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Global long-term thyroid cancer death rate trends over the past 30 years

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Li M et al 2020 Long term declines of thyroid cancer mortality: An international age-period-cohort analysis. Thyroid. Epub 2020 Jan 22. PMID: 31964280.

Not all enlarging papillary microcarcinomas require thyroid surgery

Multiple studies have shown that papillary microcarcinomas are very low risk and are unlikely to grow and/or spread. As such, there is significant interest in confirming whether or not thyroid surgery can be avoided for at least some people diagnosed with papillary microcarcinoma. The purpose of the study is to provide better understanding of the risk of cancer growth and spread for patients diagnosed with papillary thyroid microcarcinoma to determine whether or not thyroid surgery is needed for such patients.

Ito Y et al. 2019 Kinetic analysis of growth activity in enlarging papillary thyroid microcarcinomas. Thyroid. Epub 2019 Nov 21. PMID: 31650907.

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Liu L et al 2020 Prognostic value of pre-ablation stimulated thyroglobulin in children and adolescents with differentiated thyroid cancer. Thyroid. Epub 2020 Jan 22. PMID: 31964278.

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Hales C et al. Controlled antenatal thyroid screening II: Effect of treating maternal suboptimal thyroid function on child behavior. J. Clin. Endocrinol. Metab. 2020. 105:e417-e427. PMID: 3166532

THYROID AND PREGNANCYII

Subclinical hypothyroidism and thyroid autoimmunity are associated with pre-term delivery

The *Consortium on Thyroid and Pregnancy* was developed as a means to study the association of thyroid problems and thyroid autoimmunity in the mother with pre-term birth. The purpose of this study was to investigate whether mild/subclinical hypothyroidism, isolated hypothyroxinemia, and thyroid autoimmunity in the mother are risk factors for pre-term birth.

Korevaar TIM et al for the Consortium on Thyroid and Pregnancy—Study Group on Preterm Birth, 2019 Association of thyroid function test abnormalities and thyroid autoimmunity with preterm birth: a systematic review and meta-analysis. JAMA 2019;322:632–641. PMID: 31429897.

THYROID SURGERY......**13** Looking beyond readmissions as an outcome for outpatient thyroidectomy

Over the past decade, there has been an increase in thyroid surgery done as an outpatient procedure, meaning no overnight stay. Multiple studies demonstrating that these same-day discharges after thyroid surgery is a safe practice in appropriately selected patients. The aim of this study was to use a large database to compare outcomes (complications) of thyroid surgery patients that were discharged on the same day vs those that stayed in the hospital 1-2 nights.

Hu QL et al. 2020 Same-day discharge is not associated with increased readmissions or complications after thyroid operations. Surgery 167:117–123. PMID: 31582306.

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Editor

Alan P. Farwell, MD, FACE

Boston Medical Center Boston University School of Medicine 720 Harrison Ave., Boston, MA 02115 American Thyroid Association Email: thyroid@thyroid.org www.thyroid.org/patients/ct/index.html

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Designed by Karen Durland, kdurland@gmail.com

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EDITOR'S COMMENTS

Welcome to another issue of *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through <u>Twitter</u> at *@* thyroidfriends and on <u>Facebook</u>. 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, MCT8 – AHDS Foundation, ThyCa: Thyroid Cancer Survivors' Association, Thyroid Cancer Canada, Thyroid Cancer Alliance* and *Thyroid Federation International*.

We invite all of you to join our **Friends of the ATA** community. It is for you that the American Thyroid Association (ATA) is dedicated to carrying out our mission of providing reliable thyroid information and resources, clinical practice guidelines for thyroid detection and treatments, resources for connecting you with other patients affected by thyroid conditions, and cutting edge thyroid research as we search for better diagnoses and treatment outcomes for thyroid disease and thyroid cancer. We thank all of the *Friends of the ATA* who support our mission and work throughout the year to support us. We invite you to help keep the ATA mission strong by choosing to make a donation that suits you — it takes just one moment to give online at: www.thyroid.org/donate and all donations are put to good work. The ATA is a 501(c)3 nonprofit organization and your gift is tax deductible.

The Covid-19 pandemic has caused an unprecedented upheaval in our daily lives and presented extremely difficult challenges to our healthcare system. There is a lot of information circulating around. We at the American Thyroid Association would like to make sure that you all have access to most accurate, reliable, fact-based and updated information. (https://www.thyroid.org/covid-19/)

June is Differentiated Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- Has the mortality rate for thyroid cancer changes in the past 30 years?
- Do patients with small papillary thyroid cancers need surgery?
- Can stimulated thyroglobulin levels predict prognosis in children with thyroid cancer?
- Is levothyroxine overtreatment during pregnancy harmful?
- Is subclinical hypothyroidism during pregnancy associated with pre-term delivery?
- Can thyroid surgery be done in an outpatient setting?

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

THYROID CANCER

Global long-term thyroid cancer death rate trends over the past 30 years

BACKGROUND

The number of patients diagnosed with thyroid cancer has increased significantly in the last several decades in many countries, especially papillary thyroid cancer. However, the overall mortality (death) rate has been largely unchanged. The increasing number of thyroid cancer patients can be partly explained by an increased detection of small cancers due to the widespread use of imaging techniques, such as ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) and use of fine needle aspiration biopsy. This phenomenon is called overdiagnosis, since most of these small thyroid cancers do not result in symptoms or death if left untreated. However, more recent studies looking at the data from the Surveillance, Epidemiology, and End Results (SEER) cancer registry found a significant increase in the occurrence of advancedstage papillary thyroid cancer and large papillary thyroid cancers greater than 5 cm in diameter. Further, they found an increase in mortality in the United States, especially in patients with advanced-stage papillary thyroid cancer. An increase in exposure to possible risk factors for thyroid cancer (obesity, smoking, endocrine-disrupting chemicals) has been suggested to play a role. This comprehensive study analyzed long-term thyroid cancer mortality data from five continents using a model know as age-periodcohort models to understand the impact of risk factors on thyroid cancer mortality.

THE FULL ARTICLE TITLE

Li M et al 2020 Long term declines of thyroid cancer mortality: An international age-period-cohort analysis. Thyroid. Epub 2020 Jan 22. PMID: 31964280.

SUMMARY OF THE STUDY

Thyroid cancer mortality data by age group (ranging from 25 to 84 years), year of death, and gender were obtained from the World Health Organization (WHO) mortality database for 24 countries spanning five continents. Data for Canada, the United States, and South Africa were also

obtained from United Nations World Population Prospects reports. The study time span for each country varied from 20 to 60 years. Data were divided and analyzed as 5-year time periods and 5-year age groups. In age-period-cohort (APC) models, age effects reflect risk factors associated with a certain age, period effects reflect risk factors that occur at a certain time affecting all age groups in a similar way, while cohort effects reflect unique risk factors for a generation as it moves across time.

Age-standardized mortality rates of thyroid cancer were uniformly less than 1 per 100,000 in most countries and similar for both sexes between 2011 and 2015. The highest rates were observed in Israel (0.89 per 100,000 and 0.79 per 100,000 for women and men, respectively), while the lowest rates were in France and Switzerland for women (0.38 per 100,000) and South Africa for men (0.28 per 100,000). Long-term mortality rates have declined over time in most countries. The countries with the prior highest levels and largest subsequent decrease in mortality were Switzerland and Austria. The fastest annual declines between 1986-1990 and 2011-2015 were noted in women from Switzerland, Austria, Czechia, China/Hong Kong, France, Italy, and Hungary. Declines were generally slower in men than in women. A small but statistically significant annual increase in mortality during 1986–2015 was noted for both sexes in the United States and for men in Canada. Thyroid cancer death rates increased significantly with age.

The steepest decline by period was observed in iodinedeficient regions that implemented iodine supplementation programs early (Northern and Central Europe; Alpine regions such as Austria, Switzerland, and Italy; and United States). In the United States, the initial decline stabilized after 1990 and increased slightly more recently. Cohort effects also declined in most countries over years, with more pronounced changes noted in women from Switzerland.

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THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study showed a global long-term decline in thyroid cancer mortality across countries and genders over the past 30 years with downward trends in both period and cohort effects. Possible explanations include iodine supplementation programs (since iodine deficiency and goiter are risk factors for thyroid cancer), earlier diagnosis and improved treatment for thyroid cancer. The mortality trends suggest no significant impact of exposure to known or new risk factors. Since the decrease in mortality is in contrast with the increase in the number of thyroid cancers diagnosed, the difference could be explained by overdiagnosis of small cancers that may not require treatment.

— Alina Gavrila, MD, MMSc

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer (PTC): the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

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.

Surveillance, Epidemiology, and End Results (SEER) Cancer Registry: provides information on cancer statistics in the U.S. population. It is supported by the National Cancer Institute (NCI), which is a part of the National Institutes of Health (NIH) in Bethesda, MD and the federal government's primary agency for cancer research and training.

SEER: Surveillance, Epidemiology and End Results program, a nation-wide anonymous cancer registry generated by the National Cancer Institute that contains information on 26% of the United States population. Website: http://seer.cancer.gov/

Age-Period-Cohort (APC) models: age effects reflect risk factors associated with a certain age, *period effects* reflect risk factors that occur at a certain time affecting all age groups in a similar way, *cohort effects* reflect unique risk factors for a generation as it moves across time.

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THYROID CANCER

Not all enlarging papillary microcarcinomas require thyroid surgery

BACKGROUND

In general, the initial treatment of thyroid cancer requires thyroid surgery. This is because surgical removal of thyroid cancer prevents its growth and spread outside of the thyroid, and preventing associated health problems and possible premature death. However, over the last decade, multiple studies have shown that a subset of small thyroid cancers, called papillary microcarcinomas, are very low risk and are unlikely to grow and/or spread. These microcarcinomas are papillary thyroid cancers measuring less than 1 cm and may not need to be removed surgically. Instead, these small thyroid cancers can be followed with ultrasound, something known as active surveillance. Although the risk of complications from thyroid surgery is generally very small, especially when this surgery is performed by an expert thyroid surgeon, such risk can only be completely prevented by avoiding surgery altogether. For this reason, there is significant interest in confirming whether or not thyroid surgery can be avoided for at least some people diagnosed with papillary microcarcinoma.

The purpose of this study is to provide better understanding of the risk of cancer growth and spread for patients diagnosed with papillary thyroid microcarcinoma and to therefore estimate whether or not thyroid surgery is needed for such patients.

FULL ARTICLE TITLE

Ito Y et al. 2019 Kinetic analysis of growth activity in enlarging papillary thyroid microcarcinomas. Thyroid. Epub 2019 Nov 21. PMID: 31650907.

SUMMARY OF THE STUDY

In this study, the authors reviewed the medical records for 824 people diagnosed with papillary thyroid microcarcinoma at their institution between 2005 and 2011. None of the 824 patients were treated by thyroid surgery at the time their thyroid microcarcinoma was first diagnosed but instead were monitored for cancer growth. This monitoring was performed at least once a year using neck ultrasound, which is the best method for appraising thyroid cancer growth, as well as determining if the cancer has spread to neighboring neck lymph nodes. Thyroid microcarcinoma growth was measured by cancer diameter and estimated cancer volume. Thyroid surgery was recommended for patients for whom significant cancer growth (growth of 3 mm or more and/or increase in tumor volume of at least 50%) was identified during follow-up monitoring, although not all patients in this category chose to undergo surgery.

Among the 824 patients included in the study, 399 (48%) showed no growth of their cancers during the follow-up period, which averaged just over 6 years. Among the 425 (52%) patients experiencing initial cancer growth, 369 continued ultrasound monitoring for their thyroid cancer, rather than undergoing thyroid surgery. Of these patients, 62 (~17%) continued to experience yearly cancer growth, while 142 (~38%) actually showed cancer shrinkage and 165 (~45%) had cancers that remained stable in size.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors of this study found that roughly half of the papillary microcarcinomas they monitored were stable in size over the duration of their investigation. Moreover, they found that among those microcarcinomas that did initially show significant growth, most subsequently remained stable in size or even shrank. On the basis of these findings, the authors suggest that most patients with thyroid microcarcinomas, including those that demonstrate an initial increase in size, may not need to undergo thyroid surgery.

It is important to note that the risk that any given papillary thyroid microcarcinoma will spread outside of the thyroid is not perfectly linked to its growth behavior. It is also important to note that, because papillary thyroid cancer grows and spreads slowly (usually over the course of many years), this study was not long enough to determine

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THYROID CANCER, continued

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outcomes other than cancer growth. Additional studies are needed to determine long-term outcomes. As always, the decision to monitor a papillary thyroid microcarcinoma for growth over time, versus proceed with thyroid surgery, will depend on a discussion between the patient and their doctors as to the specific risks and personal treatment preferences for each individual patient.

— Jason D. Prescott, MD PhD

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u>

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

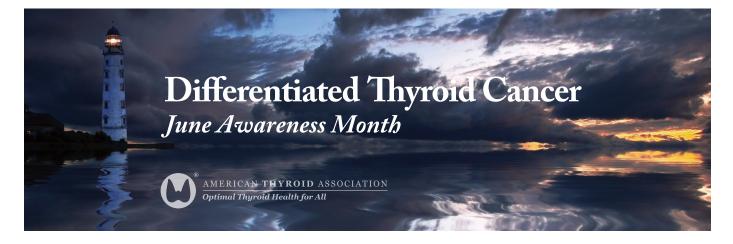
Papillary microcarcinoma: a papillary thyroid cancer smaller than I cm in diameter.

Cancer metastasis: spread of the cancer from the initial organ where it developed to other organs, such as the lungs and bone.

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

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

Thyroidectomy: surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a *partial thyroidectomy*.



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PEDIATRIC THYROID CANCER

Postoperative TSH-stimulated thyroglobulin may predict outcome of thyroid cancer in children

BACKGROUND

While much less common, children can develop thyroid cancer. Fortunately, most children who develop thyroid cancer have an excellent outcome. This is true even if the cancer has spread outside the thyroid and into the lungs. As with adults, treatment with radioactive iodine is indicated when there is persistent thyroid cancer after the initial surgery. In order to treat with radioactive iodine, the remaining thyroid tissue, including any remaining cancer, needs to be stimulated by TSH, either by stopping the thyroid hormone and having the patient become hypothyroid or by treating with Thyrogen[™]. In adults, the level of the thyroid-specific protein thyroglobulin prior to this stimulation helps predict how the patient will do long term. This data does not exist in children. This study was performed to look at how a stimulated thyroglobulin level prior to radioactive iodine therapy predicts outcomes for pediatric thyroid cancer patients.

THE FULL ARTICLE TITLE

Liu L et al 2020 Prognostic value of pre-ablation stimulated thyroglobulin in children and adolescents with differentiated thyroid cancer. Thyroid. Epub 2020 Jan 22. PMID: 31964278.

SUMMARY OF THE STUDY

The cases of thyroid cancer in patients under the age of 21 who were treated at one academic medical center in China were evaluated over a 9-year period. All the children had a total thyroidectomy and a central lymph node dissection as well as a lateral lymph node dissection if abnormal lymph nodes were seen on imaging prior to surgery. Patients were prepared for radioactive iodine therapy by stopping the thyroid hormone, causing the TSH to increase and having the patient become hypothyroid. Thyroglobulin and thyroglobulin antibody levels were measure under this TSH stimulation, prior to radioactive iodine therapy and those with positive thyroglobulin antibodies were excluded from the study. Patients were categorized by the American Thyroid Association (ATA) pediatric thyroid cancer risk categories and followed with testing every 6 to 12 months. Their response to treatment was determined by thyroglobulin testing and radiology imaging studies and they were defined as either having no disease or with evidence of thyroid cancer at their last follow up. The primary result was the level of thyroglobulin before radioactive iodine therapy as related to both evidence of thyroid cancer at the last follow up visit and the ATA pediatric risk category.

There were 118 patients age 5-20 with an average age of 16 in the study. All had a total thyroidectomy and all had lymph nodes removed from the central part of the neck. In addition, $\sim 2/3$ rds of the patients had a lateral neck lymph node dissection. The majority had classic papillary thyroid cancer. About 1/4 of patients had spread of the cancer to the lungs. The average follow up was just over 5 years.

The stimulated thyroglobulin before radioactive iodine therapy was an average of 15.1 ng/ml with a range of <1 to > 4000 ng/ml. Those who had no evidence of their cancer at the end of the study had an average stimulated thyroglobulin level of 4.82 ng/ml while the stimulated thyroglobulin level was an average of 184.1 ng/ml in those with those with persistent thyroid cancer. A stimulated thyroglobulin level of 17.8 or less was predictive of no evidence of cancer in follow up evaluations almost 9 out of 10 times. In patients who were classified as having high risk cancer based on the initial thyroid cancer pathology and staging, a stimulated thyroglobulin level of 17.8 ng/ml or less had a much lower incidence of persistent cancer (5.6% compared to > 90% if the level was > 17.8 ng/ml).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Stimulated thyroglobulin levels prior to radioactive iodine therapy help predict clinical outcomes in pediatric thyroid cancer patients. A lower stimulated thyroglobulin level, even in high risk disease, predicts a high likelihood of a good outcome after at least 5 years of follow up. This is

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PEDIATRIC THYROID CANCER, continued

important to these patients and their parents as it can provide comfort for those with lower risk disease and low stimulated thyroglobulin levels. It is also useful for clinicians to have a sense of the likelihood of persistent cancer and the intensity of follow up testing needed for pediatric thyroid cancer patients.

— Joshua Klopper, MD

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u> Radioactive Iodine Therapy: <u>https://www.thyroid.org/radioactive-iodine/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u>

ABBREVIATIONS & DEFINITIONS

Thyroidectomy: surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a *partial thyroidectomy*.

Total thyroidectomy: surgery to remove the entire thyroid gland.

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.

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.

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-I3I is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the nondestructive 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*).

Thyroid Hormone Withdrawal: this is used to produce high levels of TSH in patients by stopping thyroid hormone pills and causing short-term hypothyroidism. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan.

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 recombinant human TSH, then levels of thyroglobulin are measured. Sometimes this test is combined with a whole body iodine scan.

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

Central neck compartment: the central portion of the neck between the hyoid bone above, and the sternum and collar bones below and laterally limited by the carotid arteries.

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THYROID AND PREGNANCY

Overtreatment of mild hypothyroidism in the mother during pregnancy may lead to behavior problems in the children

BACKGROUND

Normal thyroid hormone levels in the mother during pregnancy is critical for normal brain development in the baby. Many studies have shown the importance of maintaining normal thyroid hormone levels during pregnancy for the best pregnancy outcomes. Earlier studies demonstrated that untreated overt hypothyroidism in the mother was associated with impaired brain development and lower IQ (intelligence quotient) scores in the children. Later studies examined the effect of milder forms of hypothyroidism in the mother on brain function in babies and did not find a benefit of thyroid hormone replacement. A large randomized controlled trial, known as the Controlled Antenatal Thyroid Screening (CATS) trial, investigated the effect of thyroid hormone treatment of women with mildly low thyroid function during pregnancy on the brain function of their children and did not find an overall benefit. The current study is an extension of the CATS trial. The investigators examined the effect of thyroid function in the mother during pregnancy on the behavior of the children as assessed by questionnaires designed to evaluate mental health, ADHD symptoms and autism spectrum symptoms. They specifically examined the effects of thyroid hormone overtreatment in the mother with mild hypothyroidism on the subsequent behavior of the children.

THE FULL ARTICLE TITLE

Hales C et al. Controlled antenatal thyroid screening II: Effect of treating maternal suboptimal thyroid function on child behavior. *J. Clin. Endocrinol. Metab.* 2020. 105:e417-e427. PMID: 3166532

SUMMARY OF THE STUDY:

The CATS trial is a randomized trial of thyroid hormone replacement in women living in the United Kingdom or Italy with mild hypothyroidism during pregnancy compared to a control group of women with normal thyroid levels. The investigators randomized women at approximately 13 weeks of pregnancy to either a screen or a control group. All women had blood drawn for thyroid function (TSH, Free T_4). The screen group had the measurement done immediately whereas the control group had the measurements done after pregnancy. In the screen group, if the women were found to have mild hypothyroidism, defined as either an elevated TSH or low Free T_4 , they were treated with 150 mcg of levothyroxine and then had doses titrated to a TSH value 0.1-1 mIU/L throughout the duration of the pregnancy. The control group of women did not receive thyroid hormone therapy during pregnancy. Women living in the United Kingdom from this original study were asked to participate in a series of questionnaires about their children's behavior when they were between the ages of 7 and 10 years (average age 9.5 years). These questionnaires included the Strengths and Difficulties Questionnaire, Child ADHD Questionnaire and the Social Communications Questionnaire, which are designed to evaluate mental health difficulties, ADHD symptoms and autism spectrum behaviors.

A total of 475 mother/child pairs completed the questionnaires for inclusion in the study. Comparisons were made between children born to mothers with normal thyroid function during pregnancy, mothers with treated mild hypothyroidism and untreated mild hypothyroidism. Overall, there were no significant group differences for any of the 3 questionnaires. Higher questionnaire scores indicating worse childhood behavior/mental health difficulties were noted in male children, children born to younger mothers and children from families with more social challenges. Further analyses indicated higher scores on some subsets of the questionnaires (worse behavior problems) in children born to mothers that had been overtreated (defined as a high Free T_4) with thyroid hormone during their pregnancy. These data suggest that overtreatment of suboptimal thyroid dysfunction (hypothyroidism) can be associated with more childhood behavioral difficulties.

WHAT ARE THE IMPLICATIONS OF THE STUDY?

This study suggests that overtreatment with thyroid hormone for mild hypothyroidism in the mother during

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THYROID AND PREGNANCY, continued

pregnancy may negatively affect the behavior of children during later development. Close monitoring of thyroid function in women on thyroid hormone during pregnancy is recommended to maintain normal thyroid function (with the goal being normal TSH and free T_4 levels during pregnancy).

- Whitney W. Woodmansee MD

ATA THYROID BROCHURE LINKS

Thyroid Disease in Pregnancy: https://www.thyroid.org/thyroid-disease-pregnancy/

ABBREVIATIONS & DEFINITIONS

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

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

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

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

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

ADHD: Attention Deficit Hyperactivity Disorder

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The American Thyroid Association (ATA) – Searching for Answers to Thyroid Cancer April 17, 2016



Differentiated Thyroid Cancer – Support ATA's ongoing Research April 17, 2016



Medullary Thyroid Cancer – Help the ATA Find a Cure April 17, 2016



Anaplastic Thyroid Cancer – Support Research for Treatments April 17, 2016

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THYROID AND PREGNANCY

Subclinical hypothyroidism and thyroid autoimmunity are associated with pre-term delivery

BACKGROUND

Thyroid hormone is essential to normal brain development in babies. Several studies have shown an increased risk poor pregnancy outcomes when the mother has overt hypothyroidism. These poor outcomes can be decreased or prevented in women with overt hypothyroidism that are treated with thyroid hormone. Poor pregnancy outcomes also are seen in mothers with mild/ subclinical hypothyroidism but to a much lesser degree and the effects of treatment with thyroid hormone are less clear. Further, the impact of other thyroid disorders, such as isolated hypothyroxinemia and thyroid autoimmunity with normal thyroid function, on pregnancy outcomes is unclear and controversial.

One particular poor pregnancy outcome is pre-term delivery, meaning the baby is born <37 weeks of pregnancy when the baby is not quite fully developed. Pre-term delivery is increased in mothers with overt hypothyroidism but the impact of mild/subclinical hypothyroidism, isolated hypothyroxinemia and thyroid autoimmunity with normal thyroid function on pre-term delivery has remained unclear.

Given the large variability across study populations and variable patient numbers in previous studies, it is difficult to generalize the available results to provide evidencebased guidelines and recommendations. To address these limitations, the *Consortium on Thyroid and Pregnancy* was developed as a means to study the association of thyroid problems and thyroid autoimmunity in the mother with pre-term birth. The purpose of this study was to investigate whether mild/subclinical hypothyroidism, isolated hypothyroxinemia, and thyroid autoimmunity in the mother are risk factors for pre-term birth.

THE FULL ARTICLE TITLE

Korevaar TIM et al for the Consortium on Thyroid and Pregnancy—Study Group on Preterm Birth, 2019 Association of thyroid function test abnormalities and thyroid autoimmunity with preterm birth: a systematic review and meta-analysis. JAMA 2019;322:632–641. PMID: 31429897.

SUMMARY OF THE STUDY

In this analysis, 19 studies from the United States, Europe, Chile, Australia, Pakistan, and Japan were included, totaling 47,045 study participants. Included participants had data available on serum TSH, FT₄, thyroid peroxidase antibody (TPOAb), or thyroglobulin antibody concentration, as well as gestational age at birth. Participants who had received treatment for abnormal thyroid-function tests or had preexisting thyroid disease, thyroid-interfering medication use, miscarriage, *in vitro* fertilization, or multiple pregnancies were excluded. The primary outcome of the study was preterm birth, defined as delivery at less than 37 weeks' gestation. Secondary outcomes included gestational age at birth, and very preterm birth (<32 weeks).

Of the study participants, 1234 (3.1%) had subclinical hypothyroidism, 904 (2.2%) had isolated hypothyroxinemia, and 3043 (7.5%) were TPOAb-positive, 226 of whom had serum TSH <2.5 mIU/L. Pre-term birth occurred in 2357 (5.0%) of pregnancies; very pre-term birth occurred in 349 pregnancies (0.7%). As compared with women with normal thyroid function and negative TPOAb, pre-term birth was more common in women with subclinical hypothyroidism (6.1% vs. 5.0), isolated hypothyroxinemia (7.1% vs. 5.0%) and in TPOAbpositive women (6.6% vs. 4.9%). There was also a higher risk of very pre-term birth in women with isolated hypothyroxinemia (1.9% vs. 0.8%) and in TPOAbpositive women (1.7% vs. 0.7%). After adjustment for TPOAb status, subclinical hypothyroidism was no longer associated with pre-term birth. Finally, TPOAb positivity remained a risk factor for pre-term birth even in women with serum TSH <2.5 mIU/L.

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THYROID AND PREGNANCY, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is an important study that clearly shows that mild/ subclinical hypothyroidism, isolated hypothyroxinemia, and TPOAb positivity in pregnant women are associated with a higher risk of pre-term birth. What is unknown is whether thyroid hormone therapy can affect the rate of pre-term birth in any of these groups. The most current American Thyroid Association guidelines for management of thyroid disease during pregnancy state that treatment with thyroid hormone can be "considered" in TPOAbpositive women with TSH >2.5 mIU/L. This study suggests that thyroid hormone treatment may be beneficial to all TPOAb-positive pregnant women. Finally, the issue of screening pregnant women for thyroid disease is controversial, but this study suggests that if screening is done, then testing for TPOAbs should be included. Further studies are needed to help sort out and resolve these complicated and controversial issues.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

Thyroid Disease in Pregnancy: <u>https://www.thyroid.org/thyroid-disease-pregnancy/</u> Hypothyroidism (Underactive): <u>https://www.thyroid.org/hypothyroidism/</u>

ABBREVIATIONS & DEFINITIONS

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

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

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

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). **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.

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.

Isolated hypothyroxinemia: low levels of thyroxine (T_4) with normal TSH levels, no evidence for pituitary disease and no clinical symptoms for hypothyroidism

Gestational age: how many weeks along the pregnancy has been, with normal delivery being at 40 weeks.

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THYROID SURGERY

Looking beyond readmissions as an outcome for outpatient thyroidectomy

BACKGROUND

Thyroid surgery is done regularly for cancer and benign non-cancerous reasons. The usual procedure has been admitting on the day of surgery, staying in the hospital overnight for observation of potential serious postoperative complications, such as severe hypocalcemia or a bleeding requiring urgent reoperation, then going home the next day. Over the past decade, there has been an increase in thyroid surgery done as an outpatient procedure, meaning no overnight stay. This has mainly been done by high volume surgeons, meaning those that do >100 thyroid operations a year. Multiple studies demonstrating that these same-day discharges after thyroid surgery is a safe practice in appropriately selected patients. However, most previous studies have used the "outpatient" term to also include patients that stay overnight and <23 hours for observation.

A large national database has been capturing endocrine specific outcomes for the past few years and therefore, the aim of this study was to use this large database to compare outcomes (complications) of thyroid surgery patients that were discharged on the same day vs those that stayed in the hospital 1-2 nights.

THE FULL ARTICLE TITLE

Hu QL et al. 2020 Same-day discharge is not associated with increased readmissions or complications after thyroid operations. Surgery 167:117–123. PMID: 31582306.

SUMMARY OF THE STUDY

The authors were able to look at just over 10,000 patients that had thyroid surgery that remained in the central neck (ie not including a lateral neck dissection). About ¹/₄ were discharged on the same day whereas ³/₄ were discharged after 1-2 nights in the hospital. Without taking other factors into account, patients that had only half of their thyroid removed as opposed to a total thyroidectomy, as well as those that were younger and healthier, were much more likely to be discharged without staying overnight. When all factors were taken into account, multiple patient and operative factors were predictive of being discharged the same day of surgery. When patients that were discharged on the same day were matched with patients that stayed 1-2 nights, there was no difference in any complications or readmissions.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that same-day discharge for most patients after thyroid surgery is safe and without any increased risk of complications or readmission. This is especially true for patients that have only half of their thyroid taken out. It is reasonable for patients to discuss this option with their surgeons.

- Melanie Goldfarb, MD, FACS

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

Thyroidectomy: surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in

removal of a lobe, it is termed a partial thyroidectomy.

Lobectomy: surgery to remove one lobe of the thyroid.

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A publication of the American Thyroid Association®

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Volume 13 | Issue 6 | June 2020



THYROID SURGERY, continued

AMERICAN **THYROID** ASSOCIATION

Total thyroidectomy: surgery to remove the entire thyroid gland.

Hypocalcemia: low calcium levels in the blood, a complication from thyroid surgery that is usually short-

term and relatively easily treated with calcium pills. If left untreated, low calcium may be associated with muscle twitching or cramping and, if severe, can cause seizures and/or heart problems.



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AMERICAN THYROID ASSOCIATION Optimal Thyroid Health for All

Volume 13 | Issue 6 | June 2020

Clinical Thyroidology[®] for the Public

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.





CANCER











American Thyroid Association

Foundation

www.thyroid.org

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

Bite Me Cancer

www.bitemecancer.org info@bitemecancer.org

Graves' Disease and Thyroid Foundation

www.gdatf.org (Toll-free): 877-643-3123 info@ngdf.org

Light of Life Foundation

www.checkyourneck.com info@checkyourneck.com

MCT8 – AHDS Foundation

mct8.info Contact@mct8.info

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

(Toll-free): 877-588-7904 thyca@thyca.org

Thyroid Cancer Alliance

www.thyroidcanceralliance.org www.thyroidcancerpatientinfo.org Rotterdam. The Netherlands

Thyroid Cancer Canada

www.thyroidcancercanada.org 416-487-8267 info@thyroidcancercanada.org

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





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www.thyroid.org

Get the latest thyroid health information. You'll be among the first to know the latest cutting-edge thyroid research that is important to you and your family.

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

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

- *Friends of the ATA e-news*, providing up-to-date information on thyroid issues, summaries of recently published articles from the medical literature that covers the broad spectrum of thyroid disorders., and invitations to upcoming patient events
- Updates on the latest patient resources through the ATA website and elsewhere on the world wide web
- Special e-mail alerts about thyroid topics of special interest to you and your family

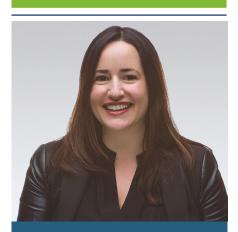
We will use your email address to send you *Friends of the ATA e-news* and occasional email updates. We won't share your email address with anyone, and you can unsubscribe at any time.

www.thyroid.org

AMERICAN THYROID ASSOCIATION

ATA | Founded 1923

Donate Now!



The ATA was a valuable resource for our family when my dad was diagnosed with Anaplastic Thyroid Cancer. When you're faced with a detrimental diagnosis where even a few days can make the difference in life or death, understanding your options quickly is critical. The ATA website offers a one-stop shop for patients and caregivers to find specialists, current clinical trials, general thyroid cancer information, and links to other patient support groups and information.

Mary Catherine Petermann

- Father who was diagnosed with Anaplastic Thyroid Cancer in 2006
- He was treated at Mayo Clinic
- He has clean scans as of October 2016

JOIN US

PLEASE JOIN OUR JOURNEY TO ADVANCED DISCOVERIES AND TREATMENT FOR THYROID DISEASE AND THYROID CANCER

As patients with thyroid disease navigate the challenges to their quality of life and researchers and physicians look for more effective directions, we at the ATA have our own destination– **funding for critical thyroid research, prevention, and treatment.** For 94 years, the ATA has led the way in thyroidology. It's a daily obstacle course to find new drugs, better treatments, advanced surgical methods, and more rapid diagnoses for the 20 million Americans who have some form of thyroid disease.

The ATA has paved the way with management guidelines for clinicians who diagnose and treat thyroid disease. For physicians treating pregnant women diagnosed with thyroid disease, our recent publication presents 97 evidence-based recommendations making sure that best practices are implemented with the latest, most effective treatment.



Through your generous support and donations, research takes the lead and hope is on the horizon. **Will you join us** in our campaign to raise **\$1.5 million** for thyroid research, prevention, and treatment? Your compassionate, tax-deductible gift will provide funds for:

- Research grants that pave the way for 1,700 ATA physicians and scientists who have devoted their careers to understanding the biology of and caring for patients affected by thyroid disease.
- Patient education for individuals and families looking for life-changing clinical trials, the best thyroid specialists, and cutting edge treatment and drugs.
- Professional education that offers a wealth of knowledge and leading-edge research for trainees and practitioners.
- A website that is the go-to resource for thyroid information for patients and practitioners alike. In 2016 alone, there were more than 3,700,000 website views of ATA's library of online thyroid information patient brochures.

Donations **of all sizes** will change the future for thyroid patients. You will make a direct impact on patients like Mary Catherine's father as he deals with Anaplastic Thyroid Cancer. You will help scientists like ATA Associate Member Julia Rodiger, Ph.D., a scientist at the National Institutes of Health, as she analyzes thyroid hormones for intestinal stem cell development.

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.

WHAT ARE THE TYPES OF THYROID CANCER?

Papillary thyroid cancer. Papillary thyroid cancer is the most common type, making up about 70% to 80% of all thyroid cancers. Papillary thyroid cancer can occur at any age. It tends to grow slowly and often spreads to lymph nodes in the neck. However, unlike many other cancers, papillary cancer has a generally excellent outlook, even if there is spread to the lymph nodes.

Follicular thyroid cancer. Follicular thyroid cancer makes up about 10% to 15% of all thyroid cancers in the United States. Follicular cancer can spread to lymph nodes in the neck, but this is much less common than with papillary cancer. Follicular cancer is also more likely than papillary cancer to spread to distant organs, particularly the lungs and bones. Papillary and follicular thyroid cancers are also known as Well-Differentiated Thyroid Cancers (DTC). The information in this brochure refers to the differentiated thyroid cancers. The other types of thyroid cancer listed below will be covered in other brochures

Medullary thyroid cancer. Medullary thyroid cancer (MTC), accounts for approximately 2% of all thyroid cancers. Approximately 25% of all MTC runs in families and is associated with other endocrine tumors (see *Medullary Thyroid Cancer brochure*). In family members of an affected person, a test for a genetic mutation in the RET proto-oncogene can lead to an early diagnosis of medullary thyroid cancer and, as a result, to curative surgery.

Anaplastic thyroid cancer. Anaplastic thyroid cancer is the most advanced and aggressive thyroid cancer and the least likely to respond to treatment. Anaplastic thyroid cancer is very rare and is found in less than 2% of patients with thyroid cancer. (See *Anaplastic thyroid cancer brochure*.)

WHAT ARE THE SYMPTOMS OF THYROID CANCER?

Thyroid cancer often presents as a lump or nodule in the thyroid and usually does not cause any symptoms (see *Thyroid Nodule brochure*). Blood tests generally do not help to find thyroid cancer and thyroid blood tests such as TSH are usually normal, even when a cancer is present. Neck examination by your doctor is a common way in which thyroid nodules and thyroid cancer are found. Often, thyroid nodules are discovered incidentally on imaging tests like CT scans and 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. Rarely, thyroid cancers and nodules may cause symptoms. In these cases, patients 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 a thyroid cancer invades the nerve that controls the vocal cords.

The important points to remember are that cancers arising in thyroid nodules generally do not cause symptoms, thyroid function tests are typically normal even when cancer is present, and the best way to find a thyroid nodule is to make sure that your doctor examines your neck as part of your periodic check-up.

WHAT CAUSES THYROID CANCER?

Thyroid cancer is more common in people who have a history of exposure to high doses of radiation, have a family history of thyroid cancer, and are older than 40 years of age. However, for most patients, we do not know the specific reason or reasons why thyroid cancer develops.

High dose radiation exposure, especially during childhood, increases the risk of developing thyroid cancer. Prior to the 1960s, X-ray treatments were often used for conditions such as acne, inflamed tonsils and adenoids, enlarged lymph nodes, or to treat enlargement of a gland in the chest called the thymus. All these treatments were later found to be associated with an increased risk of developing thyroid cancer later in life. Even X-ray therapy used to treat cancers such as Hodgkin's disease (cancer of the lymph nodes) or breast cancer has been associated with an increased risk for developing thyroid cancer if the treatment included exposure to the head, neck or chest. Routine X-ray exposure such as dental X-rays, chest X-rays and mammograms have not been shown to cause thyroid cancer.

Exposure to radioactivity released during nuclear disasters (1986 accident at the Chernobyl power plant in Russia or the 2011 nuclear disaster in Fukushima, Japan) has also been associated with an increased risk of developing thyroid cancer, particularly in exposed children, and thyroid cancers can be seen in exposed individuals as many as 40 years after exposure.

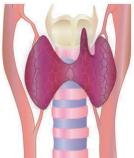
You can be protected from developing thyroid cancer in the event of a nuclear disaster by taking potassium iodide (see *Nuclear Radiation and the Thyroid brochure*). This prevents the absorption of radioactive iodine and has been shown to reduce the risk of thyroid cancer. The American Thyroid Association recommends that anyone living within 200 miles of a nuclear accident be given potassium iodide to take prophylactically in the event of a nuclear accident. If you live near a nuclear reactor and want more information about the role of potassium iodide, check the recommendations from your state at the following link: www.thyroid.org/web-links-for-importantdocuments-about-potassium-iodide/.

HOW IS THYROID CANCER DIAGNOSED?

A diagnosis of thyroid cancer can be suggested by the results of a fine needle aspiration biopsy of a thyroid nodule and can be definitively determined after a nodule is surgically excised (see *Thyroid Nodule brochure*). Although thyroid nodules are very common, less than 1 in 10 will be a thyroid cancer.

WHAT IS THE TREATMENT FOR THYROID CANCER?

Surgery. The primary therapy for all types of thyroid cancer is surgery (see Thyroid Surgery brochure). The extent of surgery for differentiated thyroid cancers (removing only the lobe involved with the cancer- called a lobectomyor the entire thyroid – called a total thyroidectomy) will depend on the size of the tumor and on whether or not the tumor is confined to the thyroid. Sometimes findings either before surgery or at the time of surgery – such as spread of the tumor into surrounding areas or the presence of obviously involved lymph nodes - will indicate that a total thyroidectomy is a better option. Some patients will have thyroid cancer present in the lymph nodes of the neck (lymph node metastases). These lymph nodes can be removed at the time of the initial thyroid surgery or sometimes, as a later procedure if lymph node metastases become evident later on. For very small cancers (<1 cm) that are confined to the thyroid, involving only one lobe and without evidence of lymph node involvement a simple lobectomy (removal of only the involved lobe) is considered sufficient. Recent studies even suggest that small tumors - called micro papillary thyroid cancers may be observed without surgery depending on their location in the thyroid. After surgery, most patients need to



FURTHER INFORMATION

2 This page and its contents are Copyright © 2016 the American Thyroid Association 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

be on thyroid hormone for the rest of their life (see *Thyroid Hormone Treatment brochure*). Often, thyroid cancer is cured by surgery alone, especially if the cancer is small. If the cancer is larger, if it has spread to lymph nodes or if your doctor feels that you are at high risk for recurrent cancer, radioactive iodine may be used after the thyroid gland is removed.

Radioactive iodine therapy. (Also referred to as I-131 therapy). Thyroid cells and most differentiated thyroid cancers absorb and concentrate iodine. That is why radioactive iodine can be used to eliminate all remaining normal thyroid tissue and potentially destroy residual cancerous thyroid tissue after thyroidectomy (see Radioactive lodine brochure). The procedure to eliminate residual thyroid tissue is called radioactive iodine ablation. This produces high concentrations of radioactive iodine in thyroid tissues, eventually causing the cells to die. Since most other tissues in the body do not efficiently absorb or concentrate iodine, radioactive iodine used during the ablation procedure usually has little or no effect on tissues outside of the thyroid. However, in some patients who receive larger doses of radioactive iodine for treatment of thyroid cancer metastases, radioactive iodine can affect the glands that produce saliva and result in dry mouth complications. If higher doses of radioactive iodine are necessary, there may also be a small risk of developing other cancers later in life. This risk is very small, and increases as the dose of radioactive iodine increases. The potential risks of treatment can be minimized by using the smallest dose possible. Balancing potential risks against the benefits of radioactive iodine therapy is an important discussion that you should have with your doctor if radioactive iodine therapy is recommended.

If your doctor recommends radioactive iodine therapy, your TSH will need to be elevated prior to the treatment. This can be done in one of two ways.

The first is by stopping thyroid hormone pills (levothyroxine) for 3-6 weeks. This causes high levels of TSH to be produced by your body naturally. This results in hypothyroidism, which may involve symptoms such as fatigue, cold intolerance and others, that can be significant. To minimize the symptoms of hypothyroidism your doctor may prescribe T3 (Cytomel[®], liothyronine) which is a short acting form of thyroid hormone that is usually taken after the levothyroxine is stopped until the final 2 weeks before the radioactive iodine treatment.

Alternatively, TSH can be increased sufficiently without stopping thyroid hormone medication by injecting TSH into your body. Recombinant human TSH (rhTSH, Thyrogen[®]) can be given as two injections in the days prior to radioactive iodine treatment. The benefit of this approach is that you can stay on thyroid hormone and avoid possible symptoms related to hypothyroidism.

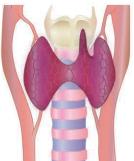
Regardless of whether you go hypothyroid (stop thyroid hormone) or use recombinant TSH therapy, you may also be asked to go on a low iodine diet for 1 to 2 weeks prior to treatment (see *Low Iodine Diet FAQ*), which will result in improved absorption of radioactive iodine, maximizing the treatment effect.

TREATMENT OF ADVANCED THYROID CANCER.

Thyroid cancer that spreads (metastasizes) outside the neck area is rare, but can be a serious problem. Surgery and radioactive iodine remain the best way to treat such cancers as long as these treatments continue to work. However, for more advanced cancers, or when radioactive iodine therapy is no longer effective, other forms of treatment are needed. External beam radiation directs precisely focused X-rays to areas that need to be treated—often tumor that has recurred locally or spread to bones or other organs. This can kill or slow the growth of those tumors. Cancer that has spread more widely requires additional treatment.

New chemotherapy agents that have shown promise treating other advanced cancers are becoming more widely available for treatment of thyroid cancer. These drugs rarely cure advanced cancers that have spread widely throughout the body but they can slow down or partially reverse the growth of the cancer. These treatments are usually given by an oncologist (cancer specialist) and often require care at a regional or university medical center.

FURTHER INFORMATION



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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*

WHAT IS THE FOLLOW-UP FOR PATIENTS WITH THYROID CANCER?

Periodic follow-up examinations are essential for all patients with thyroid cancer because the thyroid cancer can return-sometimes several 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 an important tool to view the neck and look for nodules, lumps or cancerous lymph nodes that might indicate the cancer has returned. Blood tests are also important for thyroid cancer patients. Most patients who have had a thyroidectomy for cancer require thyroid hormone replacement with levothyroxine once the thyroid is removed (see *Thyroid Hormone Treatment brochure*). The dose of levothyroxine prescribed by your doctor will in part be determined by the initial extent of your thyroid cancer. More advanced cancers usually require higher doses of levothyroxine to suppress TSH (lower the TSH below the low end of the normal range). In cases of minimal or very low risk cancers, it's typically safe to keep TSH in the normal range. The TSH level is a good indicator of whether the levothyroxine dose is correctly adjusted and should be followed periodically by your doctor.

Another important blood test is measurement of thyroglobulin (Tg). Thyroglobulin is a protein produced by normal thyroid tissue and thyroid cancer cells, and is usually checked at least once a year. Following thyroidectomy and radioactive iodine ablation, thyroglobulin levels usually become very low or undetectable when all tumor cells are gone. Therefore, a rising thyroglobulin level should raise concern for possible cancer recurrence. Some patients will have thyroglobulin antibodies (TgAb) which can make it difficult to rely on the Tg result, as this may be inaccurate.

In addition to routine blood tests, your doctor may want to repeat a whole-body iodine scan to determine if any thyroid cells remain. Increasingly, these scans are only done for high risk patients and have been largely replaced by routine neck ultrasound and thyroglobulin measurements that are more accurate to detect cancer recurrence, especially when done together.

WHAT IS THE PROGNOSIS OF THYROID CANCER?

Overall, the prognosis of differentiated thyroid cancer is excellent, especially for patients younger than 45 years of age and those with small cancers. Patients with papillary thyroid cancer who have a primary tumor that is limited to the thyroid gland have an excellent outlook. Ten year survival for such patients is 100% and death from thyroid cancer anytime thereafter is extremely rare. For patients older than 45 years of age, or those with larger or more aggressive tumors, the prognosis remains very good, but the risk of cancer recurrence is higher. The prognosis may not be quite as good in patients whose cancer is more advanced and cannot be completely removed with surgery or destroyed with radioactive iodine treatment. Nonetheless, these patients often are able to live a long time and feel well, despite the fact that they continue to live with cancer. It is important to talk to your doctor about your individual profile of cancer and expected prognosis. It will be necessary to have lifelong monitoring, even after successful treatment.

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FURTHER INFORMATION

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