american thyroid association

Clinical Thyroidology for the Public

VOLUME 9 • ISSUE 10 • OCTOBER 2016

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CLINICAL **THYROIDOLOGY** FOR THE **PUBLIC**
A publication of the American Thyroid Association
VOLUME 9 • ISSUE 10 • OCTOBER 2016

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*.

October is Thyroid Nodule Awareness Month.

In this issue, the studies ask the following questions:

1. Are low TSH levels early in pregnancy normal or abnormal?
2. Does increasing levothyroxine doses early in pregnancy affect miscarriage?
3. What predicts lack of compliance with thyroid hormone during pregnancy in hypothyroid women?
4. Does thyroid autoimmunity affect fertility?
5. How often does the Afirma Gene Expression Classifier detect noninvasive papillary thyroid cancer?
6. What is the risk of childhood radiation on the development of thyroid cancer in adults?

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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THYROID AND PREGNANCY

Low TSH levels early on in pregnancy may be normal

BACKGROUND

Thyroid hormone is essential for the normal development of the baby during pregnancy. During the first half of pregnancy, the presence of thyroid hormones in the developing baby is entirely dependent on the mother since the baby's thyroid does not begin to function until the 2nd trimester. Abnormal thyroid function in the mother during pregnancy may increase the risk of miscarriage and other pregnancy complications. The American Thyroid association has published several guidelines for the detection and management of thyroid problems during pregnancy. Thyroid hormone levels in the mother do change during pregnancy. This study examined these changes to determine the normal ranges of thyroid hormones during pregnancy.

THE FULL ARTICLE TITLE

Laurberg P et al Dynamics and predictors of serum TSH and fT_4 reference limits in early pregnancy: a study within the Danish National Birth Cohort. J Clin Endocrinol Metab 2016;101:2484-92. Epub April 26, 2016.

SUMMARY OF THE STUDY

Pregnant women under study were part of the Danish National Birth Cohort, in which participants had their first pregnancy visit in a general practice, including the sampling of blood to be stored deep-frozen at the Danish National Biobank. About 50% of Danish pregnant women were invited; 60% of these women agreed to participate. The pregnancy included in the present study was the woman's first pregnancy recorded in the DNBC, with the delivery of a single child. Gestational age at birth had to be in the 25-to-45-week range. Women were interviewed before gestational week 30 with regard to smoking during the pregnancy, prepregnancy alcohol intake, and prepregnancy BMI. Information was also available by linking to Danish nationwide health registers and Statistic Denmark for population characteristics. Among the 71,706 women who fulfilled the criteria, 8605 were selected as a 12% random sample. Of this sample, 6671 healthy participants with normal thyroid function initially were included in the study.

TSH levels decreased gradually at weeks 5 to 6 to the lowest point at weeks 9 to 12 (range 0.07 - 3.28 mU/L). This is followed by a rise back to an intermediate value at weeks 15 to 19 (range 1.29 - 3.29 mU/L). The largest changes occurred at the lower end of the range as the lower limit of TSH was 0.37 at weeks 5 to 6, 0.059 at weeks 10 to 11 and 0.11 at weeks 13 to 19. Serum FT_4 changes were the reverse of those of TSH, but much less pronounced. The authors considered two phases with relatively stable TSH levels: (a) a normal TSH period corresponding to gestational weeks 5 to 6, during which non-pregnant reference TSH and FT_4 values are appropriate, and (b) a low TSH period, corresponding to weeks 9 to 12 with TSH reference limit values lower and FT_4 reference limit values slightly higher than non-pregnant levels. In general, the low range of TSH was higher in obese women. Smoking did not affect TSH values, but the FT_4 was slightly higher in nonsmoking pregnant women.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This article clearly shows that TSH values vary significantly during the first trimester of pregnancy. Changes encompass two stable periods, the normal TSH one at the very beginning of pregnancy and the low TSH one at weeks 9 to 12. This is followed a partial return of TSH to the initial values. This is important for the evaluation of thyroid function in women during pregnancy and clearly shows that a low TSH can be normal early on in pregnancy and should not be treated.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

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

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

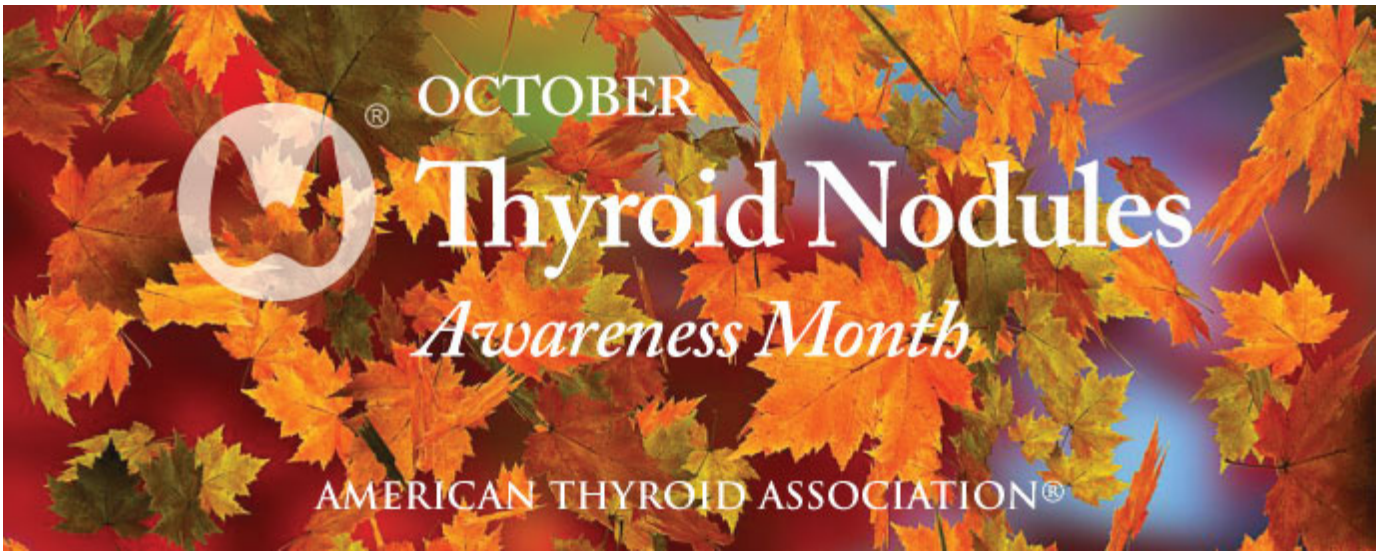
THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

Body-mass index (BMI): a standardized measure of obesity calculated by dividing the weight in kilograms by the square of the height. A normal BMI is 18.5-24.9, overweight is 25-30 and obese is >30.

Miscarriage: this occurs when a baby dies in the first few months of a pregnancy, usually before 22 weeks of pregnancy.

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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THYROID AND PREGNANCY

Increasing levothyroxine doses early in pregnancy is associated with a lower risk for pregnancy loss in hypothyroid women

BACKGROUND

In pregnancy, appropriate treatment of hypothyroidism is very important because low levels of thyroid hormone in the mother may harm her baby or even cause pregnancy loss or miscarriage. Higher levels of thyroid hormone are needed during pregnancy and, in women with normal thyroid function, the thyroid gland increases the production of thyroid hormone to meet this increased need. In hypothyroid women, this often means that the dose of Levothyroxine needs to be increased during pregnancy. Many endocrinologists advise pregnant women to take a higher dose of Levothyroxine as soon as pregnancy is confirmed and to come in to have blood tests for TSH more often to ensure that the level remains normal. This study was done to evaluate the effect of increasing Levothyroxine dose in preventing pregnancy loss in women with hypothyroidism.

THE FULL ARTICLE TITLE

Maraka S et Effects of increasing levothyroxine on pregnancy outcomes in women with uncontrolled hypothyroidism. Clin Endocrinol (Oxf). August 3, 2016 [Epub ahead of print].

SUMMARY OF THE STUDY

In this study, 96 hypothyroid women who were treated in Mayo Clinic in Rochester, Minnesota from 2011 to 2013 were included. They were between 18 to 45 years old and all were treated with Levothyroxine before becoming pregnant and all had a blood test for TSH in first trimester of pregnancy with level of more than 2.5 mIU/L (the goal level of TSH in first trimester of pregnancy is less than 2.5).

The information about the age, body mass index, medical conditions, ethnicity, level of education, employment, smoking and use of illegal drugs, complications and course of pregnancy was obtained by reviewing medical charts The patients were divided into two groups; group 1 consisted of 85 women who had immediate increase of Levothyroxine dose after the thyroid blood test in first trimester of pregnancy showed abnormal TSH and group 2 consisted of 11 women who did not have any adjustment in levothyroxine dose. The rate of miscarriage and death of baby after 22nd week of pregnancy was compared between the two groups. Women who did not have any adjustment in Levothyroxine dose had a higher level of TSH in their last pregnancy blood test; 36% of women in this group had lost their pregnancy due to miscarriage. The rate of pregnancy loss was 2.4% in women who took a higher dose of thyroid hormone after pregnancy. No difference was found between the two groups in the rate of other pregnancy complications.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study confirms that the dose requirements for Levothyroxine increase during pregnancy and shows that an increase in the Levothyroxine dose early in pregnancy may prevent some cases of pregnancy loss and miscarriage. The result of this study is important for young women and their physicians and re-affirms the need for close monitoring of thyroid levels during pregnancy.

— Shirin Haddady, MD

ATA THYROID BROCHURE LINKS

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

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

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

THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

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

Levothyroxine (T_4): 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.

Body-Mass Index (BMI): a standardized measure of obesity calculated by dividing the weight in kilograms by the square of the height. A normal BMI is 18.5-24.9, overweight is 25–30 and obese is >30.

Miscarriage: this occurs when a baby dies in the first few months of a pregnancy, usually before 22 weeks of pregnancy.

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HYPOTHYROIDISM

What predicts lack of compliance with thyroid hormone during pregnancy in hypothyroid women?

BACKGROUND

It is well known that untreated and under-treated hypothyroidism during pregnancy leads to increased miscarriage and pregnancy complications. Women that take their thyroid hormone regularly and keep their TSH values in the normal range will have less problems during pregnancy and their babies will have improved developmental outcomes.

There are studies that show that there are many women who do not take their thyroid hormone regularly while pregnant. Sometimes, a woman's concern about the safety of the medication or a particular personality trait may influence their compliance with this medication. The goal of this study was to identify certain factors that may predict lack of compliance with thyroid hormone during pregnancy. This, in turn, will allow for more specific interventions, such as education, targeted to women identified to be less likely to be compliant.

THE FULL ARTICLE TITLE

Juch H et al Medication adherence among pregnant women with hypothyroidism—missed opportunities to improve reproductive health? A cross-sectional, web-based study. Patient Educ Couns. April 11, 2016 [Epub ahead of print].

SUMMARY OF THE STUDY

This study was done using an anonymous online questionnaire available in 18 countries in North America, Australia and Europe that was accessed via websites and social networks for pregnant women. Data was collected during a period of two months. Pregnant women with self-reported hypothyroidism were included in the study.

The questionnaire was comprehensive and included questions about marital status, education, age, immigration status among others. A section asked for information about the type of medication used to treat the hypothyroidism and about other health problems and their treatment. Depression and certain personality traits were also addressed.

A total of 5095 women completed the questionnaire and of these, 231 women reported being hypothyroid. Of these women, 197 were using levothyroxine, 16 were using other treatments including iodine and T_3 hormone and 16 reported not taking any medication. Among women taking medications, 17% said that they had low adherence to taking their thyroid medicine; 44% reported medium adherence and 39% reported high adherence. The reasons given for not taking their medications regularly included forgetfulness or just being hassled about their treatment plan. When further analysis of data was done to eliminate other factors, younger age, not taking prenatal vitamins and agreement with the general statement that it is better to not take medications while pregnant were associated with low medication adherence. Women who reported believing that untreated hypothyroidism was more risky than the medication itself, and those women with high scores for conscientiousness were more likely to be adherent.

The 16 hypothyroid women who did not use thyroid medicines during pregnancy were more likely to smoke, less likely to be married or live with a partner, less likely to take prenatal or over the counter medicines, and had higher scores for neuroticism as a personality trait than the women who did use medications.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Surprisingly, 17% of hypothyroid women reported low adherence to thyroid medication during pregnancy and 7% of pregnant hypothyroid women reported not taking any thyroid medication. The high percentage of patients reporting poor compliance with a simple and safe regimen of treatment for a common condition is worrisome. More patient education is essential regarding the treatment of hypothyroidism during pregnancy.

— Jesse Block-Galaraza, MD

ATA THYROID BROCHURE LINKS

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

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

HYPOTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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

Triiodothyronine (T3): the active thyroid hormone, usually produced from thyroxine.

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.

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 September is **Thyroid Nodule 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 AND PREGNANCY

Thyroid autoimmunity and infertility treatments

BACKGROUND

Autoimmune thyroid disease is very common in women of childbearing age and can lead to either an overactive (Graves' disease, hyperthyroidism) or underactive thyroid (Hashimoto's thyroiditis, hypothyroidism). Autoimmune thyroid disease occurs when the body makes antibodies that attack the thyroid and turn it on or off. This is characterized by positive TPO and/or thyroglobulin antibodies and is most commonly associated with in increased risk of developing hypothyroidism. Women with positive TPO antibodies have been shown to have an increased risk of pregnancy complications, including miscarriage and preterm labor. Autoimmune thyroid disease has been shown to be more common in women seeking treatment for infertility. This study sought to determine the effect of autoimmune thyroid disease on the success of assisted reproduction techniques (infertility treatments), specifically in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI).

THE FULL ARTICLE TITLE

Busnelli A et al. The impact of thyroid autoimmunity on IVF/ICSI outcome: a systematic review and meta-analysis. Hum Reprod Update. June 20, 2016 [Epub ahead of print].

SUMMARY OF THE STUDY

These investigators examined 12 studies identified in the medical literature to investigate the relationship between autoimmune thyroid disease and pregnancy outcomes. Autoimmune thyroid disease was defined by positive TPO and/or thyroglobulin antibodies and the primary outcome examined was live births in women who received the infertility treatments of IVF or ICSI. Women with autoimmune thyroid disease had a significantly lower (35%) live birth rate than women without autoimmune thyroid disease. Interestingly, these investigators found that having autoimmune thyroid disease did not seem to negatively impact the success of the fertility procedure itself and there were no differences identified in number of eggs retrieved, fertilization rates, implantation rates or confirmed pregnancy rates. They did report that women with autoimmune thyroid disease had a higher miscarriage rate and that this presumably explained the lower live birth rate. Although all of the women had normal thyroid function as measured by TSH, women with autoimmune thyroid disease had higher TSH values as a group than women without autoimmune thyroid disease. Despite the fact that hypothyroidism is known to have an adverse effects on pregnancy success, TSH levels did not predict live birth or miscarriage rates in this study. In summary, women with autoimmune thyroid disease had lower live birth rates and higher miscarriage rates following infertility treatment, independent of thyroid function. Further studies are warranted to understand the mechanism(s) leading to less successful pregnancy outcomes in women with autoimmune thyroid disease.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Women with autoimmune thyroid disease and normal thyroid function have less successful pregnancy outcomes (fewer live births and more likely to have a miscarriage) following fertility treatments (IVF or ICSI) than women without autoimmune thyroid disease. The underlying mechanism is not known but future studies should be designed to better understand this process and hopefully lead to identification of appropriate prevention strategies.

— Whitney W. Woodmansee MD

ATA THYROID BROCHURE LINKS

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

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

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

THYROID AND PREGNANCY, continued

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).

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

Thyroglobulin 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.

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.

Miscarriage: this occurs when a baby dies in the first few months of a pregnancy, usually before 22 weeks of pregnancy.

In-Vitro Fertilization (IVF): a procedure when an egg is fertilized outside of the body and then implanted in a woman to achieve a pregnancy. A specific type of IVF is intracytoplasmic sperm injection (ICSI).

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THYROID CANCER

Suspicious readings of the Afirma gene-expression classifier include some noninvasive encapsulated follicular variant of papillary thyroid carcinomas

BACKGROUND

Thyroid nodules are commonly found on ultrasound of the neck and the evaluation of a thyroid nodule may include thyroid biopsy. Thyroid nodule biopsies are used to identify if a nodule is cancerous or determine the risk that a thyroid nodule may be cancerous. Sometimes, thyroid biopsy specimens are indeterminate, meaning that thyroid cancer cannot be definitively ruled in or out. In such cases, testing of molecular markers related to thyroid cancer may help determine the risk of cancer. One such molecular marker test is the Afirma gene expression classifier (GEC) test. The results of the GEC are either read as suspicious for cancer or benign.

Papillary thyroid cancer is the most common type of thyroid cancer. A group of expert pathologists have recently identified a subgroup of papillary thyroid cancer called noninvasive follicular variant papillary thyroid cancer that has a very low risk of relapsing after surgical removal. Because of this rather benign course, some pathologists have even questioned whether this subgroup is a cancer after all.

The aim of this study was to find out how often indeterminate thyroid biopsy specimens which were read as "suspicious" by the GEC test were ultimately diagnosed as noninvasive follicular variant papillary thyroid cancer after surgery.

THE FULL ARTICLE TITLE

Wong KS et al. Noninvasive follicular variant of papillary thyroid carcinoma and the Afirma gene-expression classifier. Thyroid 2016;26:911-5.

SUMMARY OF THE STUDY

In this study from Boston, 63 thyroid surgical specimens were reviewed from patients whose thyroid biopsy samples were read as indeterminate and in whom the GEC test was reported as suspicious. The authors reported the following rates of final diagnoses for these specimens: 65% of cases had no cancer (ie. benign), 25% of cases had follicular variant papillary thyroid cancer, 2% of cases had classical papillary thyroid cancer and 8% of cases had follicular thyroid cancer. Of the 16 cases of follicular variant papillary thyroid cancer, 14 of them were noninvasive follicular variant of papillary thyroid cancer (88%).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that a GEC suspicious test result may include noninvasive follicular variant papillary thyroid cancer as well as classical papillary thyroid cancer. An important limitation of this study is that the authors did not examine the rate of noninvasive follicular variant papillary thyroid cancer in specimens that were not reported as suspicious by the GEC test. This study suggests that more research is needed to determine if the noninvasive follicular variant thyroid cancer can be diagnosed by molecular markers without proceeding to surgery.

— Anna Sawka, MD

ATA THYROID BROCHURE LINKS

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

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

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

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

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

Thyroid Fine Needle Aspiration Biopsy (FNAB): a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

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

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. There are 3 variants of papillary thyroid cancer: classic, follicular and tall-cell.

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.

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THYROID CANCER

Exposure to radiation in childhood increases risk for thyroid cancer even in low doses

BACKGROUND

Exposure to ionizing radiation has been demonstrated to increase thyroid cancer risk over time. It is known that children's exposure to radiation leads to a higher risk for thyroid cancer in adulthood. This is because children's thyroid glands are more sensitive to radiation than adult thyroid glands. Previous studies showed an elevated risk for thyroid cancer in childhood cancer survivors. However, smaller radiation doses were previously also used for non-cancer disorders, such as treatment for fungal skin infections, thymus (a gland just below the thyroid) or tonsillar enlargement, and benign hemangiomas (non-cancerous growths of blood vessels under the skin) in infants and children. One of the studies included environmental radiation exposure, as the Japanese atomic bomb survivors were included.

This study was done to further characterize the risk of even small doses of radiation on developing thyroid cancer in children. In particular, this study was done to evaluate the dose-response pattern of radiation in children, to determine the role of chemotherapy drugs in this risk and to evaluate other factors such as age at exposure in risk for thyroid cancer.

THE FULL ARTICLE TITLE

Veiga LH et al Thyroid Cancer after Childhood Exposure to External Radiation: An Updated Pooled Analysis of 12 Studies. Radiat Res. 2016;185(5):473-84. Epub April 29, 2016.

SUMMARY OF THE STUDY

Original data from 12 studies of people exposed to radiation at ages under 20 years old were used. These studies contained information about thyroid cancers that developed after treatment for other cancers. This expanded upon a previous report in 1995 of 7 studies with additional information and longer follow-up. The study used a complex statistical analysis to determine the risk of use of radiation. Age at exposure, calendar year of follow-up, time since exposure, age reached, exposure to chemotherapy drugs, thyroid radiation dose, and number of treatments were evaluated. They considered thyroid cancer cases as secondary if the patients had been treated with radiation for cancer, or primary if the patient had been treated with radiation for non-cancerous reasons.

A total of 1070 thyroid cancers were recorded and 79% of the cancers were papillary cancer. However, even the non-papillary thyroid cancers were shown to have a similar radiation risk pattern. The average age at radiation exposure was 5 years old and the average age at thyroid cancer diagnosis was 41 years old.

The risk of thyroid cancer increased with increasing doses of radiation exposure, even with very low doses. Interestingly, high radiation doses were shown to decrease the risk, probably because high doses are likely to cause cell death. Chemotherapy drugs causes a 4-fold increased risk. The risks were not different in boys and girls. This increased risk of thyroid cancer from radiation exposure may occur as soon as 5-10 years after treatment and may persist for patients for 50 years or more after the radiation. There was some variability in this result, however.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The risk of thyroid cancer increased after radiation exposure, even at very low doses. Chemotherapy drugs had an additive association with thyroid cancer risk. Thyroid cancer risk is elevated as soon as 5-10 years from treatment for many decades thereafter. This information adds to the knowledge base and understanding of patients at high risk for thyroid cancer and identification of those at risk based upon the treatment history and duration of time since the exposure

— Julie Hallanger Johnson, MD

ATA THYROID BROCHURE LINKS

Childhood Head and Neck Irradiation:
http://www.thyroid.org/pediatric-endocrinology/

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

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THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Ionizing Radiation: radiation that can damage cells, causing cell death or mutation. It can originate from radioactive materials, x-ray tubes or specialized machines. It is invisible and not directly detectable by human senses.

Chemotherapy: cancer fighting drugs that kill cancer cells. These drugs can also damage normal cells.

Papillary Thyroid Cancer: the most common type of thyroid cancer. There are 3 variants of papillary thyroid cancer: classic, follicular and tall-cell.

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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 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-portal/
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

BITE ME CANCER!

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

Thyroid Cancer Canada
Cancer de la thyroïde Canada

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.

continued on next page

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

Light of Life Foundation
checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

Thyroid Federation International

BITE ME CANCER!

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

Thyroid Cancer Canada
Cancer de la thyroïde Canada

ATA Alliance for Thyroid Patient Education

Continued...

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

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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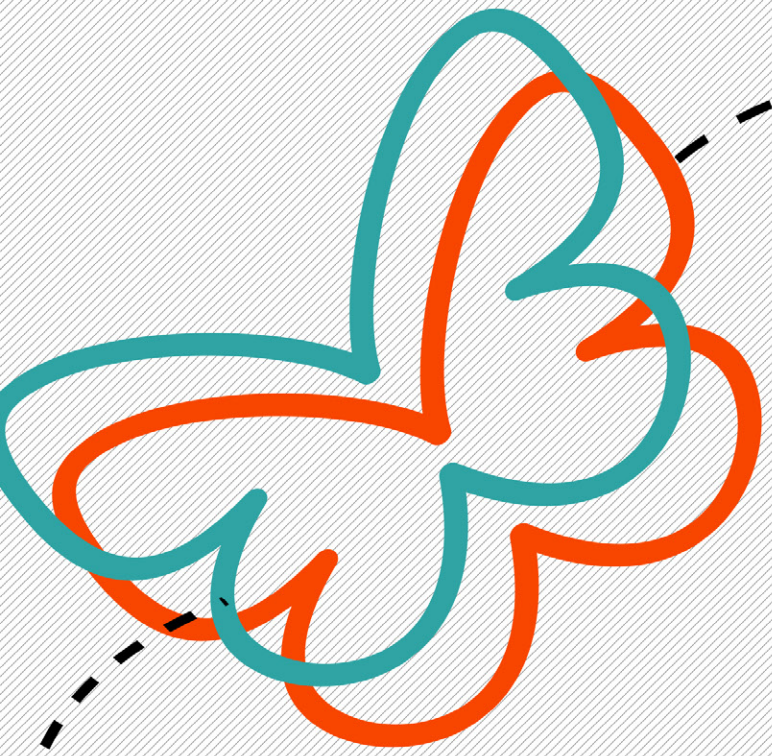
Reasons to #GIVE2THYROID

www.thyroid.org/donate



Reason 1

Public & Thyroid Patients

The American Thyroid Association® is dedicated to serving as an educational resource for the public by supporting thyroid research and promoting the prevention, treatment and cure of thyroid-related diseases and thyroid cancer. Help support the continuation of our patient/public education programs and resources including:

+thyroid brochures
+summarized medical literature
+endocrinologist referral
+monthly newsletters
+support links
+patient alliance community
+health and education forums

Reason 2

Thyroid Physicians, Scientists & Professionals

The American Thyroid Association® provides outstanding leadership in thyroidology by promoting excellence and innovation in clinical management, research, education, and patient care. Help support thyroid specialists and the development of resources that advance our understanding of thyroid disorders and cancer including:

+clinical practice guidelines
+position statements
+early career training
+research and education grants
+leadership & service awards
+community for collaboration
+continuing education programs
+peer-review biomedical journals
+summarized medical literature
+up to date thyroid news & publications
+patient education

American Thyroid Association

#GIVE2THYROID

www.thyroid.org/donate

Thyroid Nodules

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 A THYROID NODULE?

The term thyroid nodule refers to an abnormal growth of thyroid cells that forms a lump within the thyroid gland. Although the vast majority of thyroid nodules are benign (noncancerous), a small proportion of thyroid nodules do contain thyroid cancer. In order to diagnose and treat thyroid cancer at the earliest stage, most thyroid nodules need some type of evaluation.

WHAT ARE THE SYMPTOMS OF A THYROID NODULE?

Most thyroid nodules do not cause symptoms. Often, thyroid nodules are discovered incidentally during a routine physical examination or on imaging tests like CT scans or neck ultrasound done for completely unrelated reasons. Occasionally, patients themselves find thyroid nodules by noticing a lump in their neck while looking in a mirror, buttoning their collar, or fastening a necklace. Abnormal thyroid function tests may occasionally be the reason a thyroid nodule is found. Thyroid nodules may produce excess amounts of thyroid hormone causing hyperthyroidism (see *Hyperthyroidism brochure*). However, most thyroid nodules, including those that cancerous, are actually non-functioning, meaning tests like TSH are normal. Rarely, patients with thyroid nodules may complain of pain in the neck, jaw, or ear. If a nodule is large enough to compress the windpipe or esophagus, it may cause difficulty with breathing, swallowing, or cause a "tickle in the throat". Even less commonly, hoarseness can be caused if the nodule invades the nerve that controls the vocal cords but this is usually related to thyroid cancer.

The important points to remember are the following:

- Thyroid nodules generally do not cause symptoms.
- Thyroid tests are most typically normal—even when cancer is present in a nodule.
- The best way to find a thyroid nodule is to make sure your doctor checks your neck!

WHAT CAUSES THYROID NODULES AND HOW COMMON ARE THEY?

We do not know what causes most thyroid nodules but they are extremely common. By age 60, about one-half of all people have a thyroid nodule that can be found either through examination or with imaging. Fortunately, over 90% of such nodules are benign. Hashimoto's thyroiditis, which is the most common cause of hypothyroidism (see *Hypothyroidism brochure*), is associated with an increased risk of thyroid nodules. Iodine deficiency, which is very uncommon in the United States, is also known to cause thyroid nodules.

HOW IS A THYROID NODULE EVALUATED AND DIAGNOSED?

Once the nodule is discovered, your doctor will try to determine whether the rest of your thyroid is healthy or whether the entire thyroid gland has been affected by a more general condition such as hyperthyroidism or hypothyroidism. Your physician will feel the thyroid to see whether the entire gland is enlarged and whether a single or multiple nodules are present. The initial laboratory tests may include measurement of thyroid hormone (thyroxine, or T4) and thyroid-stimulating hormone (TSH) in your blood to determine whether your thyroid is functioning normally.

Since it's usually not possible to determine whether a thyroid nodule is cancerous by physical examination and blood tests alone, the evaluation of the thyroid nodules often includes specialized tests such as thyroid ultrasonography and fine needle biopsy.

Thyroid Nodules

THYROID ULTRASOUND:

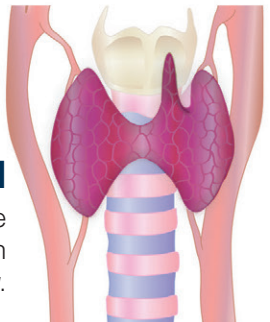
Thyroid ultrasound is a key tool for thyroid nodule evaluation. It uses high-frequency sound waves to obtain a picture of the thyroid. This very accurate test can easily determine if a nodule is solid or fluid filled (cystic), and it can determine the precise size of the nodule. Ultrasound can help identify suspicious nodules since some ultrasound characteristics of thyroid nodules are more frequent in thyroid cancer than in noncancerous nodules. Thyroid ultrasound can identify nodules that are too small to feel during a physical examination. Ultrasound can also be used to accurately guide a needle directly into a nodule when your doctor thinks a fine needle biopsy is needed. Once the initial evaluation is completed, thyroid ultrasound can be used to keep an eye on thyroid nodules that do not require surgery to determine if they are growing or shrinking over time. The ultrasound is a painless test which many doctors may be able to perform in their own office.

THYROID FINE NEEDLE ASPIRATION BIOPSY (FNA OR FNAB):

A fine needle biopsy of a thyroid nodule may sound frightening, but the needle used is very small and a local anesthetic may not even be necessary. This simple procedure is often done in the doctor's office. Sometimes, medications like blood thinners may need to be stopped for a few days before to the procedure. Otherwise, the biopsy does not usually require any other special preparation (no fasting). Patients typically return home or to work after the biopsy without even needing a bandaid! For a fine needle biopsy, your doctor will use a very thin needle to withdraw cells from the thyroid nodule. Ordinarily, several samples will be taken from different parts of the nodule to give your doctor the best chance of finding cancerous cells if they are present. The cells are then examined under a microscope by a pathologist.

The report of a thyroid fine needle biopsy will usually indicate one of the following findings:

1. The nodule is benign (noncancerous).
   - This result is obtained in up to 80% of biopsies. The risk of overlooking a cancer when the biopsy is benign is generally less than 3 in 100 tests or 3%. This is even lower when the biopsy is reviewed by an experienced pathologist at a major medical center. Generally, benign thyroid nodules do not need to be removed unless they are causing symptoms like choking or difficulty swallowing. Follow up ultrasound exams are important. Occasionally, another biopsy may be required in the future, especially if the nodule grows over time.
2. The nodule is malignant (cancerous) or suspicious for malignancy .
   - A malignant result is obtained in about 5% of biopsies and is most often due to papillary cancer, which is the most common type of thyroid cancer. A suspicious biopsy has a 50-75% risk of cancer in the nodule. These diagnoses require surgical removal of the thyroid after consultation with your endocrinologist and surgeon.
3. The nodule is indeterminate. This is actually a group of several diagnoses that may occur in up to 20% of cases. An Indeterminate finding means that even though an adequate number of cells was removed during the fine needle biopsy, examination with a microscope cannot reliably classify the result as benign or cancer.
   - The biopsy may be indeterminate because the nodule is described as a Follicular Lesion. These nodules are cancerous 20-30% of the time. However, the diagnosis can only be made by surgery. Since the odds that the nodule is not a cancer are much better here (70-80%), only the side of the thyroid with the nodule is usually removed. If a cancer is found, the remaining thyroid gland usually must be removed as well. If the surgery confirms that no cancer is present, no additional surgery to "complete" the thyroidectomy is necessary.
   - The biopsy may also be indeterminate because the cells from the nodule have features that cannot be placed in one of the other diagnostic categories. This diagnosis is called atypia, or a follicular lesion of undetermined significance. Diagnoses in this category will contain cancer rarely, so repeat evaluation with FNA or surgical biopsy to remove half of the thyroid containing the nodule is usually recommended.
4. The biopsy may also be nondiagnostic or inadequate. This result is obtained in less than 5% of cases when an ultrasound is used to guide the FNA. This result indicates that not enough cells were obtained to make a diagnosis but is a common result if the nodule is a cyst. These nodules may require reevaluation with second fine needle biopsy, or may need to be removed surgically depending on the clinical judgment of your doctor.



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*.

Thyroid Nodules

NUCLEAR THYROID SCANS:

Nuclear scanning of the thyroid was frequently done in the past to evaluate thyroid nodules. However, use of thyroid ultrasound and biopsy have proven so accurate and sensitive, nuclear scanning is no longer considered a first-line method of evaluation. Nuclear scanning still has an important role in the evaluation of rare nodules that cause hyperthyroidism. In this situation, the nuclear thyroid scan may suggest that no further evaluation or biopsy is needed. In most other situations, neck ultrasound and biopsy remain the best and most accurate way to evaluate all types of thyroid nodules.

MOLECULAR DIAGNOSTICS:

Can any other tests assist in evaluation of thyroid nodules?

Yes! While still mainly research tests and not widely available, new tests that examine genes in the DNA of thyroid nodules are being developed. These tests can provide helpful information about whether cancer may be present or absent. These tests are particularly helpful when the specimen evaluated by the pathologist is indeterminate. These specialized tests are done on samples obtained during the normal biopsy process. There are also specialized blood tests that can assist in the evaluation of thyroid nodules. These are currently available only at highly specialized medical centers, however, their availability is increasing rapidly. Ask your doctor if these tests are available and might be helpful for evaluating your thyroid nodule.

HOW ARE THYROID NODULES TREATED?

All thyroid nodules that are found to contain a thyroid cancer, or that are highly suspicious of containing a cancer, should be removed surgically by an experienced thyroid surgeon. Most thyroid cancers are curable and rarely cause life-threatening problems (see *Thyroid Cancer brochure*). Thyroid nodules that are benign by FNA or too small to biopsy should still be watched closely with ultrasound examination every 6 to 12 months and annual physical examination by your doctor. Surgery may still be recommended even for a nodule that is benign by FNA if it continues to grow, or develops worrisome features on ultrasound over the course of follow up.

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***.