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Carlé A et al. Hypothyroid symptoms fail to predict thyroid insufficiency in old people: a population-based case-control study. *Am J Med.* July 6, 2016

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Iodine is a micronutrient needed for thyroid hormone production. Iodine deficiency during pregnancy remains the most common cause of preventable mental retardation in the world. While severe iodine deficiency is not seen in the US, recent surveys indicate that US pregnant women are considered mildly iodine deficient. This study was a survey of U.S. midwives and obstetricians to assess their perceptions of iodine nutrition, as well as how often they recommend that their patients take an iodine supplement.

De Leo S et al. Iodine Supplementation in Women During Preconception, Pregnancy, and Lactation: Current Clinical Practice by U.S. Obstetricians and Midwives. *Thyroid* 2016 (ePub)

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The incidence of thyroid cancer has increased dramatically during the past three decades and it is now the fastest growing cancer in women. The current study is a worldwide review of the incidence of thyroid cancer that attempts to identify risk factors for the increasing incidence.

Wiltshire JJ et al. Systematic review of trends in the incidence rates of thyroid cancer. *Thyroid* 2016;26:1541-52.

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Thyroid cancer diagnoses in South Korea increased 15-fold between 1993 and 2011, and South Korea now has the world's highest rate of thyroid cancer. It is unclear whether the rise in thyroid cancer represents over-diagnosis due to increased screening or whether there has been a true increase in the number of thyroid cancers. The aim of this study was to examine the increase in South Korean thyroid cancer diagnoses.

Park S et al Association between screening and the thyroid cancer "epidemic" in South Korea: evidence from a nationwide study. *BMJ* 2016;355:i5745. doi: 10.1136/bmj.i5745.

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Kakarmath S et al Clinical, sonographic, and pathological characteristics of RAS-positive versus BRAF-positive thyroid carcinoma. *J Clin Endocrinol Metab* 2016;101:4938-44. Epub September 30, 2016.

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Clinical Thyroidology for the Public

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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 will be providing summaries of research studies that were discussed in a recent issue of *Clinical Thyroidology*, a publication of the American Thyroid Association for physicians. These summaries are present in lay language to allow the rapid dissemination of thyroid research to the widest possible audience. This means that you are getting the latest information on thyroid research and treatment almost as soon as your physicians. As always, we are happy to entertain any suggestions to improve *Clinical Thyroidology for the Public* so let us know what you want to see.

We also provide even faster updates of late-breaking thyroid news through **Twitter** at [@thyroidfriends](https://twitter.com/thyroidfriends) and on **Facebook**. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room.

Also check out our friends in the **Alliance for Thyroid Patient Education**. The Alliance member groups consist of: the *American Thyroid Association*, *Bite Me Cancer*, the *Graves' Disease and Thyroid Foundation*, the *Light of Life Foundation*, *ThyCa: Thyroid Cancer Survivors Association*, *Thyroid Cancer Canada* and *Thyroid Federation International*.

February is **Hypothyroidism Awareness Month**.

In this issue, the studies ask the following questions:

1. Is subclinical thyroid disease associated with early dementia?
2. Should patient age and gender influence screening for hypothyroidism?
3. How often is iodine supplementation recommended to pregnant women?
4. Is the incidence of thyroid cancer actually increasing all over the world?
5. Do screening programs lead to an over-diagnosis of thyroid cancer?
6. Do thyroid cancers differ depending on which gene mutations are associated with the 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, FACE



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**SUBCLINICAL THYROID DYSFUNCTION****Subclinical hyperthyroidism, but not subclinical hypothyroidism, is associated with increased dementia risk****BACKGROUND**

Overt thyroid disease means that both the TSH levels and the thyroid hormone levels are abnormal, while subclinical disease is defined by abnormal TSH levels only — the thyroid hormone levels are normal. Overt hypothyroidism and hyperthyroidism has been clearly shown to be associated with a decline in thinking and understanding (cognitive function) and possibly developing early dementia. It is still unclear whether subclinical hypothyroidism and/or hyperthyroidism are similarly associated with worsening cognitive function and early dementia. The aim of this study was to examine published studies to determine whether subclinical hypothyroidism or subclinical hyperthyroidism is associated with increased risk for dementia or impaired thought processes.

THE FULL ARTICLE TITLE

Rieben C et al Subclinical Thyroid Dysfunction and the Risk of Cognitive Decline: a Meta-Analysis of Prospective Cohort Studies. *J Clin Endocrinol Metab*. September 30, 2016 [Epub ahead of print].

SUMMARY OF THE STUDY

The authors included studies which involved adults with subclinical hypothyroidism and/or hyperthyroidism as well as people without thyroid disease. An evaluation for early dementia was performed using the Mini Mental State Examination (MMSE) ([page 18](#)). A total of 11 studies, including 16,805 participants, were eligible for inclusion. Some reported information on dementia, others reported outcomes from the MMSE and some on both. In most studies the average age of the participants was >70 years and the average follow-up was 44.4 months. Subjects on thyroid hormone or on medications that could change thyroid function were excluded when analyzing the results.

The authors found that 5 studies reported associations between subclinical hyperthyroidism and dementia, and three studies showed associations between subclinical hyperthyroidism and Alzheimer's disease, when compared to participants with normal thyroid function. There was no significant association between subclinical hypothyroidism and dementia in any of the studies. Neither subclinical hyperthyroidism nor subclinical hypothyroidism was associated with worsening MMSE scores in any of the studies that evaluated this outcome.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Current guidelines from the American Academy of Neurology recommend routine thyroid function testing in all patients newly diagnosed with dementia. Even though this study found that subclinical hyperthyroidism was associated with dementia, there was a lot of variation in the reference ranges for thyroid hormone used and methods for assessing cognition and dementia diagnosis between the included studies. It is still uncertain whether subclinical thyroid dysfunction is truly associated with dementia and whether normalization of thyroid function in these patients would improve cognitive outcomes.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

Thyroid Disease in the Older Patient: <http://www.thyroid.org/thyroid-disease-older-patient/>

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

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

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.

Overt Hypothyroidism: clear hypothyroidism an increased TSH and a decreased T₄ level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.



SUBCLINICAL THYROID DYSFUNCTION, continued

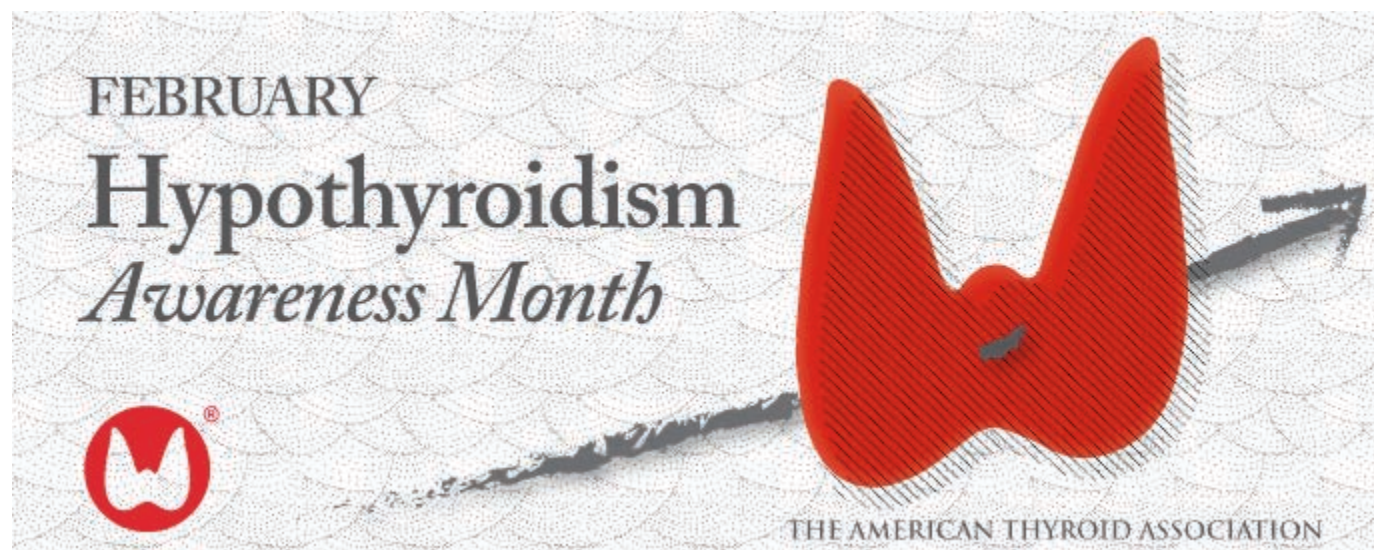
Overt Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Subclinical 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.

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

Cognition: the mental processes involved in gaining knowledge and comprehension. These processes include thinking, knowing, remembering, judging and problem-solving.

Mini Mental State Examination (MMSE) (page 18): a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. It is commonly used in medicine and allied health to screen for dementia.





HYPOTHYROIDISM

Should patient age and gender influence screening for autoimmune hypothyroidism?

BACKGROUND

Hypothyroidism is most often caused by an autoimmune process where the body makes antibodies that attack and destroy the thyroid. The thyroid gland then is unable to make enough thyroid hormone and becomes underactive. Patients with hypothyroidism usually complain of symptoms like tiredness, dry skin, constipation, hair loss, moodiness and weight gain. In contrast, patients with an overactive thyroid (hyperthyroidism) frequently note symptoms like feeling jumpy, jittery, anxious, heart racing, difficulty sleeping and weight loss. For a very long time, physicians had noticed that the symptoms of thyroid disease may differ in elderly, especially in patients with hyperthyroidism. Sometimes older patients with hyperthyroidism have more symptoms that are associated with hypothyroidism, a condition called “apathetic hyperthyroidism.” The association of age with symptoms of hypothyroidism is less studied, but it is a very important subject. Hypothyroidism is diagnosed more frequently in older age. Generally physicians rely on patient’s symptoms to choose tests necessary to make a diagnosis, it is important to identify how symptoms of elderly with hypothyroidism differ from younger patients. The purpose of this present paper is to evaluate the symptoms of hypothyroidism in different ages and compare them in younger and older groups.

THE FULL ARTICLE TITLE

Carlé A et al. Hypothyroid symptoms fail to predict thyroid insufficiency in old people: a population-based case-control study. *Am J Med.* July 6, 2016

SUMMARY OF THE STUDY

The study was done in Denmark and the subjects were selected from an existing Danish project about iodine intake and thyroid disease (Investigation of Iodine Intake and Thyroid Diseases (DanThyr) project). This project consisted of 538,734 participants, from whom 578 were newly diagnosed patients with autoimmune hypothyroidism. A total of 247 patients were invited to participate in the current study and 147 patients agreed to do so. All study subjects in DanThyr project had to fill out questionnaires periodically which asked about 13 symptoms (stuck sensation in the neck, difficulty swallowing, neck pain, wheezing, shortness of breath,

palpitations, constipation, hair loss, sensitive and dry skin, restlessness, mood liability, dizziness and tiredness). [Click here to link to the questionnaire.](#)

For every patient with hypothyroidism, 4 individuals with normal thyroid function were chosen to serve as control group. The symptoms that were recorded by participants in the questionnaire were compared between younger (younger than 50) and older (older than 60) patients as well as between the individuals with hypothyroidism and healthy controls.

The study showed that all the above 13 symptoms were seen more frequently in younger hypothyroid patients as compared to individuals without thyroid problems. However, only 3 symptoms (tiredness, shortness of breath and wheezing) were more common in older patients with hypothyroidism as compared to individuals without thyroid problems. Thus, with advancing age, the number of symptoms at the time of diagnosis of hypothyroidism was decreased. When compared between age groups and gender, symptoms were found to be an excellent tool for predicting hypothyroidism in young men, a good test for younger women, a fair test in older men and a poor test in older women.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Symptoms of hypothyroidism may be seen with less frequency in elderly patients, especially elderly women. Physicians should not rely only on symptoms to order thyroid tests in elderly population and should have a lower threshold to suspect hypothyroidism. The symptoms classically associated with hypothyroidism are likely to be most useful in diagnosing younger men and least useful in older women.

— Shirin Haddady, MD

ATA THYROID BROCHURE LINKS

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

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

**HYPOTHYROIDISM**, continued**ABBREVIATIONS & DEFINITIONS**

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

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).

BEING TREATED FOR HYPOTHYROIDISM?**ATA INVITES YOUR FEEDBACK ON THIS SURVEY:**

www.surveymonkey.com/r/hypothyroidpatientsurvey



American Thyroid Association (ATA) encourages patients with hypothyroidism to participate, healthcare professionals to share with patients and everyone to disseminate broadly this survey intended to enhance understanding and treatment of hypothyroidism. Survey results will be discussed at the **ATA Spring Satellite Symposium: Hypothyroidism – Where are We Now?** on Friday, March 31, 2017 in Orlando, Florida by panel of thyroid experts, patients and professionals. Your responses are anonymous and should only take a few minutes to complete.

For more information regarding the ATA Spring Satellite Symposium, visit the ATA website at www.thyroid.org or <http://www.thyroid.org/2017-hypo-symposium/>.

**THYROID AND PREGNANCY****How often is iodine supplementation recommended by U.S. midwives and obstetricians to their patients?****BACKGROUND**

Thyroid hormone is needed for normal brain development. Hypothyroidism in the mother during pregnancy can cause delayed brain development leading to decreased intelligence and mental retardation in the baby. Iodine is a micronutrient needed for thyroid hormone production as the thyroid hormones contain iodine. Iodine deficiency is an important cause of hypothyroidism in parts of the world. Iodine deficiency during pregnancy remains the most common cause of preventable mental retardation in the world. While severe iodine deficiency is not seen in the US, recent surveys indicate that US pregnant women are considered mildly iodine deficient. Thus, several major medical societies recommend that women who are thinking of becoming pregnant, who are pregnant, or who are breastfeeding take a prenatal supplement containing 150 mcg of iodine daily. This study was a survey of U.S. midwives and obstetricians to assess their perceptions of iodine nutrition, as well as how often they recommend that their patients take an iodine supplement.

THE FULL ARTICLE TITLE

De Leo S et al. Iodine Supplementation in Women During Preconception, Pregnancy, and Lactation: Current Clinical Practice by U.S. Obstetricians and Midwives. *Thyroid* 2016 (ePub)

SUMMARY OF THE STUDY

Through email, all midwife members of the American College of Nurse-Midwives and all obstetrician members of the American Medical Association were invited to participate in a web-based survey between June to December 2015. The email was sent out three times to obstetricians and twice to midwives, but each respondent could submit their answers only once. The survey first asked questions regarding the midwives' and obstetricians' demographic information, such as their age, region of the country their practice was located, what type of obstetrical practice they had, and years elapsed since they finished their medical training. Later questions included what they thought was the status of iodine nutrition among U.S. pregnant women, the potential health effects of iodine deficiency during pregnancy, usefulness of iodine supplementation for women of childbearing age and for pregnant women. Respondents

were also asked how often they recommend iodine supplementation to their patients, as well as the quantity of iodine recommended daily for those that do.

Overall, there were very few respondents: only 199 midwives and 277 obstetricians answered the survey, corresponding to 3.6% and 1.2% of all U.S. midwives and obstetricians, respectively. From their answers, about one-third thought that U.S. pregnant women are iodine deficient. However, despite this, about 70% of midwives and obstetricians stated that they rarely recommend that their patients take an iodine supplement, whether in women planning a pregnancy, who are already pregnant, or are breastfeeding. Of those who do recommend iodine supplementation, only 45% would prescribe the recommended level of 150 mcg of iodine daily during pregnancy. Taken together, 75% of U.S. midwives and obstetricians who participated in this survey do not recommend or would recommend an inadequate amount of iodine during preconception, pregnancy, and lactation.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Iodine deficiency remains a major public health challenge. This is especially important among women of child-bearing age in whom poor iodine status may result in adverse health outcomes for their babies, such as mental retardation and developmental delays. Many major medical societies have recently recommended that women who are thinking of becoming pregnant, who are currently pregnant, or who are breastfeeding take an iodine supplement containing 150 mcg of iodine a day. However, this study suggests that the majority of U.S. midwives and obstetricians do not make these recommendations currently to their patients. Increased education about this important topic is needed to improve the health outcomes of pregnant women and their developing children.

— Angela M. Leung, MD, MSc

ATA THYROID BROCHURE LINKS

Iodine Deficiency: <http://www.thyroid.org/iodine-deficiency>

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

**THYROID AND PREGNANCY, continued****ABBREVIATIONS & DEFINITIONS**

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. Iodine is also present as a micronutrient in some vitamins and supplements.

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

Thyroid Awareness Monthly Campaigns

The ATA will be highlighting a distinct thyroid disorder each month and a portion of the sales for Bravelets™ will be donated to the ATA. The month of **February** is **Hypothyroidism Awareness Month** and a bracelet is available through the ATA Marketplace to support thyroid cancer awareness and education related to thyroid disease.



**THYROID CANCER****The increased incidence of thyroid cancer is worldwide****BACKGROUND**

The incidence of thyroid cancer has increased dramatically during the past three decades and it is now the fastest growing cancer in women. Almost all of this increase is in papillary thyroid cancer. The reason for this is unclear, although many point to the increase in imaging studies of the neck where small thyroid nodules are discovered before they become apparent on physical exam. This has led to some investigators stating that thyroid cancer is being over diagnosed, meaning that many of the small thyroid cancers being found would never progress to the stage where survival or health would be affected. However, there are many factors in the environment that may also cause an increase in thyroid nodules and thyroid cancer, including the release of radiation from nuclear reactor accidents. The current study is a worldwide review of the incidence of thyroid cancer that attempts to identify risk factors for the increasing incidence.

THE FULL ARTICLE TITLE

Wiltshire JJ et al. Systematic review of trends in the incidence rates of thyroid cancer. *Thyroid* 2016;26:1541-52.

SUMMARY OF THE STUDY

The authors searched 2 major databases of published scientific studies (Medline and EMBASE) for all articles on the incidence of thyroid cancer. The initial search yielded 4722 titles and abstracts, but only 60 studies were considered suitable for the final analysis. A total of 54 of the studies showed a significant increase in the incidence of thyroid cancer over the past 50 years while 2 studies found low incidence rates attributed to poor

access to health care. The largest number of studies was from Europe. All 13 reports from North America and 7 of 9 studies from Asia reported significant increases in incidence, as did 3 articles from South America. The incidence was higher in women than in men, but the trend for increasing incidence was similar in both sexes. All 4 studies that had adequate data on follicular thyroid cancer reported increasing incidence.

Of the 6 studies that evaluated exposure to ionizing radiation and thyroid cancer, 3 reported a positive association, including one from Belarus close to the Chernobyl accident. A very large table summarized each of the 60 studies, including potential risk factors. The few studies with positive data reported radiation exposure and iodine supplementation as risk factors.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This systematic review strongly supports a widespread and persistent increase in the incidence of thyroid cancer. It remains unclear if this increased incidence is simply due over diagnosis of small thyroid cancers or if it represents a true increase in thyroid cancer that may cause problems. While further studies are needed to help sort this out, the updated 2015 American Thyroid Association guidelines recommend against fine needle biopsy of thyroid nodules less than 1 cm in size and suggest consideration of active surveillance rather than surgery for very-low-risk cancers.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

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

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.

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: the second most common type of thyroid cancer.

**THYROID CANCER****Thyroid cancer over-diagnosis is a result of screening programs in South Korea****BACKGROUND**

Thyroid cancer diagnoses in South Korea increased 15-fold between 1993 and 2011, and South Korea now has the world's highest rate of thyroid cancer. In 1999, a government-funded national cancer screening program in South Korea led to the widespread use of ultrasound to screen for thyroid cancer in people without any symptoms. It is unclear whether the rise in thyroid cancer diagnoses in South Korea represents over diagnosis due to increased screening or whether there has been a true increase in the number of thyroid cancers. The aim of this study was to examine the increase in South Korean thyroid cancer diagnoses.

THE FULL ARTICLE TITLES:

Park S et al Association between screening and the thyroid cancer “epidemic” in South Korea: evidence from a nationwide study. *BMJ* 2016;355:i5745. doi: 10.1136/bmj.i5745.

SUMMARY OF THE STUDY

The National Epidemiologic Survey of Thyroid cancer (NEST) sampled the national Korean Central Cancer Registry to select a representative group of Korean thyroid cancer patients with a diagnosis in 1999, 2005, or 2008. There were 3342 such patients in 1999, there were 12,659 in 2005, and there were 26,890 in 2008.

Cases were randomly selected from 24 hospitals, with the number of cases selected proportional to the number of cases diagnosed in each year. Data was collected from medical records for each case included age; sex; cancer size, stage, and histology; the presence of lymph node spread and distant metastases; and the method of cancer detection (by ultrasound screening, clinically detected based on symptoms, or unspecified). Cancers were categorized as local, regional, or distant.

A total of 5796 patients were included. Women comprised 84.5% of patients, and the average age was 46.9 years. Most cancers (94.9%) were papillary cancers. The average thyroid cancer size discovered decreased from 21.5 mm in 1999, to 13.6 mm in 2005, to 10.5 mm in 2008. As expected, cancers detected by ultrasound screening were smaller than clinically detected cancers.

The percentage of cancers detected by ultrasound screening increased from 15% in 1999 to 56% in 2008. The proportion of regional thyroid cancers was 48% in 1999 and increased to 59% by 2008; the proportion of localized disease did not change (34% in 1999 and 36% in 2008); and the proportion of distant disease decreased from 5.4% to 1.3%.

The frequency of ultrasound screening detected cancers <1 cm increased from 0.27 per 100,000 people in 1999 to 15 per 100,000 people in 2008. The incidence of clinically detected cancers <1 cm increased from 0.49 per 100,000 people in 1999 to 4.88 per 100,000 people in 2008. The incidence of clinically detected cancers >3 cm did not change, while the incidence of ultrasound screening detected cancers >3 cm increased from 0.17 in 1999 per 100,000 people to 0.61 per 100,000 people in 2008.

Cancers <2 cm accounted for 94.4% of the overall increase in thyroid cancers detected. In general, the frequency of ultrasound screening detected cancer increased 8.4-fold from 1999 to 2008, while the incidence of ultrasound screening detected regional cancer increased 38.2-fold, mostly due to an increase detection of lymph node involvement. A total of 97.1% of the increase in thyroid cancer incidence was due to increased detection of local and regional cancers.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The current high incidence of thyroid cancer in South Korea is largely due to increased detection of small local or regional cancers. Given that the vast majority of the increase in South Korea's rate of thyroid cancer diagnosis consisted of ultrasound screening detected small cancers, this argues in favor of over diagnosis, although the rate of clinically detected cancers did increase by 18.7% over the same period and an increase in true cancer incidence cannot be definitively ruled out.

In general, the vast majority of patients diagnosed with thyroid cancer do very well and relatively few actually die of the disease. Because of this, the main concern about

**THYROID CANCER**, continued

ultrasound screening of asymptomatic patients is that cancer may be identified that may never have grown or cause any problems, thus leading to unnecessary testing and treatment. The updated 2015 American Thyroid Association guidelines recommend against fine needle biopsy of thyroid nodules less than 1 cm in size and suggest consideration of active surveillance rather than surgery for very-low-risk cancers.

— Ronald B. Koppersmith, MD, FACS

ATA THYROID BROCHURE LINKS

Thyroid Nodules: <http://www.thyroid.org/what-are-thyroid-nodules>

Thyroid Surgery: <http://thyroid.org/patients/patient-brochures/surgery.html>

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid-gland>

ABBREVIATIONS & DEFINITIONS

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

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.

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



**THYROID CANCER****BRAF-positive thyroid cancer differs from RAS-positive thyroid cancer****BACKGROUND**

Thyroid cancer is the fastest rising cancer in women and papillary thyroid cancer is the most common type of thyroid cancer. Many thyroid cancers are associated with mutations in one or more cancer-associated genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. Two cancer-associated genes important in thyroid cancer are BRAF and RAS. Newer studies show that BRAF mutations may be a marker for a more aggressive type of thyroid cancer while RAS mutations appear to be a marker for the more classical type of thyroid cancer. This study tries to combine a group of features, namely patient demographics, thyroid cancer pathology, and ultrasound characteristics of the cancer to determine if there are true differences between cancers that have a BRAF mutations and those that have a RAS mutation.

THE FULL ARTICLE TITLE

Kakarmath S et al Clinical, sonographic, and pathological characteristics of RAS-positive versus BRAF-positive thyroid carcinoma. *J Clin Endocrinol Metab* 2016;101:4938-44. Epub September 30, 2016.

SUMMARY OF THE STUDY

The authors identified 101 thyroid cancers from a single institution that had either a BRAF or RAS mutation that was tested for after the cancer was removed. They had a radiologist review the pre-operative ultrasound for all the patients and added patient demographic information to compare the two mutation groups.

The majority of cancers (72%) had a BRAF mutation and the rest (28%) had a RAS mutation. Cancers containing the BRAF mutation tended to be smaller, but more likely to have concerning ultrasound features such as hypoechoogenicity (darkness) and irregular margins, more likely to have a pre-operative biopsy diagnosis of cancer and were more likely to demonstrate aggressive features such as positive lymph nodes and spread outside of the nodule.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This data can help clinicians evaluate patients with biopsy proven or suspected thyroid cancer. This may include operative planning (ie, how much surgery to do), prognosis (how likely is your thyroid cancer to come back) and monitoring (how often and for how long to follow for cancer recurrence) recommendations.

— Melanie Goldfarb, ND

ATA THYROID BROCHURE LINKS

Fine Needle Aspiration Biopsy of Thyroid Nodules:

<http://www.thyroid.org/fna-thyroid-nodules/>

Thyroid Cancer (Papillary and Follicular):

<http://www.thyroid.org/thyroid-cancer/>

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

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

ABBREVIATIONS & DEFINITIONS

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.

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.



THYROID CANCER, continued

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).

Cancer-associated genes: these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just

associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC and RAS.

Mutation: A permanent change in one of the genes.

BRAF gene: this is gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.



ATA Alliance for Thyroid Patient Education

GOAL

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

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

WHO WE ARE (in alphabetical order)

AMERICAN THYROID ASSOCIATION

www.thyroid.org

ATA Patient Resources:

<http://www.thyroid.org/thyroid-information/>

Find a Thyroid Specialist: www.thyroid.org

(Toll-free): 1-800-THYROID

thyroid@thyroid.org

BITE ME CANCER

<http://www.bitemecancer.org>

info@bitemecancer.org

GRAVES' DISEASE AND THYROID FOUNDATION

www.gdatf.org

(Toll-free): 877-643-3123

info@ngdf.org

LIGHT OF LIFE FOUNDATION

www.checkyourneck.com

info@checkyourneck.com

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

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416-487-8267

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THYROID FEDERATION INTERNATIONAL

www.thyroid-fed.org

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AMERICAN
THYROID
ASSOCIATION
FOUNDED 1923



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



Thyroid Cancer Canada
Cancer de la thyroïde Canada



Hypothyroidism

WHAT IS THE THYROID GLAND?

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

WHAT IS HYPOTHYROIDISM?

Hypothyroidism is an underactive thyroid gland. Hypothyroidism means that the thyroid gland can't make enough thyroid hormone to keep the body running normally. People are hypothyroid if they have too little thyroid hormone in the blood. Common causes are autoimmune disease, surgical removal of the thyroid, and radiation treatment.

WHAT ARE THE SYMPTOMS?

When thyroid hormone levels are too low, the body's cells can't get enough thyroid hormone and the body's processes start slowing down. As the body slows, you may notice that you feel colder, you tire more easily, your skin is getting drier, you're becoming forgetful and depressed, and you've started getting constipated. Because the symptoms are so variable and non-specific, the only way to know for sure whether you have hypothyroidism is with a simple blood test for TSH.

KEEPING OTHER PEOPLE INFORMED

Tell your family members. Because thyroid disease runs in families, you should explain your hypothyroidism to your relatives and encourage them to get regular TSH tests. Tell your other doctors and your pharmacist about your hypothyroidism and the drug and dose with which it is being treated. If you start seeing a new doctor, tell the doctor that you have hypothyroidism and you need your TSH tested every year. If you are seeing an endocrinologist, ask that copies of your reports be sent to your primary care doctor.

WHAT CAN YOU EXPECT OVER THE LONG TERM?

There is no cure for hypothyroidism, and most patients have it for life. There are exceptions: many patients with viral thyroiditis have their thyroid function return to normal, as do some patients with thyroiditis after pregnancy.

Hypothyroidism may become more or less severe, and your dose of thyroxine may need to change over time. You have to make a lifetime commitment to treatment. But if you take your pills every day and work with your doctor to get and keep your thyroxine dose right, you should be able to keep your hypothyroidism completely controlled throughout your life. Your symptoms should disappear and the serious effects of low thyroid hormone should stop getting worse and should actually improve. If you keep your hypothyroidism well-controlled, it will not shorten your life span.

WHAT CAUSES HYPOTHYROIDISM?

There can be many reasons why the cells in the thyroid gland can't make enough thyroid hormone. Here are the major causes, from the most to the least common.

- **Autoimmune disease.** In some people's bodies, the immune system that protects the body from invading infections can mistake thyroid gland cells and their enzymes for invaders and can attack them. Then there aren't enough thyroid cells and enzymes left to make enough thyroid hormone. This is more common in women than men. Autoimmune thyroiditis can begin suddenly or it can develop slowly over years. The most common forms are Hashimoto's thyroiditis and atrophic thyroiditis.
- **Surgical removal of part or all of the thyroid gland.** Some people with thyroid nodules, thyroid cancer, or Graves' disease need to have part or all of their thyroid removed. If the whole thyroid is removed, people will definitely become hypothyroid. If part of the gland is left, it may be able to make enough thyroid hormone to keep blood levels normal.
- **Radiation treatment.** Some people with Graves' disease, nodular goiter, or thyroid cancer are treated with radioactive iodine (I-131) for the purpose of destroying their thyroid gland. Patients with Hodgkin's disease, lymphoma, or cancers of the head or neck are treated with radiation. All these patients can lose part or all of their thyroid function.

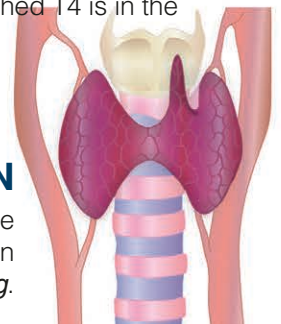
Hypothyroidism

- **Congenital hypothyroidism** (*hypothyroidism that a baby is born with*). A few babies are born without a thyroid or with only a partly formed one. A few have part or all of their thyroid in the wrong place (ectopic thyroid). In some babies, the thyroid cells or their enzymes don't work right.
- **Thyroiditis**. Thyroiditis is an inflammation of the thyroid gland, usually caused by an autoimmune attack or by a viral infection. Thyroiditis can make the thyroid dump its whole supply of stored thyroid hormone into the blood at once, causing brief hyperthyroidism (too much thyroid activity); then the thyroid becomes underactive.
- **Medicines**. Medicines such as amiodarone, lithium, interferon alpha, and interleukin-2 can prevent the thyroid gland from being able to make hormone normally. These drugs are most likely to trigger hypothyroidism in patients who have a genetic tendency to autoimmune thyroid disease.
- **Too much or too little iodine**. The thyroid gland must have iodine to make thyroid hormone. Iodine comes into the body in food and travels through the blood to the thyroid. Keeping thyroid hormone production in balance requires the right amount of iodine. Taking in too much iodine can cause or worsen hypothyroidism.
- **Damage to the pituitary gland**. The pituitary, the “master gland,” tells the thyroid how much hormone to make. When the pituitary is damaged by a tumor, radiation, or surgery, it may no longer be able to give the thyroid instructions, and the thyroid may stop making enough hormone.
- **Rare disorders that infiltrate the thyroid**. In a few people, diseases deposit abnormal substances in the thyroid and impair its ability to function. For example, amyloidosis can deposit amyloid protein, sarcoidosis can deposit granulomas, and hemochromatosis can deposit iron.

HOW IS HYPOTHYROIDISM DIAGNOSED?

The correct diagnosis of hypothyroidism depends on the following:

- **Symptoms**. Hypothyroidism doesn't have any characteristic symptoms. There are no symptoms that people with hypothyroidism always have and many symptoms of hypothyroidism can occur in people with other diseases. One way to help figure out whether your symptoms are due to hypothyroidism is to think about whether you've always had the symptom (hypothyroidism is less likely) or whether the symptom is a change from the way you used to feel (hypothyroidism is more likely).
- **Medical and family history**. You should tell your doctor:
 - about changes in your health that suggest that your body is slowing down;
 - if you've ever had thyroid surgery;
 - if you've ever had radiation to your neck to treat cancer;
 - if you're taking any of the medicines that can cause hypothyroidism— amiodarone, lithium, interferon alpha, interleukin-2, and maybe thalidomide;
 - whether any of your family members have thyroid disease.
- **Physical exam**. The doctor will check your thyroid gland and look for changes such as dry skin, swelling, slower reflexes, and a slower heart rate.
- **Blood tests**. There are two blood tests that are used in the diagnosis of hypothyroidism.
- **TSH (thyroid-stimulating hormone) test**. This is the most important and sensitive test for hypothyroidism. It measures how much of the thyroid hormone thyroxine (T4) the thyroid gland is being asked to make. An abnormally high TSH means hypothyroidism: the thyroid gland is being asked to make more T4 because there isn't enough T4 in the blood.
- **T4 tests**. Most of the T4 in the blood is attached to a protein called thyroxine-binding globulin. The “bound” T4 can't get into body cells. Only about 1%–2% of T4 in the blood is unattached (“free”) and can get into cells. The free T4 and the free T4 index are both simple blood tests that measure how much unattached T4 is in the blood and available to get into cells.



FURTHER INFORMATION

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

Hypothyroidism

HOW IS HYPOTHYROIDISM TREATED?

THYROXINE (T4) REPLACEMENT.

Hypothyroidism can't be cured. But in almost every patient, hypothyroidism can be completely controlled. It is treated by replacing the amount of hormone that your own thyroid can no longer make, to bring your T4 and TSH back to normal levels. So even if your thyroid gland can't work right, T4 replacement can restore your body's thyroid hormone levels and your body's function. Synthetic thyroxine pills contain hormone exactly like the T4 that the thyroid gland itself makes. All hypothyroid patients except those with severe myxedema (life-threatening hypothyroidism) can be treated as outpatients, not having to be admitted to the hospital.

SIDE EFFECTS AND COMPLICATIONS.

The only dangers of thyroxine are caused by taking too little or too much. If you take too little, your hypothyroidism will continue. If you take too much, you'll develop the symptoms of hyperthyroidism—an overactive thyroid gland. The most common symptoms of too much thyroid hormone are fatigue but inability to sleep, greater appetite, nervousness, shakiness, feeling hot when other people are cold, and trouble exercising because of weak muscles, shortness of breath, and a racing, skipping heart. Patients who have hyperthyroid symptoms at any time during thyroxine replacement therapy should have their TSH tested. If it is low, indicating too much thyroid hormone, their dose needs to be lowered.

FOLLOW-UP

You'll need to have your TSH checked about every 6 to 10 weeks after a thyroxine dose change. You may need tests more often if you're pregnant or you're taking a medicine that interferes with your body's ability to use thyroxine. The goal of treatment is to get and keep your TSH in the normal range. Babies with hypothyroidism must get all their daily treatments and have their TSH levels checked as they grow, to prevent mental retardation and stunted growth. Once you've settled into a thyroxine dose, you can return for TSH tests about once a year.

YOU NEED TO RETURN SOONER IF ANY OF THE FOLLOWING APPLY TO YOU:

- Your symptoms return or get worse.
- You want to change your thyroxine dose or brand, or change taking your pills with or without food.
- You gain or lose a lot of weight (as little as a 10-pound difference for those who weren't overweight to begin with).
- You start or stop taking a drug that can interfere with absorbing thyroxine (such as certain antacids, calcium supplements and iron tablets), or you change your dose of such a drug. Medications containing estrogen also impact thyroxine doses, so any change in such a medication should prompt a re-evaluation of your thyroxine dose.
- You're not taking all your thyroxine pills. Tell your doctor honestly how many pills you've missed.
- You want to try stopping thyroxine treatment. If ever you think you're doing well enough not to need thyroxine treatment any longer, try it only under your doctor's close supervision. Rather than stopping your pills completely, you might ask your doctor to try lowering your dose. If your TSH goes up, you'll know that you need to continue treatment.



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