THYROID AND PREGNANCY

Mild abnormalities in thyroid hormone levels in one blood test in early pregnancy may become normal when repeated.

Thyroid hormone levels in pregnant women change during pregnancy. Most of the time, these changes are short-lived and resolve without therapy, but some do need to be treated. This study investigated how often the diagnosis of thyroid problems remains the same when thyroid hormone levels in pregnant women were checked more than once during early pregnancy.


GRAVES’ DISEASE

Eye surgery for thyroid eye disease and quality of life

Symptoms of thyroid eye disease can be severe and affect quality of life in many ways. Treatment options are limited and surgery may be needed. This study was done by reviewing and analyzing existing studies to help assess whether the different types of eye surgery improved the quality of life in patients with thyroid eye disease.


GRAVES’ DISEASE

Rituximab may increase remission in young patients with Graves’ disease.

Graves’ disease is an autoimmune condition causing hyperthyroidism and antithyroid drugs may affect the autoimmune process and cause it to go into remission. Rituximab is a monoclonal antibody that has been shown to be effective in treating other autoimmune diseases. In the current study, disease remission and treatment safety were evaluated in young patients with Graves’ disease when Rituximab was administered together with antithyroid drugs.


THYROID AND CANCER

Pre-existing thyroid autoimmunity is associated with increased thyroid cancer risk

Autoimmune disease is a major cause of thyroid problems in the US. Previous studies have suggested an association between autoimmune thyroid disease and thyroid cancer. The aim of this study is to determine whether there is an association of thyroid cancer with autoimmune thyroid disease.


Lack of an impact of education and income on the increase of thyroid cancer in Denmark

Similar to the United States, thyroid cancer has been increasing in other parts of the world. Indeed, the occurrence of new cases of thyroid cancer in Denmark has increased considerably from 1980 to 2014. The goal of the study was specifically to evaluate how the level of education and income of adults in Denmark was associated with the increase in thyroid cancer.

Sørensen SM et al 2022 Temporal trends in papillary and follicular thyroid cancer incidence from 1995 to 2019 in adults in Denmark according to education and income. Thyroid. Epub 2022 Apr 22. PMID: 35459415.

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ATA ALLIANCE FOR THYROID PATIENT EDUCATION

Friends of the ATA
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 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, 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. 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/)

August is Thyroid Disease and Pregnancy Awareness Month.

In this issue, the studies ask the following questions:

- Do mild abnormalities in thyroid levels during pregnancy need to be treated?
- How does thyroid surgery for thyroid eye disease affect patient’s quality of life?
- Does Rituximab increase remission rates in Graves’ disease?
- Does thyroid autoimmunity increase the risk for thyroid cancer?
- Does patient education and income impact the diagnosis of thyroid cancer in Denmark?

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

www.thyroid.org

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A publication of the American Thyroid Association®
Mild abnormalities in thyroid hormone levels in one blood test in early pregnancy may become normal when repeated.

**BACKGROUND**
Thyroid hormone from the mother is essential for a baby’s normal development during pregnancy. Importantly, thyroid hormone levels in pregnant women change during pregnancy. Thyroid hormone requirements increase during pregnancy and this may result in an increased TSH and possibly hypothyroidism. Pregnancy hormones (HCG) can stimulate the thyroid, causing thyroid hormone levels to increase and TSH to decrease. Most of the time, these changes are short-lived and resolve without therapy but some do need to be treated. However, some people may not be able to appropriately respond, leading to diagnosis of either hypothyroidism or hyperthyroidism. Abnormal thyroid hormone levels, both high and low, in mothers during pregnancy have been associated with harmful outcomes for pregnancy and baby’s development. Therefore, it is important to correctly diagnose thyroid disease in pregnancy. Hypothyroidism or hyperthyroidism during pregnancy is often diagnosed based on a single blood test. This study investigated how often the diagnosis of thyroid problems remains the same when thyroid hormone levels in pregnant women were checked more than once during early pregnancy.

**THE FULL ARTICLE TITLE**

**SUMMARY OF THE STUDY**
A total of 1466 pregnant women from a national Danish database were included in the study. The authors collected the results of thyroid blood tests from the database, including thyroid stimulating hormone (TSH), free thyroxine (FT4), thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb) levels. Women had initial blood tests at an average of 8 weeks of pregnancy and repeat blood tests at an average of 12 weeks of pregnancy. Hypothyroidism or hyperthyroidism were defined using the pregnancy-specific normal ranges established from this population.

About 39% of women who were classified as having thyroid problems in the first measurement again had thyroid problems in the second measurement, so in 61% the problems resolve. Only 18% of pregnant women who had low FT4 levels only in the first measurement had again low FT4 in the second measurement. On the other hand, 88% of women who had high levels of thyroid antibodies (TPOAb or TgAb) in the first measurement had high levels of thyroid antibodies in the second measurement. Those with lower TSH level (<0.01mIU/L in hyperthyroidism) or the higher TSH level (>7.0mIU/L in hypothyroidism) in the first measurement were more likely to have persistent thyroid abnormalities in the second measurement, compared to those who had only mild thyroid abnormalities. Thyroid problems were more likely to continue from the first to the second measurements if women had high thyroid antibody levels.

**WHAT ARE THE IMPLICATIONS OF THIS STUDY?**
In this study, the diagnosis of hypothyroidism or hyperthyroidism did not persist in more than half of pregnant women when blood thyroid levels were repeatedly measured several weeks apart in early pregnancy. Only about 2 in 5 women who had thyroid problems identified in the first blood tests still had thyroid problems in the second blood tests. Very high or very low levels of TSH and presence of thyroid antibody increased likelihood of having persistent thyroid dysfunction.

Given many studies showing adverse effects of thyroid problems in pregnant women on pregnancy and baby’s developmental outcomes, it would be important to correctly diagnose thyroid problems for treatment. Universal screening of thyroid problems pregnancy is currently not recommended, because large randomized
THYROID AND PREGNANCY, continued

controlled trials have not shown benefit of treating mild thyroid problems, which is more likely to be identified with universal screening. The findings of this study suggest a potential need for confirming mild thyroid problems in pregnancy with repeat testing. As women with TSH levels at either extreme (very low or very high) were more likely to still have abnormal levels on repeat measurements, it would be reasonable to start treatment in these women. Women with positive thyroid antibody levels would be also reasonable to treat, as they were likely to have persistent thyroid dysfunction on repeat measurements. However, those with only mild thyroid problems on one thyroid blood test may benefit from repeating them to confirm the diagnosis. In addition, studies regarding the impact of one-time abnormalities of thyroid levels on pregnancy outcomes are needed to assess long-term effects.

— Sun Y. Lee, MD, MSc

ATA THYROID BROCHURE LINKS
Thyroid Function Tests: https://www.thyroid.org/thyroid-function-tests/
Thyroid Disease in Pregnancy: https://www.thyroid.org/thyroid-disease-pregnancy/

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. T4 gets converted to the active hormone T3 in various tissues in the body.

TPO antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

Thyroglobulin antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

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

Eye surgery for thyroid eye disease and quality of life

BACKGROUND

Graves’ disease is an autoimmune condition that affects thyroid function and causes hyperthyroidism. This occurs when the body develops antibodies that attack and turn on the thyroid. These antibodies are known as thyroid stimulating immunoglobulins, or TSI. Approximately 30-50% of patients may also develop an associated condition that affects the eyes, known as thyroid eye disease, or Graves’ Ophthalmopathy. However, only a relatively small percentage of patients with thyroid eye disease develop significant symptoms. These symptoms can include burning, itching, increasing tearing, double vision and decreased vision. The most severe symptom is inflammation of the eye muscles that causes bulging of the eyes that can alter a patient’s appearance. Risk factors for developing thyroid eye disease include female sex, smoking, having been treated with radioactive iodine, elevated TSI, and, possibly, the duration and severity of hyperthyroidism.

The symptoms of thyroid eye disease can be severe and affect quality of life in many ways. The treatments available at this time depend on the severity of the eye disease and include eye drops, eye patches, medications to decrease muscle inflammation, treatment of the hyperthyroidism, external radiation to the eye muscles and surgery. There are different types of surgeries that are offered that may include eyelid surgery, eye muscle surgery to correct double vision and surgery of the eye sockets to make more room for the inflamed eye muscles.

This study was done by reviewing and analyzing existing studies to help assess whether the different types of eye surgery improved the quality of life in patients with thyroid eye disease.

THE FULL ARTICLE TITLE


SUMMARY OF THE STUDY

The authors analyzed data from 10 studies which included a total of 632 patients, with a mean age of 48.4 years. The instrument used was the Graves’ Ophthalmopathy Quality of Life questionnaire. The results of this analysis suggest that eye surgery is associated with improved quality of life in regards to appearance but also in regards to visual function.

For improvement in appearance, surgery of the eye sockets had the most improvement, followed by eyelid surgery. Overall surgery of the eye sockets resulted in improved appearance and eye muscle surgery improved function and appearance, while eyelid surgery improved only eye appearance.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Thyroid eye disease can be highly debilitating and have substantial long-term negative connotations for patients’ wellbeing and quality of life. This study showed that surgery can improve quality of life in these patients, but the type of surgery chosen impacts different aspects of quality of life.

Importantly, there is a new medical treatment that has shown to be very effective, so future studies should include evaluation of quality of life in patients treated with this new medication.

— Jessie Block-Galarza, MD
GRAVES’ DISEASE, continued

ATA THYROID BROCHURE LINKS
Graves’ Disease: https://www.thyroid.org/graves-disease/
Graves' Eye Disease: https://www.thyroid.org/graves-eye-disease/

ABBREVIATIONS & DEFINITIONS

**Thyroid Eye Disease:** Also known as Graves Ophthalmopathy. TED is most often seen in patients with Graves’ disease but can also be seen in patients with Hashimoto’s thyroiditis. 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.

**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).

**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.

AUGUST
Thyroid & Pregnancy
Awareness Month

AMERICAN THYROID ASSOCIATION
www.thyroid.org
GRAVES’ DISEASE

Rituximab may increase remission in young patients with Graves’ disease

BACKGROUND
Graves’ disease is the most common cause of hyperthyroidism in the United States. It is an autoimmune condition and occurs when the body develops antibodies that attack and turn on the thyroid. These antibodies are known as thyroid stimulating immunoglobulins, or TSI. Treatment options include antithyroid drugs (ATDs), radioactive iodine and surgery. ATDs may affect the autoimmune process and cause the Graves’ disease to go into remission. In general, when patients are treated with ATDs for 1 to 3 years, rates of remission are generally 20 to 30%.

Rituximab is a monoclonal antibody that suppresses an overactive immune response and has been shown to be effective in treating other autoimmune diseases such as rheumatoid arthritis. Several clinical trials using Rituximab for adult patients with Graves’ disease have been performed, but there were no reports of its use in young patients. In the current study, disease remission and treatment safety were evaluated in young patients with Graves’ disease when Rituximab was administered together with ATDs.

THE FULL ARTICLE TITLE

SUMMARY OF THE STUDY
This study was phase 2 trial, meaning it was a small study testing safety and effectiveness prior to moving to large scale trials (phase 3). A total of 27 patients diagnosed with Graves’ disease between the ages of 12 and 20 years were enrolled within 6 weeks after the initiation of ATDs (carbimazole and propylthiouracil). After a single 500-mg intravenous dose of Rituximab, the ATDs were titrated according to thyroid function and were stopped at 12 months. Remission outcomes were assessed at 24 months. If patients were still hyperthyroid at 12 months, ATD therapy was continued. Participants were reviewed and had laboratory blood tests at week 4 after the end of Rituximab therapy and thereafter at regular intervals.

The proportion of Graves’ disease patients in remission at 24 months was 48% (13 of 27). At 12 months, the daily carbimazole dose was less than 5 mg in 21 of 27 participants. There were no differences in the time taken for serum free thyroxine (FT4) and free triiodothyronine (FT3) concentrations to normalize between the remission group and the relapse group. There were no serious adverse effects as the Rituximab was well tolerated.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study shows that adding a single dose of Rituximab to ATD therapy in patients with Graves’ disease may increase the likelihood of remission without severe side effects in young patients. This is an important finding and larger, phase 3, trials are warranted.

— Alan Farwell, MD

ATA THYROID BROCHURE LINKS
Graves’ Disease: https://www.thyroid.org/graves-disease/
Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/
GRAVES’ DISEASE, 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 meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

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).

Rituximab: a monoclonal antibody that suppresses an overactive immune response and has been shown to be effective in treating other autoimmune diseases such as rheumatoid arthritis.
Pre-existing thyroid autoimmunity is associated with increased thyroid cancer risk

BACKGROUND
Autoimmune disease is a major cause of thyroid problems in the US. This is a group of disorders that are caused by antibodies that get confused and attack the thyroid (thyroid autoimmunity). These antibodies can either turn on the thyroid (Graves’ disease, hyperthyroidism) or turn it off (Hashimoto’s thyroiditis, hypothyroidism). Thyroid autoimmunity has been proposed to be a risk factor for the development of thyroid cancer by causing chronic inflammation in the thyroid gland. Chronic inflammation is known to come before the development of cancer in many other body tissues. Hashimoto’s thyroiditis, the most common autoimmune thyroid disease in the United States, can be diagnosed through measurement of thyroid autoantibodies in the blood, the appearance of the gland on ultrasound or after examining the gland after surgery. Previous studies have suggested an association between autoimmune thyroid disease and thyroid cancer. The aim of this study is to determine whether there is an association of thyroid cancer with autoimmune thyroid disease by evaluating for the presence of thyroid autoantibodies in thyroid cancer patients with or without diagnosed autoimmune thyroid disease.

THE FULL ARTICLE TITLE

SUMMARY OF THE STUDY
This study included U.S. active-duty military personnel diagnosed with thyroid cancer from 1996 to 2014. The study data was obtained from combining 3 groups of data related to the US military: a comprehensive dataset including demographic information and medical diagnoses, the central military cancer registry, and a serum bank that collects samples from military personnel approximately every two years. A total of 451 cases with serum available both 3-5 years and 7-10 years before the date of thyroid cancer diagnosis were randomly selected. The cases were age- and sex-matched to randomly selected controls. Serum thyroid peroxidase antibodies (anti-TPO), thyroglobulin antibodies (antiTg-Ab), and nicotine, a biomarker for exposure to tobacco were measured.

The majority of patients (61%) were male, with an average age of 36 years. Overall, 80% of patients had classical papillary thyroid cancer (PTC), while the rest had the follicular variant of PTC. Patients with pre-existing high anti-TPO antibody levels measured in banked sera collected 7 to 10 years prior to the thyroid cancer diagnosis had nearly double the odds of developing thyroid cancer. This association was 2.5 increased in females as compared to 1.6 times increased in males. In addition, the thyroid cancer risk increased as the serum anti-TPO antibody levels increased. Smoking did not affect the association between thyroid autoimmunity and thyroid cancer in this population.

Additional analysis showed that a pre-existing diagnosis of autoimmune thyroid disease accounted for 35% of the increased likelihood of these patients to be diagnosed with thyroid cancer. However, these patients had more favorable cancer features (e.g., smaller cancer size and less often spread into the neck lymph nodes), indicating a less aggressive cancer and/or diagnosis at earlier stages in thyroid cancer patients with known thyroid autoimmunity because of increased screening in this group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study showed that long-standing autoimmune thyroid disease (up to 10 years prior to thyroid cancer diagnosis) is associated with papillary thyroid cancer. Patients with higher thyroid autoantibody titers had a higher risk of developing papillary thyroid cancer. Patients with known thyroid autoimmune disease were diagnosed with thyroid cancer at earlier stages, because of close monitoring of these patients.

― Alina Gavrila, MD, MMSC
THYROID AND CANCER, continued

ATA THYROID BROCHURE LINKS
Hashimoto’s Thyroiditis: https://www.thyroid.org/hashimotos-thyroiditis/
Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS
Antibodies: proteins produced by the body’s immune cells that attack and destroy potentially harmful foreign substances, bacteria/viruses that cause infections as well as abnormal body cells. Occasionally the antibodies get confused and attack the body’s own tissues, causing autoimmune disease.

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).

Thyroid antibodies (thyroid peroxidase/TPO and thyroglobulin/Tg 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.

Hashimoto’s thyroiditis: the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy it.

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).

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

Lack of an impact of education and income on the increase of thyroid cancer in Denmark

BACKGROUND
Until recently, thyroid cancer was the fastest rising cancer in the United States. The reasons behind this increase is considered to be largely due to increased detection. Thyroid cancer is also the most common endocrine cancer. Overall the prognosis is excellent and, in the vast majority of patients, the concern is thyroid cancer recurrence rather than death from thyroid cancer. This because thyroid cancer is usually very slow growing and because we have excellent treatment options. There are different types of thyroid cancer based on how abnormal the cancer cells look under a microscope. The most frequent types are papillary thyroid cancer and follicular thyroid cancer.

Thyroid cancer also has been increasing in other parts of the world. Indeed, the occurrence of new cases of thyroid cancer in Denmark has increased considerably from 1980 to 2014. The goal of the study was specifically to evaluate how the level of education and income of adults in Denmark was associated with the increase in thyroid cancer.

THE FULL ARTICLE TITLE
Sørensen SM et al 2022 Temporal trends in papillary and follicular thyroid cancer incidence from 1995 to 2019 in adults in Denmark according to education and income. Thyroid. Epub 2022 Apr 22. PMID: 35459415.

SUMMARY OF THE STUDY
Danish nationwide health registries hold validated and accurate information on cancer diagnoses, medical history, and socioeconomic variables, with virtually complete coverage of the population. The Danish Cancer Registry contains information on nearly all primary cancers diagnosed in Denmark since 1987. Information includes date of birth, sex, age at diagnosis, and cancer characteristics. Using these registries, all adult Danish citizens during a period of 25 years (from 1995-2004 and 2005-2019) with a diagnosis of papillary thyroid cancer and follicular thyroid cancer were studied.

A total of 3,454 cases of papillary thyroid cancer and 972 cases of follicular thyroid cancer were identified and placed in categories according to age, gender, size of the cancer, education and income. The study found that there was a similar increase in papillary thyroid cancer and follicular thyroid cancer among both men and women through all levels of education and income. There was no difference observed between small and large papillary thyroid cancers regarding socioeconomic status in either gender. These results may suggest a true increase in the incidence of papillary thyroid cancer and follicular thyroid cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study done in Denmark demonstrated an increased detection of papillary thyroid cancer and follicular thyroid cancer among all levels of education and income, but there were no significant relationships. This study is important as we are increasingly challenged with variability in health care coverage from insurance companies, in addition to the lack of access and support for health care services for many underserved groups of our population in the United States. Although these findings in Denmark may not be representative of other parts of the world (especially because of the universal health care system that is in place in that country), it does suggest to us that the increase in papillary thyroid cancer and follicular thyroid cancer may be a result of many variables different than level of education and income.

—Juan Vasquez Mendez, MD
Maria del Pilar Brito, MD
THYROID CANCER, continued

ABAECIATIONS AND 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).

**Follicular thyroid cancer:** is a tumor of the follicular cells that are lined by cuboidal epithelial cells and have capsular and vascular invasive properties.

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): [https://www.thyroid.org/thyroid-cancer/](https://www.thyroid.org/thyroid-cancer/)

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