid-gland

ABBREVIATIONS & DEFINITIONS

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 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.

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.

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THYROID CANCER, continued

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.

Indeterminate thyroid biopsy: this happens usually when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

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

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

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

Anaplastic thyroid cancer: a very rare but very aggressive type of thyroid cancer. In contrast to all other types of thyroid cancer, most patients with anaplastic thyroid cancer die of their cancer and do so within a few years.

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ATA Alliance for Thyroid Patient Education

WELCOME

The American Thyroid Association is pleased to welcome our two newest members, **Thyroid Federation International** and **Thyroid Cancer Canada**, to the 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

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.

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.

continued on next page

AMERICAN THYROID ASSOCIATION FOUNDED 1923

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

GRAVES' DISEASE & THYROID FOUNDATION

Thyroid Cancer Canada
Cancer de la thyroïde Canada

Light of Life Foundation
checkyourneck.com

Thyroid Federation International

ATA Alliance for Thyroid Patient Education

Continued...

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.

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.

Sixth International Thyroid awareness Week

May 25-31, 2014

Thyroid Federation International (TFI)
takes great pleasure in announcing the topic for the sixth International Thyroid Awareness Week (25 - 31 May 2014). The topic for ITAW 2014 is:

"Thyroid High Five" 5 Reasons to be aware of Thyroid Disease - Thyroid Cancer, Auto-Immune Disease, Infertility, Anxiety/Depression and Iodine Deficiency.

I wanted to share these dates with you so that you can plan ITAW activities accordingly. Please share this topic for ITAW 2014 (International Thyroid Awareness Week) with your members, colleagues, thyroid organizations and academic and community forums for Thyroid education and awareness.

Even till this day too many thyroid related issues go unnoticed. Symptoms are overlooked or misinterpreted as pure signs of stress or depression. The aim of the initiative "International Thyroid Awareness Week" is to raise awareness on thyroid related issues and problems. By conducting programs during and around the ITAW May 25-31, 2014 on this topic you may be able to help patients understand their thyroid related issues better.

Wishing each one of you a very happy New Year.

Ashok Bhaseen, M.Pharm, MMS
President, Thyroid Federation International
A Global Thyroid Patient Organization

www.thyroid-fed.org
www.thyroidweek.org
ashok.bhaseen@thyroid-fed.org