american thyroid association

Clinical Thyroidology for the Public

VOLUME 10 • ISSUE 3 • MARCH 2017

www.thyroid.org

Air pollution is a mixture of several particles, including metals, nitrate and organic materials, which have been shown to affect endocrine glands. Exposure to air pollution has also been associated with an increased risk for low birth weight and preterm birth. This study was done to determine whether exposure to air pollution during late pregnancy affects the mother's and/or the baby's thyroid function and birth weight.

Janssen BG et al Fetal thyroid function, birth weight, and in utero exposure to fine particle air pollution: a birth cohort study. Environ Health Perspect. September 13, 2016

Some clinical studies have shown an increased risk of heart disease and death in patients with hypothyroidism. Further, an association has been suggested between TSH levels near the upper limit of the normal range and death in some studies. This study evaluates the risk of death associated with levels of TSH in the normal range.

Inoue K et al. Association between serum thyrotropin levels and mortality among euthyroid adults in the United States. Thyroid. September 13, 2016

Atrial fibrillation is common in hyperthyroidism and if severe, can lead to heart failure and is a cause of the rare deaths due to hyperthyroidism. However, information regarding hyperthyroidism and sudden cardiac death is limited. Further, there is no information linking thyroid hormone levels and sudden cardiac death. The present study examined the relationship between sudden cardiac death and thyroid function tests, focusing on subjects who would be considered not to be hyperthyroid.

Chaker L et al. Thyroid function and sudden cardiac death: a prospective population-based cohort study. Circulation 2016;134:713-22.

There have been studies suggesting that higher levels of free T_4 in the blood may be associated with an increased risk of developing a solid cancers. Other studies have not agreed with this finding. This study looks at a large group of people to determine whether T_4, even within the normal range, may increase the risk of developing any solid cancer.

Khan SR et al. Thyroid function and cancer risk: the Rotterdam Study. J Clin Endocrinol Metab. September 20, 2016 [Epub ahead of print].

Patients with Graves' disease can be treated with antithyroid drugs with the goal of the patient eventually going into remission. However, approximately in half of the patients, Graves' disease relapses after the initial ATD treatment, requiring a second ATD course or different treatments for control of the hyperthyroidism. Several studies have reported risk factors that might predict relapse after the ATD discontinuation. The goal of this analysis is to evaluate all previously reported risk factors and find a prediction rule for relapse after discontinuation of the initial ATD treatment in patients with Graves' disease.

Struja T et al Can we predict relapse in Graves' disease? Results from a systematic review and meta-analysis. Eur J Endocrinol 2017; 176:87-97. Epub October 25, 2016.

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CLINICAL **THYROIDOLOGY** FOR THE **PUBLIC**
A publication of the American Thyroid Association
VOLUME 10 • ISSUE 3 • MARCH 2017

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*.

March is Medullary Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

1. Does air pollution affect the baby's thyroid function during pregnancy?
2. Are high TSH levels a risk factor for death from all causes?
3. Are high FT_4 levels a risk factor for sudden cardiac death?
4. Are high FT_4 levels a risk factor for cancer?
5. Can we predict which Graves disease patients will relapse after antithyroid drugs are stopped?

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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HYPOTHYROIDISM

Air pollution may alter the baby's thyroid function during pregnancy

BACKGROUND

Thyroid hormones are critical for the growth and development of babies during pregnancy. During the first trimester of pregnancy, the mother supplies thyroid hormones. However, starting in the second trimester, the developing baby is able to produce his/her own thyroid hormone. T_4 is the major form of thyroid hormone released by the thyroid gland and T_3 is the most active form of thyroid hormone. Both are controlled by thyroid stimulating hormone (TSH). Chemicals that disrupt endocrine glands (endocrine disruptors) are being studied. Organic compounds, chemicals such as cadmium and cigarette smoking may affect thyroid regulation. Air pollution is a mixture of several particles, including metals, nitrate and organic materials, which have been shown to affect endocrine glands. Exposure to air pollution has also been associated with an increased risk for low birth weight and preterm birth. However, the role of air pollution on the baby's thyroid during pregnancy is not known. This study was done to determine whether exposure to air pollution during late pregnancy affects the mother's and/or the baby's thyroid function and birth weight.

THE FULL ARTICLE TITLE

Janssen BG et al Fetal thyroid function, birth weight, and in utero exposure to fine particle air pollution: a birth cohort study. Environ Health Perspect. September 13, 2016

SUMMARY OF THE STUDY

The authors studied 640 mother–child pairs from the East Limburg Hospital in Genk, Belgium, between February 2010 and June 2014. Mother-children pairs were part of the ENVIRONAGE birth cohort study. They obtained data from small particles in the air, with a diameter equal or less to 2.5 μm, based on the mother's home address using a system that permits correlation with space and time from satellite images. Using this system, they were able to obtain daily air small particle values using data from the Belgian network that studies air-quality. The outcomes were obtained for the third trimester of pregnancy and the average exposure value was used after correction for environmental factors such as temperature and humidity. Data on subject characteristics was obtained through questionnaires. They also reviewed other factors associated with pregnancies, by reviewing the medical files of the hospital. Umbilical cord and blood samples from the mother were collected at the time of delivery or up to 1 day after delivery. They had data for 499 newborns and 431 mothers.

The range of the small particles in the air was divided into 4 ranges. For each higher range, cord-blood TSH concentrations were 11.6% lower; cord-blood FT_4 concentrations were 3.7% lower and cord-blood FT_3 concentrations were 6.4% higher. The effect on the mother's laboratory tests did not reach significance. Only free T_4 levels were associated with birth weight. An 11% decrease in cord blood free T_4 was associated with a decrease of 56 grams in birth weight, after adjusting for other variables.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows for the first time that exposure to air pollution decreases cord Free T_4 and increases cord Free T_3 level. Lower cord Free T_4 levels were also associated with lower birth weight. This study is important because, although the data is limited, it highlights the need to do more research in environmental health and air pollution.

— Liuska Pesce, 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, continued

ABBREVIATIONS & DEFINITIONS

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

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

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.

Endocrine disruptors: chemical pollutants in the environment that can affect the action of endocrine glands. Examples include bisphenol A (BPA), polychlorinated biphenols (PCBs), perfluoroalkyl substances (PFAs) and organochlorines (OCs).

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THYROID AND THE HEART

TSH levels and the risk of death

BACKGROUND

There are clear effects of thyroid hormone on the heart. Some clinical studies have shown an increased risk of heart disease and death in patients with hypothyroidism, both mild and overt. Similarly, there have been some reports of and increased risk of death in patients with overt hyperthyroidism (Graves' disease) and there is a clear risk of a normal heart rhythms (atrial fibrillation) in individuals with a low TSH for any reason. Further, an association has been suggested between TSH levels near the upper limit of the normal range and death in some studies. This study evaluates the risk of death associated with levels of TSH in the normal range.

THE FULL ARTICLE TITLE

Inoue K et al. Association between serum thyrotropin levels and mortality among euthyroid adults in the United States. Thyroid. September 13, 2016

SUMMARY OF THE STUDY

This study looked at approximately 13,000 adults who had a TSH blood test. The data was obtained from individuals who participated in the National Health and Nutrition Examination Survey (NHANES) III from the years 1988 through 1994. Associations between thyroid tests (TSH) and death from all causes, heart disease and cancer was studied. The reference normal range for the TSH test in this survey was 0.39 to 4.60 mIu/l. A similar study was then also done in the survey from later years (between 2001 to 2010) that also had the thyroid hormone free T_4 levels available.

Overall, a higher risk of death from heart disease and cancer as well as death from all causes was noted in those individuals who had the TSH levels in the low normal (average 0.83) or high normal (average 2.64) range. Further analysis of the groups from 2000 to 2010 no such association with high TSH or low free T_4 levels.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Although the study suggests an association between an increased risk of death and either low or high normal TSH levels, the data is not conclusive. Importantly, this study looked at associations, not causes, and is not saying that thyroid function in the normal range contributed to the increased risk of death. There were limitations including the inconsistencies between the older and newer surveys. There were also age differences noted among groups. Perhaps normal TSH reference levels for a population will need to be defined better in the future.

—Vibhavasu Sharma, MD

ATA THYROID BROCHURE LINKS

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

Hypothyroidism (Underactive): http://www.thyroid.org/hypothyroidism/

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

ABBREVIATIONS & DEFINITIONS

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

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

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HYPERTHYROIDISM

Relatively high serum free thyroxine concentrations are associated with higher risk of sudden cardiac death in the Rotterdam study

BACKGROUND

Sudden cardiac death is defined as "unexpected natural death from a cardiac cause within 1 hour from the onset of symptoms in a person without any previous condition that would appear fatal". Thyroid hormone has clear effects on the heart. A major symptom of hyperthyroidism is palpitations, or heat racing. Indeed, an irregular heart rhythm know as atrial fibrillation is also common in hyperthyroidism. If severe, atrial fibrillation can lead to heart failure and is a cause of the rare deaths due to hyperthyroidism. However, information regarding hyperthyroidism and sudden cardiac death is limited. Further, there is no information linking thyroid hormone levels and sudden cardiac death. The present study examined the relationship between sudden cardiac death and thyroid function tests, focusing on subjects who would be considered not to be hyperthyroid.

THE FULL ARTICLE TITLE

Chaker L et al. Thyroid function and sudden cardiac death: a prospective population-based cohort study. Circulation 2016;134:713-22.

SUMMARY OF THE STUDY

The study included a group of middle to older aged subjects from the Rotterdam Study in the Netherlands which investigated a variety of medical conditions in older people. There were 3 groups analyzed: Cohort I (C1) included those in whom baseline data were collected from 1990 to 1993 and were 55 years of age or older during the baseline period and Cohort II (C2) included participants in whom baseline data were collected from 2000 to 2001 who were also 55 years of age or older during the baseline period. Cohort III (C3) were 45 years of age or older during the period from 2006 to 2008, when their baseline data were collected. Most of the people had serum TSH and FT_4 measured at the first visit. A total of 10,318 participants were followed from the time of baseline testing until sudden cardiac death or death from other causes. Of these, 8881 participants had serum TSH values in the reference range of 0.4 to 4.4 mIU/L. Medical records and death certificates were the source of information regarding the diagnosis of sudden cardiac death. Baseline evaluations included a physical examination, electrocardiogram, a panel of laboratory measurements, and a detailed history.

The 10,318 study participants were followed for a maximum of 21.2 years, with an average follow-up of 9.2 years. There were 261 cases of sudden cardiac death. In the entire group, higher levels of FT_4 were associated with an 87% increase in the risk of sudden cardiac death. In euthyroid participants, higher levels of FT_4 were associated with a >2-fold risk of sudden cardiac death. In euthyroid participants, the 10-year risk for sudden cardiac death increased from 1% to almost 4% with increasing FT_4 values.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In subjects 45 years of age or older at baseline who are euthyroid by conventional criteria, higher FT_4 levels at baseline are associated with an increased occurrence of sudden cardiac death over the next decade. However, this study demonstrates only an association and not a cause and effect. Further, there is nothing in this study that would suggest any therapy would be indicated. Additional clinical trials are also needed to confirm these results.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

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

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

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

HYPERTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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

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.

MARCH
Medullary Thyroid Cancer
Awareness Month

THE AMERICAN THYROID ASSOCIATION

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 **March** is **Medullary Thyroid Cancer 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 FUNCTION TESTS

Higher Free T_4 levels are associated with an increased risk of any solid cancer

BACKGROUND

Thyroid hormone levels can be measured in the blood by a simple lab test. Thyroxine (T_4) is the major hormone produced by the thyroid gland and it can be measured as free T_4 in the blood. There have been studies suggesting that higher levels of free T_4 in the blood may be associated with an increased risk of developing a solid cancers (for example, lung, breast, prostate, gastrointestinal (GI) cancers). Other studies have not agreed with this finding. This study looks at a large group of people to determine whether T_4, even within the normal range, may increase the risk of developing any solid cancer.

THE FULL ARTICLE TITLE

Khan SR et al. Thyroid function and cancer risk: the Rotterdam Study. J Clin Endocrinol Metab. September 20, 2016 [Epub ahead of print].

SUMMARY OF THE STUDY

The study included a group of middle to older aged subjects from the Rotterdam Study in the Netherlands which investigated a variety of medical conditions in older people. Using this population, the authors were able to include 10,318 participants who all had thyroid hormone blood tests (TSH, FT_4), who did not have a history of cancer, and who they could follow from 1990 to 2012 or death to determine if the subject developed a solid cancer. The subject's average age was 61 years and 57% were women. There were 1465 cases of solid cancer over an average follow up time of 10.4 years. Based on the complicated statistical methods which included adjusting the statistics for other potential causes or risk factors for developing cancer, they found that there was a significant positive association between FT_4 level and lung cancer and breast cancer, but not for prostate or GI cancers.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

If we assume that this study is correct that higher FT_4 levels, even within the normal range (euthyroid), increase the risk for solid cancers, it profoundly impacts all people, not just those who take thyroid hormone as treatment of hypothyroidism. The authors propose mechanisms by which thyroxine can initiate the path toward developing a malignancy, but these mechanisms need to be studied further. Additional clinical trials are also needed to confirm these results.

—Wendy Sacks, MD

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

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

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

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

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HYPERTHYROIDISM

Can we predict relapse after antithyroid drugs are discontinued in patients with Graves' disease?

BACKGROUND

Patients with Graves' disease can be treated with antithyroid drugs (ATDs), radioactive iodine therapy, or thyroid surgery. ATDs are frequently used with the goal of the patient eventually going into remission. In this case, the drugs can usually be discontinued after 12-18 months of treatment. However, in approximately half of the patients, Graves' disease relapses after the initial ATD treatment, requiring a second ATD course or different treatments for control of the hyperthyroidism. In addition, although rare, ATDs can have serious side effects, such as inflammation of the liver or very low white blood cell counts (agranulocytosis) and infection. Several studies have reported risk factors that might predict relapse after the ATD discontinuation, such as a younger age, male gender, smoking, large goiter size, severe hyperthyroidism at diagnosis, and high TSH receptor antibodies. However, each of these factors appears to increase the risk of relapse only slightly. The goal of this analysis is to evaluate all previously reported risk factors and find a prediction rule for relapse after discontinuation of the initial ATD treatment in patients with Graves' disease. This could be used to individualize the treatment and chose the best initial treatment option for each patient.

THE FULL ARTICLE TITLE

Struja T et al Can we predict relapse in Graves' disease? Results from a systematic review and meta-analysis. Eur J Endocrinol 2017; 176:87-97. Epub October 25, 2016.

SUMMARY OF THE STUDY

This analysis included 31 studies of patients diagnosed with a first episode of Graves' disease who took ATDs for at least 12 months and had follow-up for at least 12 months after they stopped this treatment. Out of a total of 4346 patients, 2322 (53%) had a relapse, most relapses occurring between months 6 and 18 after stopping the ATD treatment.

Among the risk factors studied, smoking, thyroid gland size evaluated by exam and ultrasound, eye disease, antibody level, and T_4/T_3 levels, but not age and gender were significantly associated with relapse in at least one type of statistical analysis used. There was a progressive increase in the risk of relapse with greater goiter size and higher antibody and T_4/T_3 levels measured before treatment initiation. However, none of these factors had a major impact on the risk of relapse. The risk factors with major significance in one analysis, had only minor significance or lost significance in other analyses. No new risk factors were identified. Certain genetic tests (HLA types) were reported as significant risk factors in several individual studies but this analysis is not clinically useful.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This analysis showed that most of the previously reported factors predict relapse after the initial ATD treatment in patients with Graves' disease, however, the contribution of each individual factor does not seem to be significant. Additional well designed studies are needed to evaluate whether a combination of these factors or new factors could be a stronger predictor of relapse that could be used clinically. It might be advisable to use alternative treatment options rather than ATDs in new patients with Graves' disease who smoke, have a large goiter, eye disease, and high antibody levels because of a high relapse risk.

— Alina Gavrila, MD, MMSC

ATA THYROID BROCHURE LINKS

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

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

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HYPERTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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.

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

Thyroid eye disease (TED): also known as Graves' ophthalmopathy. TED includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

Antithyroid drugs (ATDs): medications that block the thyroid from making thyroid hormone. Methimazole, carbimazole and propylthiouracil (PTU) are used to treat hyperthyroidism, especially when it is caused by Graves' disease.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and hyperthyroidism.

Thyroidectomy: surgery to remove the entire thyroid gland.

Agranulocytosis: a marked decrease in the neutrophil count, the most abundant type of white blood cells that causes a patient to be more likely to develop an infection. This is commonly associated with a fever and/or a sore throat.

Goiter: a thyroid gland that is enlarged for any reason is called a goiter.

TSH receptor antibody (TRAb): antibodies often present in the serum of patients with Graves' disease that are directed against the thyrotropin (TSH) receptor located on the thyroid cell. The antibodies activate the TSH receptor and stimulate the thyroid hormone production within the thyroid cells, thus resulting in hyperthyroidism.

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

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

ATA Alliance for Thyroid Patient Education

GOAL

The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases.

We look forward to future collaborations and continuing to work together toward the improvement of thyroid education and resources for patients.

WHO WE ARE (in alphabetical order)

AMERICAN THYROID ASSOCIATION
www.thyroid.org
ATA Patient Resources:
http://www.thyroid.org/thyroid-information/
Find a Thyroid Specialist: www.thyroid.org
(Toll-free): 1-800-THYROID
thyroid@thyroid.org

BITE ME CANCER
http://www.bitemecancer.org
info@bitemecancer.org

GRAVES' DISEASE AND THYROID FOUNDATION
www.gdatf.org
(Toll-free): 877-643-3123
info@ngdf.org

LIGHT OF LIFE FOUNDATION
www.checkyourneck.com
info@checkyourneck.com

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.
www.thyca.org
(Toll-free): 877-588-7904
thyca@thyca.org

THYROID CANCER CANADA
www.thyroidcancercanada.org
416-487-8267
info@thyroidcancercanada.org

THYROID FEDERATION INTERNATIONAL
www.thyroid-fed.org
tfi@thyroid-fed.org

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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

Medullary Thyroid Cancer

WHAT IS THE THYROID GLAND?

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

CANCER OF THE THYROID

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

MEDULLARY THYROID CANCER

Medullary Thyroid Cancer (MTC) accounts for 1%–2% of thyroid cancers in the United States. MTC is different from other types of thyroid cancers (which are derived from thyroid follicular cells – the cells that make thyroid hormone), because it originates from the parafollicular C cells (also called "C cells") of the thyroid gland. These cells do not make thyroid hormone and instead make a different hormone called calcitonin.

MTC can, and frequently does, spread to lymph nodes and can also spread to other organs. MTC is likely to run in families (inherited forms) in up to 25% of diagnoses, and inherited forms can be associated with other endocrine tumors, in syndromes called Multiple Endocrine Neoplasia (MEN) 2A and MEN 2B. In addition to MTC, patients with MEN2A may have tumors of the adrenal glands called pheochromocytomas or in the parathyroid glands (parathyroid adenomas). Patients with MEN2B, have MTC, pheochromocytomas and neuromas (typically a benign growth or tumor of nerve tissue) in the lining of the mouth and/ or gastrointestinal track.

Patients with an inherited form of MTC usually have a mutation in a gene called the RET proto-oncogene. This mutation is present in all of the cells in their body (a germline mutation) and these mutations cause the development of MTC. This is important because in family members of a person with an inherited form of MTC, a blood test for a mutation in the RET proto-oncogene can lead to an early diagnosis of MTC and, to curative surgery to remove it. However, in the majority of patients (~ 75%) a germline mutation is not found - indicating that MTC is not an inherited or inheritable condition. In these cases, MTC is called sporadic.

Whether MTC is sporadic or familial can be determined by a blood test for the RET proto-oncogene. Anyone diagnosed with MTC should have this test run to determine whether the MTC is familial (meaning other family members may also have MTC that has not yet been diagnosed) or sporadic.

Medullary Thyroid Cancer

WHAT ARE THE SYMPTOMS OF MEDULLARY THYROID CANCER?

Medullary thyroid cancer usually presents as a lump or nodule in the thyroid. It may be noted by the patient or discovered during routine neck examination by the doctor. Sometimes, the nodule is discovered incidentally by imaging studies done for other unrelated reasons (CT of the neck, PET scan, or carotid ultrasound). The nodule may cause no symptoms, but in some cases the tumor may have spread to lymph nodes in the neck, which may be enlarged on physical examination.

Patients with advanced MTC may complain of pain in the neck, jaw, or ear. If a nodule is large enough to compress the windpipe or the esophagus, it may cause difficulty with breathing or swallowing. Hoarseness can be present if the cancer invades the nerve that controls the vocal cords.

MTC is usually more aggressive than the other more common types of thyroid cancer (See *Thyroid Cancer- papillary and follicular- brochure*), and it is usually easier to treat and control if it is found before it spreads to lymph nodes in the neck or other parts of the body.

Thyroid function tests such as TSH are usually normal, even when MTC is present.

If you have a family history of MTC and have tested positive for the RET mutation, then you should see an endocrinologist to help determine how best to follow you or treat you.

HOW IS MEDULLARY THYROID CANCER DIAGNOSED?

A diagnosis of thyroid cancer is usually made by a *fine needle aspiration (FNA) biopsy* of a thyroid nodule, or after the nodule is surgically removed. Patients in whom the results of an FNA biopsy (or histopathology) are suggestive or indicative of MTC should be further evaluated with measurement of the proteins calcitonin and carcinoembryonic antigen (CEA) in the blood, which are typically elevated in patients with MTC. These tests are useful to confirm the diagnosis of MTC which can help ensure the surgeon plans the correct surgery, and also serve as tumor markers during long-term follow-up to detect any remaining disease or recurrence of the cancer.

WHAT IS THE RET MUTATION?

The RET proto-oncogene is located on chromosome 10. A genetic mutation in the RET oncogene is seen in all cells in the body in patients with the hereditary forms of MTC. Mutations in RET can also be seen only in the tumor cells in patients with sporadic MTC. Since the discovery of the RET oncogene, more than 100 different mutations have been identified in the gene in patients with MTC.

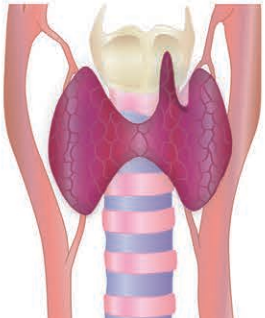
Genetic counseling and testing for RET gene mutations should be offered to patients diagnosed with MTC and first-degree relatives (parents, siblings and children of someone diagnosed with MTC) of all patients with proven germline mutations (hereditary MTC). If close relatives, especially children, are found to have the RET mutation on a blood test, the thyroid gland can be removed before MTC has a chance to develop or at least in its very early stages.

HOW IS MTC TREATED?

The primary treatment for MTC is surgery, and the currently accepted approach is to remove the entire thyroid gland (total thyroidectomy) (See *thyroid surgery brochure*). Often patients with MTC will have thyroid cancer present in the lymph nodes of the neck or upper chest. These lymph nodes are usually removed at the time of thyroid surgery or sometimes, at a later surgery if found subsequently. After surgery, patients need to take thyroid hormone replacement medication for life.

Unlike papillary and follicular thyroid cancer, medullary thyroid cancer does not take up iodine, and consequently radioactive iodine treatment is not a treatment option for patients with MTC.

Patients with MTC with very high levels of calcitonin should have imaging prior to surgery to determine whether the tumor has spread to sites outside the thyroid and/or outside the neck. If there is evidence of cancer outside the neck, surgery may be more palliative, aimed at reducing local complications caused by the tumor, rather than completely eliminating all tumor. Other treatment options (external beam radiation, or chemotherapy) may need to be used together with surgery after careful discussion with the patient.



FURTHER INFORMATION

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

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

Medullary Thyroid Cancer

New chemotherapeutic agents that have shown promise treating other advanced cancers are increasingly available for treatment of thyroid cancers. Two such agents, Vandetanib and Cabozantinib have been FDA approved for use by patients with MTC. These drugs do not cure advanced cancers that have spread widely throughout the body, but they can often slow down or partially reverse the growth of the cancer. These treatments are usually given by an oncologist (cancer specialist) and require care at specialized medical centers.

WHAT IS THE FOLLOW-UP FOR PATIENTS WITH MTC?

Periodic follow-up examinations are essential for all patients with MTC because the thyroid cancer can return, sometimes many years after successful initial treatment. These follow-up visits include a careful history and physical examination, with particular attention to the neck area. Neck ultrasound is also a very important tool to visualize the neck and look for nodules, lumps or enlarged lymph nodes that might indicate that the cancer has recurred.

Blood tests are also important in the follow-up of MTC patients. All patients who have had their thyroid glands removed require thyroid hormone replacement with levothyroxine. Thyroid stimulating hormone (TSH) should be checked periodically, and the dose of levothyroxine adjusted to keep TSH in the normal range. There is no need to keep TSH suppressed in patients with MTC.

Measurement of calcitonin and CEA are a necessary routine part of the follow-up of patients with MTC. Following thyroidectomy, it is hoped that calcitonin levels will be essentially undetectable for life. A detectable or rising calcitonin level should raise suspicion for possible cancer recurrence. Detectable calcitonin levels may require additional tests.

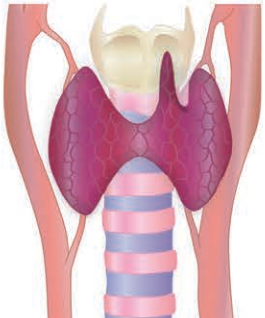
WHAT IS THE PROGNOSIS OF MEDULLARY THYROID CANCER?

The prognosis of MTC is usually not as favorable as differentiated thyroid cancers (*papillary and follicular cancer*). However, if discovered early, surgery can be curative. Even in cases where it is not caught early, MTC often progresses relatively slowly. Long-term survival depends on the stage of disease at the time of diagnosis. The blood levels of calcitonin or CEA over the first year after surgery can also be a predictor of a patient's survival.

ATA PARTNERING WITH MTC

The Medullary Thyroid Carcinoma (MTC) Registry Consortium* is partnering with the American Thyroid Association (ATA) to create a registry (list) of all new cases of MTC diagnosed in the United States over the next 10-15 years (the MTC Registry). The purpose of the MTC Registry is to help better understand what risk factors are associated with the development of MTC.

Click here for additional information:
http://www.thyroid.org/media-main/partner-relations/medullary-thyroid-carcinoma-registry-consortium/



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