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AMERICAN THYROID ASSOCIATION

Optimal Thyroid Health for All

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Kowal A et al 2020 Treatment of thyroid dysfunction and serum lipids: A systematic review and meta-analysis. *J Clin Endocrinol Metab* 105:dga672. PMID: 32954428.

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Yang X et al 2020 The association between isolated maternal hypothyroxinemia in early pregnancy and preterm birth. *Thyroid* 30:1724–1731. PMID: 32434441.

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Bervini S et al 2020. Incidence of iodine-induced hyperthyroidism after administration of iodinated contrast during radiographic procedures: A systematic review and meta-analysis of the literature. *Thyroid*. Epub 16 Dec 2020.

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Ren Y et al 2020 The presence of Hürthle cells does not increase the risk of malignancy in most Bethesda categories in thyroid fine-needle aspirates.

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The use of PET imaging may change treatment and improve long-term survival of patients with thyroid cancer who have increased thyroglobulin levels and negative radioiodine scanning

Thyroid cancer has a good prognosis in general, as most patients are cured after their initial treatment. However, thyroid cancer can occasionally recur, and when it recurs, thyroid cancer can become resistant to radioactive iodine therapy if the cells no longer take up iodine. The goal of this study was to evaluate whether the use of PET scans to detect cancerous areas improves survival in patients with recurrent thyroid cancer resistant to radioactive iodine therapy.

Schleupner MC et al 2020 Impact of FDG-PET on therapy management and outcome of differentiated thyroid carcinoma patients with elevated thyroglobulin despite negative iodine scintigraphy. *Nuklearmedizin* 59:356–364. PMID: 32542618.

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Clinical Thyroidology for the Public

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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 [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. 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/>)

April is [Hashimoto's Disease Awareness Month](#).

In this issue, the studies ask the following questions:

- Is combination L-T₄/L-T₄ therapy an option for management of hypothyroidism?
- What is the effect of treating hypothyroidism on elevated cholesterol levels?
- Does an isolated low T₄ in the mother cause problems with the baby during pregnancy?
- Should you worry about your thyroid after getting a CT scan?
- What do Hurtle cells mean in thyroid nodule biopsies?
- Do PET scans affect long term survival in advanced papillary thyroid cancer?

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

— Alan P. Farwell, MD,



HYPOTHYROIDISM

A joint consensus statement from the American, British, and European thyroid associations on the use of combination L-T₄/L-T₃ therapy in hypothyroidism

BACKGROUND

Hypothyroidism is common, affecting 2-3% of the US population. When you include mild forms (subclinical hypothyroidism), up to 25% of certain populations may be affected. Thyroxine (T₄) is the main thyroid hormone secreted by the thyroid gland. It is converted to triiodothyronine (T₃) in other areas of the body where thyroid hormone acts. The thyroid also secretes T₃ at a low level. Most of the actions of thyroid hormone are attributed to T₃.

Levothyroxine (L-T₄), the pill form of T₄, is the most commonly recommended treatment for hypothyroidism. Long-term experience with this therapy suggests that it is safe and effective and is accepted by most patients with hypothyroidism, resolving most, if not all, of their hypothyroid symptoms. However, despite returning the thyroid hormone levels to normal, a certain percentage of hypothyroid patients continue to have symptoms attributed to hypothyroidism. This has led to a desire by patients to find alternative treatments to L-T₄ alone. One such treatment is the use of combination therapy, adding L-T₃ (liothyronine) with L-T₄ to increase blood T₃ levels. As a consequence, combination therapy with L-T₄/L-T₃ began to be used, despite the lack of evidence suggesting a real benefit. Interesting new data have emerged to suggest a genetic basis why some patients may do better on combination therapy. Rarely, changes in the enzyme that converts T₄ to T₃ (type 2 deiodinase) causes it to not work well. In these patients, more of their blood T₃ levels may come from the thyroid rather than from the conversion of T₄. Thus, in those patients, L-T₄/L-T₃ combination therapy may be preferred.

To help address this, the American Thyroid Association (ATA), the British Thyroid Association (BTA), and the European Thyroid Association (ETA) developed a consensus statement in which they reviewed the latest evidence of hypothyroidism treatment with L-T₄/L-T₃ and developed recommendations for future clinical trials.

THE FULL ARTICLE TITLE

Jonklaas J et al 2020 Evidence based use of LT₄/LT₃ combinations in treating hypothyroidism: A consensus document. *Thyroid*. Epub 2020 Dec 4. PMID: 33276704.

SUMMARY OF THE STUDY

To draft this consensus statement, a task force consisting of 12 experts in all aspects of LT₄/LT₃ combination therapy was formed. Comments from members of all three societies, as well as input from two patients involved in the conference, were also taken into account. A total of 34 consensus items were available for voting, of which 28 received at least a 75% approval and 13 full approval. The following are selected highlights from the published statement:

The statement assessed new experimental data in the laboratory that suggests T₄ may lead to a “normal” TSH while reducing T₃ generation in other areas of the body due to effect of the type 2 deiodinase in the brain. The task force also evaluated results from available clinical trials of combination therapy (including desiccated thyroid extracts). The analysis of these trials did not show any consistent benefits of combination treatment in hypothyroid patients; however, the numerous limitations did not allow it to draw a definite conclusion on the issue.

After analyzing the numerous points of criticism of the above-mentioned trials, the task force provided some useful suggestions for a protocol for future adequately powered and high-quality randomized, controlled trials in hypothyroid patients who appear not to have full replacement by L-T₄ monotherapy despite hormone levels in the normal range. The main suggestions were to consider the severity of hypothyroidism and evaluate the presence of other medical issues (heart diseases, cancer, or psychiatric disorders). In addition, the trial studies should be at least one year in duration and include: (i) adults with normal serum TSH at baseline obtained after a stable L-T₄ replacement dose; (ii) hypothyroid patients treated with at



HYPOTHYROIDISM, continued

least 1.2 µg/kg/day of L-T₄ (thus including only patients without residual thyroid function); and (iii) patients with persistent hypothyroid symptoms or dissatisfaction and concurrently decreased baseline serum T₃ concentrations during L-T₄ monotherapy.

The task force concluded that the goal of future L-T₄/L-T₃ combination studies should give L-T₃ at least twice a day while waiting for the development of a sustained release L-T₃ preparation which is not yet available for clinical use.

Future studies need to be able to evaluate thyroid-related quality of life in a standard way, such as measured by thyroid-specific surveys like ThyroPRO. Patient preferences for thyroid hormone replacement therapy should be considered as secondary endpoint in clinical trials.

The task force also analyzed the effects of the genetic changes in the type 2 deiodinase enzyme found in some patients. Since the impact of these genetic changes is still unclear, the task force suggested that future studies be performed of the subgroup of patients with these genetic changes to clarify the potential benefit of combination therapy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Future clinical trials of L-T₄/L-T₃ combination therapy should be guided by the recommendations developed in this consensus statement. The results of such redesigned trials could lead to improved understanding of the treatment of hypothyroid patients with thyroid hormone replacement therapy.

— Alan Farwell, MD

ATA THYROID BROCHURE LINKS

Thyroid Hormone Treatment: <https://www.thyroid.org/thyroid-hormone-treatment/>

Hypothyroidism (Underactive): <https://www.thyroid.org/hypothyroidism/>

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 T₄ level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

Levothyroxine (T₄): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tirosint™ and generic preparations.

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

Desiccated thyroid extract: thyroid hormone pill made from animal thyroid glands. Currently desiccated thyroid extract is made from pig thyroids and is available as Armour Thyroid™ and Nature-Throid™.

Thyroxine (T₄): the major hormone produced by the thyroid gland. T₄ gets converted to the active hormone T₃ in various tissues in the body.



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HYPOTHYROIDISM, continued

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

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

Deiodinase enzymes: these enzymes convert T_4 to T_3 on the cellular level by removing an iodine molecule from T_4 .



APRIL
Hashimoto's
Thyroiditis
Awareness Month



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HYPOTHYROIDISM

Treating hypothyroidism decreases cholesterol levels

BACKGROUND

Cholesterol and lipoproteins have been shown to be associated with heart disease. LDL-cholesterol is known as the bad cholesterol and increased levels are associated with an increase in heart disease. Lipoprotein (a) (Lp(a)) is also associated with increased heart disease. HDL-cholesterol is known as the good cholesterol as increased levels seem to lower the risk of heart disease.

Thyroid hormone has a direct effect on cholesterol levels. Hypothyroid patients have increased cholesterol levels compared to individuals with normal thyroid function. Treatment with thyroid hormone often lowers the cholesterol levels in patients with hypothyroidism. In hyperthyroid patients, on the other hand, cholesterol levels are low and correction of the hyperthyroid state with medications may cause an increase in cholesterol levels. This study investigates the effect of thyroid hormone replacement therapy versus observation for overt and subclinical hypothyroidism and hyperthyroidism on various cholesterol and lipoprotein levels.

THE FULL ARTICLE

Kowal A et al 2020 Treatment of thyroid dysfunction and serum lipids: A systematic review and meta-analysis. *J Clin Endocrinol Metab* 105:dga672. PMID: 32954428.

SUMMARY OF THE STUDY

The authors looked at many published articles that studied patients who received thyroid hormone therapy for overt or subclinical hypothyroidism and patients with hyperthyroidism who received treatment for hyperthyroidism. They choose 166 studies that included 12,855 patients. Regarding the studies on hyperthyroid patients: the average age of the patients was 48 years and 20% were males. Treatment of patients with overt hyperthyroidism (low TSH and high FT₄ and T₃) was associated with

an increase of total cholesterol levels of about 44 mg/dL. LDL-cholesterol increased by 31 mg/dL and Lp(a) increased by 4 mg/dL. Patients treated for subclinical hyperthyroidism (low TSH and normal FT₄ and T₃) did not have changes in their lipid levels.

In the studies looking at overt hypothyroidism, the average age was also 48 years. When patients with overt hypothyroidism (high TSH and low FT₄) were treated with levothyroxine their total cholesterol levels went down by 58 mg/dL, LDL-cholesterol was lowered by 41 mg/dL, HDL-cholesterol was lowered by 4 mg/dL, triglycerides by 7 mg/dL and Lp(a) by 5 mg/dL. For patients with subclinical hypothyroidism (high TSH and normal FT₄), treatment with levothyroxine, showed a small decrease of total cholesterol levels by 12 mg/dL, LDL-cholesterol by 11 mg/dL and triglycerides by 4 mg/dL.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study confirms that treatment of hyper and hypothyroidism is associated with changes in cholesterol and lipoprotein levels. Treatment of overt hypothyroidism with levothyroxine significantly lowers cholesterol levels while treatment of hyperthyroidism with antithyroid medications causes an increase in total cholesterol, LDL-cholesterol and HDL-cholesterol. The effects of treating patients with subclinical thyroid disease resulted in much smaller changes. While overt thyroid disease requires therapy, treatment of subclinical thyroid disease is much less straightforward. One drawback of these studies is that none of the studies included looked at the risk of heart disease. However, this paper suggests that the small improvement in cholesterol after treating subclinical hypothyroidism may be of benefit for some patients.

— Susana Ebner MD



HYPOTHYROIDISM, continued

ATA BROCHURE LINKS

Hypothyroidism (Underactive): <https://www.thyroid.org/hypothyroidism/>

Hyperthyroidism (Overactive): <https://www.thyroid.org/hyperthyroidism/>

Thyroid Hormone Treatment: <https://www.thyroid.org/thyroid-hormone-treatment/>

ABBREVIATIONS & DEFINITIONS

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

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 T₄ level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

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

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

Lipids: the general term used to describe fat molecules in the blood. Examples of blood lipids include cholesterol, HDL ("good") cholesterol, LDL ("bad") cholesterol, lipoproteins and triglycerides.



THYROID AND PREGNANCY

Having low thyroid hormone level in early pregnancy may be associated with early birth of the baby

BACKGROUND

Thyroid hormone is essential for normal growth and development of the baby during pregnancy. During early pregnancy the mother makes all the thyroid hormone for the baby. Near the end of the 1st trimester, the baby's thyroid develops and begins to make thyroid hormone. For the remainder of the pregnancy, thyroid hormone from both the mother and the baby help the baby to develop normally. Lack of thyroid hormone during pregnancy, either from the mother or the baby, can cause problems with brain development and poor pregnancy outcomes, including early birth of the baby.

Hypothyroidism is diagnosed when thyroid hormone level is low and TSH is elevated. Mild/subclinical hypothyroidism is diagnosed when thyroid hormone level is normal and TSH is elevated. During pregnancy, the mother's thyroid hormone level may be low but her TSH is normal, a condition known as isolated maternal hypothyroxinemia (IMH). While it is clear that hypothyroidism can cause problems with the baby, we do not know whether IMH has any bad effect on the baby or the pregnancy. This study was done to find out whether there was an association between having IMH in early pregnancy and early birth of the baby.

THE FULL ARTICLE TITLE

Yang X et al 2020 The association between isolated maternal hypothyroxinemia in early pregnancy and preterm birth. *Thyroid* 30:1724–1731. PMID: 32434441.

SUMMARY OF THE STUDY

The study was done in Shanghai, China between January 2013 and December 2016. IMH was defined as a TSH within normal range and a low free T₄. Preterm (early) birth was defined as birth of the baby before 37 weeks of pregnancy. The researchers excluded the women who had a twin pregnancy, experienced a miscarriage, used a medication that could affect the thyroid function, or had a history of thyroid disease.

There were 41,911 patients in the study, 963 were diagnosed with IMH and 40,948 had normal thyroid function. The patients who had IMH were older, weighed more and had higher education level. There were also more women with multiple past pregnancies, diabetes mellitus during pregnancy and positive TPO antibodies in the IMH group.

Women with IMH had an increased risk of having their baby earlier than 37 weeks. An interesting finding was that the risk was higher if the baby was a girl.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In conclusion, this study found that IMH in early pregnancy may be associated with early birth of the baby and the baby's sex may also affect the risk. We need further studies to find out whether treatment with thyroid hormone would benefit these patients and their babies.

— Ebru Sulanc, MD

ATA THYROID BROCHURE LINKS

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



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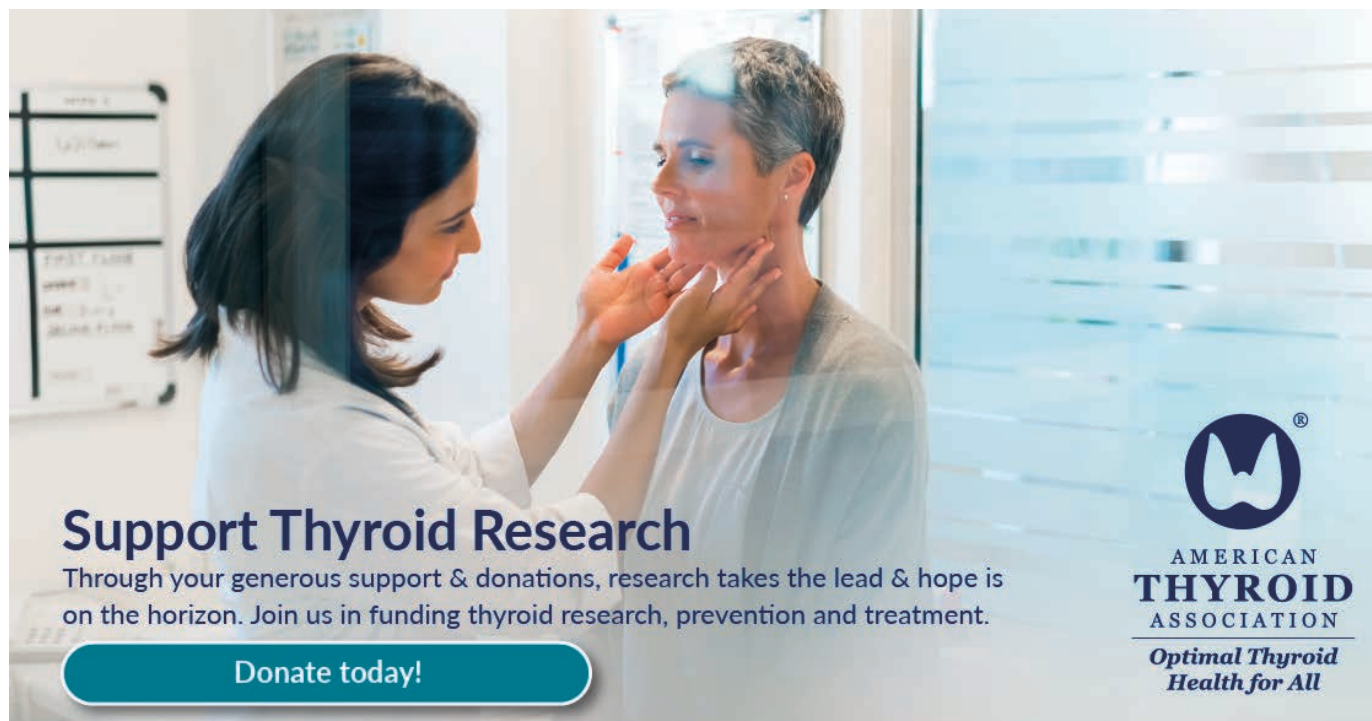
THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

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

Thyroxine (T₄): the major hormone produced by the thyroid gland. T₄ gets converted to the active hormone T₃ in various tissues in the body.

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



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HYPERTHYROIDISM

The incidence of hyperthyroidism after exposure to iodinated radiologic contrast media is extremely low

BACKGROUND

Iodine is essential for normal thyroid function, as the thyroid hormones contain iodine. World-wide, iodine deficiency is an important cause of hypothyroidism. However, exposure to an excessive amount of iodine can actually cause hyperthyroidism. This type of iodine-induced hyperthyroidism is called the Jod-Basedow effect and it typically presents a few weeks after exposure to a large amount of iodine. Those with preexisting thyroid nodules are felt to be particularly at risk. Iodinated contrast media (ICM) that is administered before specific radiologic tests, such as CT scans, contains a considerable amount of iodine. Given that over 80 million doses of ICM were provided to people in 2005 worldwide, iodine-induced hyperthyroidism may be more common than we think. As a result, some physicians choose to monitor thyroid hormone levels after ICM exposure. Some may even consider proactively treating patients at high risk of iodine-induced hyperthyroidism with antithyroid medications before radiological procedures. However, the overall risk of iodine-induced hyperthyroidism after ICM is unclear.

The authors of the current study performed a systematic review of the literature to better understand iodine-induced hyperthyroidism due to ICM.

THE FULL ARTICLE TITLE

Bervini S et al 2020. Incidence of iodine-induced hyperthyroidism after administration of iodinated

contrast during radiographic procedures: A systematic review and meta-analysis of the literature. *Thyroid*. Epub 16 Dec 2020.

SUMMARY OF THE STUDY

The authors searched the literature and identified 30 studies that were suitable to estimate the incidence of iodine-induced hyperthyroidism. Studies involving children or pregnant women were excluded. The overall incidence of overt hyperthyroidism after iodinated contrast media was 0.1% based on all the pooled data. Regarding the timing of hyperthyroidism after exposure to contrast, there were no cases of iodine-induced hyperthyroidism one week after exposure in the 6 studies that examined that time point. At 30 days following ICM exposure, the incidence of iodine-induced hyperthyroidism was 0.4%. Baseline thyroid status (i.e. whether people were hyperthyroid, euthyroid or hypothyroid at the time of contrast administration) was not a risk factor for developing iodine-induced hyperthyroidism.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Despite the widespread use of ICM, this review suggests that the incidence of hyperthyroidism following ICM exposure is extremely low. Based on these results, there is no evidence to use antithyroid medications before ICM exposure or even to monitor thyroid hormone levels afterwards on a routine basis.

— Philip Segal, MD

ATA THYROID BROCHURE LINKS

Hyperthyroidism (Overactive): <https://www.thyroid.org/hyperthyroidism/>



HYPERTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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

Iodine: an element found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. Common foods high in iodine include iodized salt, dairy products, seafood and some breads.

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



THYROID NODULES

What do Hürthle cells mean in thyroid nodule aspirates?

BACKGROUND

Thyroid nodules are very common and many require biopsy to evaluate the risk of cancer. Most biopsies are clear in terms of cancer (~5%) and non-cancer or benign (80-85%). However, up to 15% are determined to be indeterminate, meaning that a definite diagnosis of cancer vs benign cannot be made. This leads to additional testing and/or surgery.

Hurthle cells are a particular type of thyroid cell that can be found in both benign and cancerous thyroid nodules. Therefore, when seen in a thyroid biopsy sample, Hurthle cells often lead to an indeterminate diagnosis. Currently, the only distinction is whether a nodule is almost completely replaced by Hurthle cells (which is called a Hurthle cell neoplasm and a Bethesda class IV indeterminate nodule), or has some amount of Hurthle cells (which is then usually called either a Bethesda class III indeterminate nodule or a benign nodule depending on other benign features in the biopsy sample). Moreover, some of the additional testing of indeterminate nodules do not perform as well when there are a lot of Hurthle cells.

In this study, the authors aimed to determine the risk of cancer for each Bethesda biopsy category based on the amount of Hurthle cell change seen in the biopsy specimen.

THE FULL ARTICLE TITLE

Ren Y et al 2020 The presence of Hürthle cells does not increase the risk of malignancy in most Bethesda categories in thyroid fine-needle aspirates.

SUMMARY OF THE STUDY

This was a study of 203 biopsy slides at a single institution where the cytology reports contained the words Hurthle cell or oncocytes (another name for Hurthle cells) and the patients had a subsequent surgery. A single senior cytopathologist reviewed all the slides and classified them as mild, moderate, or predominate Hurthle cells in the specimen. The rate of cancer was then determined for each Bethesda biopsy category (they range from I-VI) and the amount of Hurthle cells in a biopsy specimen. These were also compared to historical controls of the risk of cancer for each Bethesda category at 5 institutions.

Overall, the risk of cancer was 3% for mild Hurthle cells, 15% for moderate Hurthle cells, and 21.4% for predominant Hurthle cells. Moreover, the risk of cancer for the entire group was equal or lower for each Bethesda category except for Bethesda II/Benign biopsies. These biopsies that were classified as predominantly Hurthle cell (>75%) had a higher risk of cancer (27.3% vs 9.3%) compared to the historical control group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In general, the presence of Hurthle cells did not change or increase the risk of cancer for biopsy specimens. This is reassuring for patients that see the words “Hurthle cells” on their biopsy report, that there is generally no increased risk of cancer.

— Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

Thyroid Nodules: <https://www.thyroid.org/thyroid-nodules/>

Fine Needle Aspiration Biopsy of Thyroid Nodules: <https://www.thyroid.org/fna-thyroid-nodules/>



THYROID NODULES, continued

ABBREVIATIONS & DEFINITIONS

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

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

Indeterminate thyroid biopsy: this happens a few atypical cells are seen but not enough to be abnormal

(atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

Hurthle cells: are a particular type of thyroid cell that can be found in both benign and cancerous thyroid nodules.



THYROID CANCER

The use of PET imaging may change treatment and improve long-term survival of patients with thyroid cancer who have increased thyroglobulin levels and negative radioiodine scanning

BACKGROUND:

Thyroid cancer has a good prognosis in general, as most patients being cured after their initial treatment. This initial treatment almost always includes surgery and, when the thyroid cancer is advanced, includes radioactive iodine therapy. The radioactive iodine works as a “magic bullet” as the cancerous cells take it up, which then destroys the cells once trapped inside. However, thyroid cancer can occasionally recur, especially if it was advanced when it was initially discovered. When it recurs, thyroid cancer can become resistant to radioactive iodine therapy if the cells no longer take up iodine. In this situation, a radioactive iodine whole body scan will also fail to identify the recurrent cancer sites. However, a positron-emission tomography (PET scan) that uses a small amount of radiolabeled glucose will often detect the cancerous areas, since recurrent thyroid cancer is often more aggressive and active, thus taking up larger amounts of glucose which is measured by the PET scan. The goal of this study was to evaluate whether the use of PET scans to detect cancerous areas improves survival in patients with recurrent thyroid cancer resistant to radioactive iodine therapy.

THE FULL ARTICLE TITLE:

Schleupner MC et al 2020 Impact of FDG-PET on therapy management and outcome of differentiated thyroid carcinoma patients with elevated thyroglobulin despite negative iodine scintigraphy. *Nuklearmedizin* 59:356–364. PMID: 32542618.

SUMMARY OF THE STUDY:

This study included 194 patients with recurrent thyroid cancer who underwent initial treatment consisting of total thyroidectomy followed by radioactive iodine therapy between 1996 and 2014 at an institution in Germany. During follow-up, these patients had elevated serum thyroglobulin (Tg) levels without corresponding cancerous areas noted on radioactive iodine whole body scans.

Elevated Tg was defined as a baseline Tg higher or equal to 1 mg/L or a stimulated Tg higher or equal to 2 mg/L. Patients were divided into those who underwent PET scanning (PET group) and those who did not (non-PET group) at any time during follow-up. Patients were initially imaged using a single-modality PET scanner until 2004 and then a hybrid scanner combined with computed tomography (CT) was used until 2014.

Between 1996 and 2004, 42 of 70 patients (60%) underwent single-modality PET imaging, while 107 of 149 patients (86%) underwent hybrid PET/CT between 2004 and 2014. Overall, 149 patients (77%) were imaged with PET or PET/CT, while 45 patients (23%) were not. The patients in the PET group had more severe cancer and higher stimulated Tg levels at the time of study enrollment, and they already received higher radioactive iodine doses prior to participating in this study. The average Tg levels at enrolment were 3.7 vs. 3.3 mg/L, while stimulated Tg was 13.9 vs. 3.1 mg/L in the PET and non-PET groups, respectively.

During the first nine months following PET imaging, more patients underwent surgery (28% vs. 13%), while fewer patients received radioactive iodine therapy (63% vs. 82%) as compared to the non-PET group. External-beam radiotherapy was rarely used in both groups (4% vs. 2%). On long-term follow-up of up to 15 years, the patients in the PET group received all types of treatments more often as compared to the non-PET patients (radioactive iodine therapy: 54% vs. 40%, surgery: 24% vs. 11%, and external beam radiotherapy: 18% vs. 2%, respectively). A total of 21% vs. 32% of patients attained complete remission, while 26% vs. 10% showed progressive disease in the PET vs. non-PET groups. The overall survival and event-free survival (time from study enrollment until recurrence was diagnosed) rates were similar in the PET and non-PET groups (15.8 vs. 16.4 years, and 11.9 vs. 13.5 years, respectively).



THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Patients with thyroid cancer who present with elevated serum Tg levels and negative radioiodine scanning after their initial treatment and are evaluated with PET scanning had similar long-term survival and outcomes to patients treated without PET, despite having more advanced disease at baseline. Early use of PET scanning

in these patients can lead to treatment changes by identifying cancer sites that are not detectable and treatable with radioiodine, but might respond to other therapies, such as surgery and external radiation therapy. Further research is needed to evaluate the long-term clinical benefit of PET imaging in this group of patients.

— Alina Gavrilă, MD, MMSc

ATA THYROID BROCHURE LINKS

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

Radioactive Iodine Therapy: <https://www.thyroid.org/radioactive-iodine/>

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid cancer (DTC): accounts for more than 90% of all thyroid cancers and has a high cure rate. It includes papillary and follicular thyroid cancer.

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

Thyroglobulin (Tg): 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, since measurable blood levels indicate recurrence.

Thyroidectomy: surgery to remove the 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.

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

Radioiodine Whole Body Scan (WBS): this imaging test uses a small amount of a radioactive iodine, to take pictures of the whole body to look for thyroid cancer metastases. The radioactive iodine scans are performed under TSH stimulation, either after thyroid hormone withdrawal or after injections of recombinant human TSH (Thyrogen), and usually include measuring serum thyroglobulin levels.

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.

Positron-emission tomography (PET): a nuclear medicine imaging test that uses a small amount of radiolabeled glucose to identify cancer. Since cancer cells are more active than normal cells, the cancer cells take up more of the radiolabeled glucose and show up on the PET scan. FDG-PET scans are frequently combined with CT scans to accurately identify where the cancer is located. Its role in thyroid cancer is still being studied.



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.



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www.thyroid.org

ATA Patient Resources:

www.thyroid.org/thyroid-information/

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(Toll-free): 1-800-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.

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Thyroid Cancer Alliance

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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 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

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.
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- 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.

Hashimoto's Thyroiditis

(Lymphocytic Thyroiditis)

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 hormones help the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

WHAT IS HASHIMOTO'S THYROIDITIS?

The term "Thyroiditis" refers to "inflammation of the thyroid gland". There are many possible causes of thyroiditis (see [Thyroiditis brochure](#)). Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis, is the most common cause of hypothyroidism in the United States. It is an autoimmune disorder involving chronic inflammation of the thyroid. This condition tends to run in families. Over time, the ability of the thyroid gland to produce thyroid hormones often becomes impaired and leads to a gradual decline in function and eventually an underactive thyroid (Hypothyroidism). Hashimoto's thyroiditis occurs most commonly in middle aged women, but can be seen at any age, and can also affect men and children.

WHAT ARE THE SYMPTOMS OF HASHIMOTO'S THYROIDITIS?

There are no signs or symptoms that are unique to Hashimoto's thyroiditis.

Because the condition usually progresses very slowly over many years, people with Hashimoto's thyroiditis may not have any symptoms early on, even when the characteristic thyroid peroxidase (TPO) antibodies are detected in blood tests. TPO is an enzyme that plays a role in the production of thyroid hormones. If Hashimoto's thyroiditis causes cell damage leading to low thyroid hormone levels, patients will eventually develop symptoms of hypothyroidism (see [Hypothyroidism brochure](#)). Hypothyroid symptoms may include fatigue, weight gain, constipation, increased sensitivity to cold, dry skin, depression, muscle aches and reduced exercise tolerance, and irregular or heavy menses. In some cases, the inflammation causes the thyroid to become enlarged (goiter), which rarely may cause neck discomfort or difficulty swallowing.

HOW IS THE DIAGNOSIS OF HASHIMOTO'S THYROIDITIS MADE?

The diagnosis of Hashimoto's thyroiditis may be made when patients present with symptoms of hypothyroidism, often accompanied by a goiter (an enlarged thyroid gland) on physical examination, and laboratory testing of hypothyroidism, which is an elevated thyroid stimulating hormone (TSH) with or without a low thyroid hormone (Free thyroxine [Free T4]) levels. TPO antibody, when measured, is usually elevated.

Occasionally, the disease may be diagnosed early, especially in people with a strong family history of thyroid disease. TPO antibody may be positive, but thyroid hormone levels may be normal or there may only be isolated mild elevation of serum TSH is seen. Symptoms of hypothyroidism may be absent.

HOW IS HASHIMOTO THYROIDITIS TREATED?

Patients with elevated TPO antibodies but normal thyroid function tests (TSH and Free T4) do not require treatment. Patient with only a slightly elevated TSH (mild hypothyroidism) may not require medication and should have repeat testing after 3-6 months if this has not already been done. For patients with overt hypothyroidism (elevated TSH and low thyroid hormone levels) treatment consists of thyroid hormone replacement (see [Thyroid Hormone Treatment brochure](#)). Synthetic levothyroxine taken orally at an appropriate dose, is inexpensive, very effective in restoring normal thyroid hormone levels, and results in an improvement of symptoms of hypothyroidism. Most patients with Hashimoto's thyroiditis will require lifelong treatment with levothyroxine. Finding the appropriate dose, particularly at the beginning, may require testing with TSH every 6-8 weeks after any dose adjustment, until the correct dose is determined. After that, monitoring of TSH once a year is generally sufficient.

When levothyroxine is taken in the appropriate dose, it has no side effects. However, when an insufficient dose is taken, serum TSH remains elevated and patients may have persistent symptoms of hypothyroidism (see [Hypothyroidism brochure](#)). If the dose is excessive, serum TSH will become suppressed and patients may develop symptoms of hyperthyroidism or have other side effects (see [Hyperthyroidism brochure](#)).



FURTHER INFORMATION

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

For information on thyroid patient support organizations, please visit the [Patient Support Links](#) section on the ATA website at www.thyroid.org

