



# Clinical Thyroidology<sup>®</sup> for the Public

VOLUME 11 | ISSUE 1 | JANUARY 2018

**EDITOR'S COMMENTS .....2****HYPERTHYROIDISM .....3****Subclinical hyperthyroidism with a suppressed TSH is associated with increased dementia risk in older adults**

Severe thyroid disease is associated with cognitive deficits that could be misdiagnosed as dementia. The association of milder forms of these thyroid conditions and cognitive deficits is less well understood. It is also unclear of the association between dementia and thyroid disease. The purpose of this study was to determine whether subclinical thyroid disease is associated with dementia.

Aubert CE et al. The association between subclinical thyroid dysfunction and dementia: the Health, Aging and Body Composition (Health ABC) study. Clin Endocrinol (Oxf). August 29, 2017 [Epub ahead of print].

**THYROID IN THE ELDERLY .....5****The risk of dying may be higher in older patients whose levels of TSH and free T<sub>4</sub> are more variable**

While there may be minor changes in TSH levels during the course of the day, in general, both TSH and thyroid hormone levels are stable over time. However, in some individuals, TSH levels are more variable and it is known that TSH levels are generally higher in older adults than in younger people. This study aimed to determine changing thyroid function with aging and examine the association of these changes with survival, by analyzing thyroid function over time.

Mammen JS et al. Unstable thyroid function in older adults is caused by alterations in both thyroid and pituitary physiology and associated with increased mortality. Thyroid, 2017 Nov;27(11):1370-1377.

**HYPERTHYROIDISM .....7****Risk factors for liver abnormalities with hyperthyroidism**

Both hyperthyroidism as well as the medications used to treat it can affect the function of the liver, causing increases in blood levels of markers of liver function known as liver function tests. If the increase in liver function tests is due to the antithyroid medications, the medication needs to be stopped to avoid damage to the liver. This study examined the risk factors for abnormal liver tests in patients with hyperthyroidism.

Lin TY et al. Incidence of abnormal liver biochemical tests in hyperthyroidism. Clin Endocrinol (Oxf) 2017;86:755-9. Epub March 9, 2017.

**THYROID NODULES .....9****Parathyroid lesions can be diagnosed by biopsy, but will need additional testing**

Parathyroid glands can sometimes look like thyroid nodules on ultrasound and other imaging, especially when they are found in unusual locations such as inside the thyroid gland. Biopsy of a parathyroid gland usually is indeterminate, as parathyroid identification requires special stains. The goal of this study was to determine if other, less involved methods such as simple pattern recognition on cytology, could be used to accurately distinguish parathyroid from thyroid lesions with a thyroid biopsy specimen.

Cho M et al. Distinguishing parathyroid and thyroid lesions on ultrasound-guided fine-needle aspiration: a correlation of clinical data, ancillary studies, and molecular analysis. Cancer. June 16, 2017 [Epub ahead of print].

**THYROID CANCER .....11****The time it takes for lung metastases in thyroid cancer may allow more appropriate selection of patients for aggressive chemotherapy**

Patients with thyroid cancer that spreads to the lungs (metastasis) tend to have shorter survival. Some patients have faster growing lung metastases and will require oral chemotherapy drugs to try to stop the cancer growth. The authors of this study try to predict which patients will have better survival based on the amount of cancer and by measuring the rate of growth of the metastases, also referred to as cancer volume doubling times.

Sabra MM et al. Tumor volume doubling time of pulmonary metastases predicts overall survival and can guide the initiation of multikinase inhibitor therapy in patients with metastatic, follicular cell-derived thyroid carcinoma. Cancer 2017;123:2955-64. Epub April 3, 2017.

**ATA ALLIANCE FOR THYROID****PATIENT EDUCATION .....13****Friends of the ATA .....14****Support the ATA .....15****ATA Brochure: Fine Needle Aspiration****Biopsy of Thyroid Nodules. ....16**



**www.thyroid.org**

**Editor**

Alan P. Farwell, MD, FACE  
Boston Medical Center  
Boston University School of Medicine  
720 Harrison Ave., Boston, MA 02115  
American Thyroid Association  
Email: [thyroid@thyroid.org](mailto:thyroid@thyroid.org)  
[www.thyroid.org/patients/ct/index.html](http://www.thyroid.org/patients/ct/index.html)

**Editorial Board**

Jessie Block-Galaraza, MD, Albany, NY  
Gary Bloom, New York, NY  
Alina Gavrilu-Filip, MD, Boston, MA  
Melanie Goldfarb, MD, MS, FACS, FACE,  
Santa Monica, CA  
Shirin Haddady, MD, MPH, Boston, MA  
Julie E. Hallanger Johnson, MD, Tampa, FL  
Angela Leung, MD, Los Angeles, CA  
Maria Papaleontiou, MD, Ann Arbor, MI  
Liuska Pesce, MD, Iowa City, Iowa  
Wendy Sacks, MD, Los Angeles, CA  
Anna M. Sawka, MD, Toronto, ON, Canada  
Phillip Segal, MD, Toronto, ON, Canada  
Vibhavsu Sharma, MD, Albany, NY  
Whitney Woodmansee, MD, Gainesville, FL

**American Thyroid Association**

**President**

Charles H. Emerson, MD (2017–2018)

**Secretary/Chief Operating Officer**

Victor J. Bernet, MD (2015–2019)

**Treasurer**

Julie Ann Sosa, MD (2017–2021)

**President-Elect**

Elizabeth N. Pearce, MD, MSc (2017–2018)

**Past-President**

John C. Morris, MD (2017–2018)

**Executive Director**

Barbara R. Smith, CAE  
American Thyroid Association  
6066 Leesburg Pike, Suite 550  
Falls Church, VA 22041  
Telephone: 703-998-8890  
Fax: 703-998-8893  
Email: [thyroid@thyroid.org](mailto:thyroid@thyroid.org)

**Designed by**

Karen Durland, [kdurland@gmail.com](mailto:kdurland@gmail.com)

**Clinical Thyroidology for the Public**

Copyright © 2018 by the American Thyroid Association, Inc. All rights reserved.



## EDITOR'S COMMENTS

Happy New Year and welcome to another year and 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](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*, *Thyroid Cancer Alliance* and *Thyroid Federation International*.

The American Thyroid Association (ATA) extends its appreciation to all of the patients and their families that are part of the ATA community - our **Friends of the ATA**. It is for you that the 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.

As we think of all those who make a difference in our lives, we thank you for being part of the ATA family and for 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](http://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 editorial board of CTFP, the ATA Board of Directors, Members, and ATA Headquarters Staff, wish you the best this season and look forward to being part of your thyroid network in 2018.

January is **Thyroid Awareness Month**.

**In this issue, the studies ask the following questions:**

- Is subclinical thyroid disease associated with a risk of dementia?
- Are thyroid hormone levels associated with a risk death in the elderly?
- How common are liver abnormalities in patients with hyperthyroidism?
- How can parathyroid lesions be distinguished from thyroid nodules?
- Can we identify patients that will benefit the most from aggressive chemotherapy?

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



## HYPERTHYROIDISM

### Subclinical hyperthyroidism with a suppressed TSH is associated with increased dementia risk in older adults

#### BACKGROUND

Thyroid hormone has important effects on brain/cognitive functioning. Severe thyroid disease, either hyperthyroidism or hypothyroidism, is associated with cognitive deficits such as memory loss, difficulty concentrating and “brain fog”. In the elderly, these deficits could be misdiagnosed as dementia. Importantly, once the thyroid disease is treated and normal thyroid function is restored, most of these cognitive problems improve or resolve. The association of milder (subclinical) forms of these thyroid conditions and cognitive deficits is less well understood. Subclinical thyroid disease occurs when the TSH level is abnormal but the thyroid hormone levels are normal. In subclinical hyperthyroidism, the TSH is low and in subclinical hypothyroidism the TSH is high.

It is estimated that 14% of US individuals older than 71 have dementia. Therefore, understanding and potentially modifying risk factors is of great public health interest. It is also unclear of the association between dementia and thyroid disease. The purpose of this study was to determine whether subclinical thyroid disease is associated with dementia.

#### THE FULL ARTICLE TITLE

Aubert CE et al. The association between subclinical thyroid dysfunction and dementia: the Health, Aging and Body Composition (Health ABC) study. Clin Endocrinol (Oxf). August 29, 2017 [Epub ahead of print].

#### SUMMARY OF THE STUDY

This study used patient data from the Health, Aging and Body Composition study. It started in 1997-1998 and the subjects were selected at random from individuals ages 70-79 years living in Memphis, TN or Pittsburgh, PA. It included white and black participants. From an initial total of 3075 subjects, a final sample of 2558 participants were evaluated. This is because people who already had dementia, were planning to move out of the area, who had terminal cancer, or who were not independent in their daily activities were excluded. Also, basic data were needed, such as a Mini Mental State evaluation in the first year, measurements of TSH hormone amongst other. If

those were not available, then that individual was also not included in the study.

During the monitoring time, certain data was collected, such as smoking history, alcohol use, exercise, diabetes, hypertension and the use of some medications. Thyroid hormone levels were measured at the 2 year visit and the mental status evaluation was performed every couple of years. Dementia was identified based on a specific decline in the Mini Mental State test, prescription of a dementia medication or diagnosis of dementia on a hospital admission. Thyroid function was assessed by measuring a TSH. If the TSH was abnormal, then a free T<sub>4</sub> was obtained. People who had a low TSH were divided in two groups with the milder group defined as a TSH between 0.1 and 0.45, and the fully suppressed group, with a TSH of <0.1.

After adjusting for relevant variables, study results showed that dementia risk was higher in those whose TSH was suppressed <0.1 than in people with normal TSH level. Dementia risk was not increased in the group with a slightly low TSH level (0.1-0.45) or in people with a mildly elevated TSH (subclinical hypothyroidism).

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The strength of this study is the use of a large group of community based subjects, the length of the follow up and the primary outcome (dementia). The limitations were that the number of people with subclinical hyperthyroidism was relatively small (3.2% of participants), and that there was only one TSH measurement at the start of the study. These results are relevant to patients because they show that there is a relationship between what is considered to be a milder form of thyroid disease, specifically subclinical hyperthyroidism, and dementia risk. Many times, physicians are reluctant to treat subclinical thyroid problems. This study suggests that it may be important to treat subclinical hyperthyroidism, especially in the elderly with dementia symptoms.

— Jessie Block-Galarza, MD





## HYPERTHYROIDISM, continued

### ATA THYROID BROCHURE LINKS

Older Patients and Thyroid Disease: <https://www.thyroid.org/thyroid-disease-older-patient/>

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

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

Thyroid Function Tests: <https://www.thyroid.org/thyroid-function-tests/>

### ABBREVIATIONS & DEFINITIONS

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

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

**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.

**Dementia:** a broad category of brain diseases that cause a long-term and often gradual decrease in the ability to think and remember that is great enough to affect a person's daily functioning





## THYROID IN THE ELDERLY

### The risk of dying may be higher in older patients whose levels of TSH and free T<sub>4</sub> are more variable

#### BACKGROUND

Thyroid stimulating hormone (TSH) is produced by the pituitary gland in the brain, and acts on the thyroid gland to control thyroid function, which in turn controls metabolism. TSH levels are opposite thyroid hormone levels. When thyroid hormone levels are low and the gland is underactive, TSH levels are high. When the thyroid is overactive and thyroid hormone levels are high, TSH levels are low. While there may be minor changes in TSH levels during the course of the day, in general, both TSH and thyroid hormone levels are stable over time. However, in some individuals, TSH levels are more variable and it is known that TSH levels are generally higher in older adults than in younger people. This study aimed to determine changing thyroid function (variability) with aging and examine the association of these changes with survival, by analyzing thyroid function over time. The authors included participants from the Baltimore Longitudinal Study of Aging (BLSA), which is a long-term study of aging with continuous enrollment of healthy volunteers living independently in the community.

#### THE FULL ARTICLE TITLE

Mammen JS et al. Unstable thyroid function in older adults is caused by alterations in both thyroid and pituitary physiology and associated with increased mortality. *Thyroid*, 2017 Nov;27(11):1370-1377.

#### SUMMARY OF THE STUDY

The study included 1294 participants in the BLSA who had normal thyroid function tests and were not on any thyroid hormone medications or other medications known to interfere with thyroid function. Of these participants, 464 were younger than 60 years old at the start of the study, 291 were aged 60-69, 327 were aged 70-79 and 206 were over 79 years old. The study focused on a subgroup of 640 participants who had at least three tests of TSH and free T<sub>4</sub> over seven years.

The study found that while most of the participants at all ages had stable thyroid function, changes were more common among older adults. More specifically, 32.3% of those aged >80 years demonstrated changes in thyroid function (TSH and free T<sub>4</sub>) versus only 9.5% of those aged <60 years. Race and ethnicity were not associated with thyroid aging pattern, but smoking within the past 10 years increased the risk for changing thyroid function. Overall, participants who showed variability in both TSH and in free T<sub>4</sub> levels in this study seemed to be at increased risk for death.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that TSH and free T<sub>4</sub> levels tend to be more variable in the elderly, but there is a tendency for abnormal thyroid function tests to resolve. Participants who showed variability in both TSH and in free T<sub>4</sub> levels in this study seemed to be at increased risk for death. However, it is important to note that not all rising TSH levels will be associated with the same risk or carry the same treatment implications. Additionally, testing thyroid function over time may be critical in older patients to avoid treating abnormalities that may be temporary. Finally, physicians should be cautious of a mildly elevated TSH level, as it may not require treatment with thyroid hormone supplementation in some older patients.

— Maria Papaleontiou, MD

#### ATA THYROID BROCHURE LINKS

Older Patients and Thyroid Disease: <https://www.thyroid.org/thyroid-disease-older-patient/>

Thyroid Function Tests: <https://www.thyroid.org/thyroid-function-tests/>





## THYROID IN THE ELDERLY, continued

### 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.

**Pituitary gland:** this endocrine gland sits at the base of the brain and secretes hormones that control thyroid and adrenal function, growth and reproduction. The pituitary gland secretes TSH to control thyroid function.

**Thyroxine (T<sub>4</sub>):** the major hormone produced by the thyroid gland. T<sub>4</sub> gets converted to the active hormone T<sub>3</sub> in various tissues in the body.

**Free T<sub>4</sub>:** some of the T<sub>4</sub> in the blood exists as free T<sub>4</sub>. This means it hasn't bonded to protein in the blood.

**Variability:** Lack of consistency or fixed pattern, liability to change.

**Aging:** Process of becoming older.

[www.thyroid.org/donate/](http://www.thyroid.org/donate/)



Support Thyroid Research





## HYPERTHYROIDISM

### Risk factors for liver abnormalities with hyperthyroidism

#### BACKGROUND

Hyperthyroidism is a condition where the thyroid gland is overactive and produces too much thyroid hormone. A frequent treatment for hyperthyroidism is antithyroid medications, either Methimazole or Propylthiouracil. It is known that both medications, as well as hyperthyroidism itself, can affect the function of the liver, causing increases in blood levels of markers of liver function known as liver function tests. If the increase in liver function tests are due to the hyperthyroidism, treating the hyperthyroidism will cause the liver function tests to return to normal and the liver is not damaged. However, if the increase in liver function tests is due to the antithyroid medications, the medication needs to be stopped to avoid damage to the liver, and options of radioactive iodine therapy or surgery need to be considered to treat the hyperthyroidism. The effects of hyperthyroidism on the liver are not well understood. This study examined the risk factors for abnormal liver tests in patients with hyperthyroidism.

#### THE FULL ARTICLE TITLE

Lin TY et al. Incidence of abnormal liver biochemical tests in hyperthyroidism. Clin Endocrinol (Oxf) 2017;86:755-9. Epub March 9, 2017.

#### SUMMARY OF THE STUDY

This study looked at the UCLA electronic medical record database of over 1500 patients from 2002 to 2016. Nearly 80% of the patients were women, 60% were Caucasian, 14% were Asian, 9% were African-American and 14% were Hispanic. These patients were newly diagnosed

with hyperthyroidism. The liver function tests performed within 6 months of the diagnosis were reviewed. Patients on medications that can affect the liver or patients who had liver disease prior to developing hyperthyroidism were not included.

Overall, 40% of patients had at least one abnormal liver test. The abnormalities of one of the liver tests were more common in patients with severe hyperthyroidism where as others were not. Age had no effect. Men and African-American appeared to have a higher risk of having significant liver function test problems, while Hispanic patients have a higher risk of minor liver function test abnormalities.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that some liver function test problems were related to the severity of hyperthyroidism. In addition, men and African-American patients were more likely to have these abnormal tests. It was found to be less likely with non-Hispanic or Latino ethnicity.

Since many of the patients diagnosed with hyperthyroidism may require medications to treat the condition, this study suggests that it would be important to do liver function tests in these patients (especially those at a higher risk as noted above) prior to starting antithyroid drugs.

—Vibhavasu Sharma, MD

#### ATA THYROID BROCHURE LINKS:

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

#### 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.

**Methimazole:** an antithyroid medication that blocks the thyroid from making thyroid hormone. Methimazole is used to treat hyperthyroidism, especially when it is caused by Graves' disease.





## HYPERTHYROIDISM, continued

**Propylthiouracil (PTU):** an antithyroid medication that blocks the thyroid from making thyroid hormone. Propylthiouracil is used to treat hyperthyroidism, especially in women during pregnancy.

**Liver function tests:** Blood tests done to look for liver disease.

## 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 **January** is **Thyroid Awareness Month** and a bracelet is available through the **ATA Marketplace** to support thyroid cancer awareness and education related to thyroid disease.





## THYROID NODULES

### Parathyroid lesions can be diagnosed by biopsy, but will need additional testing

#### BACKGROUND

The parathyroid glands control blood calcium levels. There are 4 parathyroid glands and are found right next to the thyroid gland on both sides. The normal parathyroid gland is usually not visible on ultrasound imaging. An enlarged parathyroid gland can indicate the disorder hyperparathyroidism, where calcium levels are very high. Surgery is often required for treatment of hyperparathyroidism. Parathyroid glands can sometimes look like thyroid nodules on ultrasound and other imaging, especially when they are found in unusual locations such as inside the thyroid gland. In these cases, biopsy is often considered to evaluate whether it is thyroid vs parathyroid. However, biopsy of a parathyroid gland usually is indeterminate, as parathyroid identification requires special stains. The goal of this study was to determine if other, less involved methods such as simple pattern recognition on cytology, could be used to accurately distinguish parathyroid from thyroid lesions with a thyroid biopsy specimen.

#### THE FULL ARTICLE TITLE

Cho M et al. Distinguishing parathyroid and thyroid lesions on ultrasound-guided fine-needle aspiration: a correlation of clinical data, ancillary studies, and molecular analysis. *Cancer*. June 16, 2017 [Epub ahead of print].

#### SUMMARY OF THE STUDY

A total of 143 indeterminate thyroid biopsy specimens were reviewed by experienced pathologists. Almost 25% were confirmed to actually be parathyroid tissue and not an indeterminate thyroid lesion. In these 34 parathyroid lesions, 3 different simple cytologic patterns were identified and there were many consistent cytologic features as well.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The identification of parathyroid glands that are within the thyroid is often a challenge. This study identifies characteristics of what a parathyroid lesion looks like under the microscope and should help cytopathologists to consider that diagnosis for thyroid lesions they are determining to be indeterminate.

— Melanie Goldfarb, MD, MS, FACS, FACE

#### ATA THYROID BROCHURE LINKS

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

#### ABBREVIATIONS & DEFINITIONS

**Parathyroid glands:** usually four small glands located around the thyroid that secrete parathyroid hormone (PTH) which regulates the body's calcium levels.

**Parathyroid hormone (PTH):** the hormone that regulates the body's calcium levels. High levels of PTH cause hypercalcemia, or too much calcium in the blood. Low levels of PTH cause hypocalcemia, or too little calcium in the blood.

**Hyperparathyroidism** — a condition of too much calcium in the blood (hypercalcemia) caused by 1 or more tumors of the parathyroid glands causing elevated parathyroid hormone levels

**Thyroid biopsy:** 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.





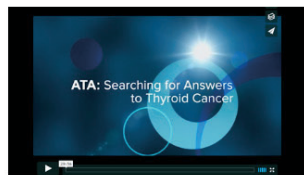
## THYROID NODULES, continued

**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.

**Cytopathologist:** a doctor that examines cells and tissues through a microscope to make a diagnosis of the cause of an abnormal lump or mass after a biopsy.

### Watch how your donations help find answers to thyroid cancer



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



13



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



19



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



10



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



11

[www.thyroid.org/donate/](http://www.thyroid.org/donate/)





## THYROID CANCER

### The time it takes for lung metastases in thyroid cancer may allow more appropriate selection of patients for aggressive chemotherapy

#### BACKGROUND

While most patients with thyroid cancer do well and most do not have spread of thyroid cancer outside of the neck, it is known that patients with thyroid cancer that spreads to the lungs (metastasis) tend to have shorter survival. This is especially true for older patients, for those with large sized cancer metastases and if the thyroid cancer is resistant to radioactive iodine therapy and seen as active on PET scans. While these factors can help physicians predict cancer growth, it really is not known how fast an individual patient's metastatic thyroid cancer will grow. Some patient's lung metastases will grow very slowly over time and will not be a problem for a long time. Other patients will have faster growing lung metastases and will require oral chemotherapy drugs to try to stop the cancer growth. The oral chemotherapy drugs that are most effective are called multikinase inhibitors (MKIs). However, MKIs have a lot of side effects so should be reserved for those at highest risk of dying of their cancer. The authors of this study try to predict which patients will have better survival based on the amount of cancer and by measuring the rate of growth of the metastases on computed tomography (CT), also referred to as cancer-volume-doubling times. Some of the patients were treated with MKIs and some were not. They found that the cancer volume doubling time can help predict overall survival and may help guide physicians when to start using MKIs.

#### THE FULL ARTICLE TITLE

Sabra MM et al Tumor volume doubling time of pulmonary metastases predicts overall survival and can guide the initiation of multikinase inhibitor therapy in patients with metastatic, follicular cell-derived thyroid carcinoma. *Cancer* 2017;123:2955–64. Epub April 3, 2017.

#### SUMMARY OF THE STUDY

The authors reviewed 199 cases of patients with thyroid cancer who also had lung metastases between the years 1992 and 2016. All the patients had been treated with surgery and radioactive iodine therapy. Some patients were treated with additional surgery, radioactive iodine

therapy, radiation treatment and/or oral chemotherapy drugs with MKIs. After reviewing the cases, 88 patients met the criteria needed to be included in the study. All patients had to have at least 4 CT scans, the largest lung cancer had to be >5 mm and they had to have adequate amount of follow up information. The average age of patients at the time of diagnosis of distant metastases was age 54. A total of 43 patients had papillary thyroid cancer, 10% follicular or follicular variant of papillary cancer, 9% Hurthle cell cancer, and 3% poorly differentiated thyroid cancer. A total of 72% of patients had <1cm lung metastases at the time of diagnosis, 52% took up iodine and 46% were active on PET scan. A total of 22% of patients had metastatic thyroid cancer to other places in the body in addition to the lungs. The average follow up was 8.5 years and 85% of the patients had progression of their disease. They used the average doubling time of the two largest lung nodules for the analysis.

The patients with a cancer volume doubling time of less than one year had the poorest survival. Of 15 patients with <1 year cancer volume doubling time, 8 were treated with MKIs and 7 were not. The 2 year survival was better for those treated (88% versus 43%) in those not treated with MKIs. If the cancer volume doubling time was greater than 1 year, they did not see improved survival.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that only the patients with the most aggressive and fastest growing thyroid cancer benefit from aggressive chemotherapy drugs known as MKIs even though there are significant side effects. Patients with metastatic cancer that is growing slowly do not show any benefit from MKIs. Thus, MKIs should be reserved for the patients at highest risk of dying from their thyroid cancer. This study provides a tool that physicians can use when trying to predict long-term survival of patients with thyroid cancer lung metastases as well as help guide when to start oral chemotherapy.

—Wendy Sacks, M.D.





## THYROID CANCER, continued

### ATA THYROID BROCHURE LINKS

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

#### ABBREVIATIONS & DEFINITIONS

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

**Follicular thyroid cancer:** the second most common type of thyroid cancer.

**Follicular variant of papillary thyroid cancer:** one of the subtypes of papillary thyroid carcinoma, which has been classified to three different forms: non-invasive follicular thyroid neoplasm with papillary-like nuclear features, invasive encapsulated and infiltrative FVPTC

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

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

of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

**Positron-Emission-Tomography (PET) scans:** 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. PET scans are frequently combined with CT scans to accurately identify where the cancer is located.

**Tyrosine kinases:** proteins that are overactive in many of the pathways that cause cells to be cancerous.

**Multi-kinase inhibitors (MKIs):** anticancer drugs that have been shown to be effective in thyroid cancer treatment. They work by inhibiting tyrosine kinases that cause cells to be cancerous. A drawback to these drugs are frequent side effects that limit their use.





## 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](http://www.thyroid.org)

ATA Patient Resources:

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

Find a Thyroid Specialist: [www.thyroid.org](http://www.thyroid.org)

(Toll-free): 1-800-THYROID

[thyroid@thyroid.org](mailto:thyroid@thyroid.org)

#### BITE ME CANCER

<http://www.bitemecancer.org>

[info@bitemecancer.org](mailto:info@bitemecancer.org)

#### GRAVES' DISEASE AND THYROID FOUNDATION

[www.gdatf.org](http://www.gdatf.org)

(Toll-free): 877-643-3123

[info@ngdf.org](mailto:info@ngdf.org)

#### LIGHT OF LIFE FOUNDATION

[www.checkyourneck.com](http://www.checkyourneck.com)

[info@checkyourneck.com](mailto:info@checkyourneck.com)

#### THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

[www.thyca.org](http://www.thyca.org)

(Toll-free): 877-588-7904

[thyca@thyca.org](mailto:thyca@thyca.org)

#### THYROID CANCER CANADA

[www.thyroidcancercanada.org](http://www.thyroidcancercanada.org)

416-487-8267

[info@thyroidcancercanada.org](mailto:info@thyroidcancercanada.org)

#### THYROID FEDERATION INTERNATIONAL

[www.thyroid-fed.org](http://www.thyroid-fed.org)

[tfi@thyroid-fed.org](mailto:tfi@thyroid-fed.org)



AMERICAN  
THYROID  
ASSOCIATION  
FOUNDED 1923



ThyCa: Thyroid Cancer  
Survivors' Association, Inc.™  
[www.thyca.org](http://www.thyca.org)



Thyroid Cancer Canada  
Cancer de la thyroïde Canada



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

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

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

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

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

**[www.thyroid.org](http://www.thyroid.org)**



AMERICAN THYROID ASSOCIATION  
ATA | Founded 1923

Donate  
Now!

## JOIN US

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



“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

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

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



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

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

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

# Fine Needle Aspiration Biopsy of Thyroid Nodules

## *Procedure and interpretation of results*

### 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 A FINE NEEDLE ASPIRATION BIOPSY (FNA OR FNAB) OF A THYROID NODULE?

A fine needle aspiration biopsy of a *thyroid nodule* is a simple and safe procedure performed in the doctor's office. Typically, the biopsy is performed under ultrasound guidance to ensure accurate placement of the needle within the *thyroid nodule*. You will be asked to lie down on your back with your head tipped backwards, so that your neck is extended. Sometimes, a pillow is placed under your shoulders to help you get in best position for the biopsy.

During the procedure you may feel some neck pressure from the ultrasound probe and from the needle. You will be asked to remain as still as possible and avoid coughing, talking and swallowing during the biopsy.

### HOW CAN YOU PREPARE FOR YOUR THYROID FNA?

Most medications can be continued. However, anticoagulants, also called "blood thinners", often need to be stopped temporarily in anticipation of your thyroid biopsy. These medications can increase the risk of bleeding. It is common to receive specific instructions regarding when to stop taking medications from your doctor's office prior to the procedure. If you have any questions about taking your medications prior to the thyroid biopsy, be sure to talk to your doctor.

Generally, you will not be required to be fasting on the day of your appointment. During the thyroid biopsy, ultrasound gel will be applied to the neck to obtain ultrasound images. This gel is water soluble and non-toxic, but may get on clothing or jewelry. You may wish to wear comfortable clothing and take off any jewelry from around the neck for the procedure.

### HOW IS A THYROID FNA PERFORMED?

The neck will first be cleaned with an antiseptic. A local or topical anesthetic may be applied. For the biopsy, your doctor will use a very thin needle to withdraw cells from the thyroid nodule. The needle used is smaller in diameter than those used in most blood draws. Your doctor will insert the needle through the skin and into the thyroid nodule. After the sampling, which only takes several seconds, the needle will be removed. New needles are used for additional samples. Several samples of cells will be obtained, by sticking a fine needle in various parts of the nodule usually between two and six times. This assures a better chance to find cancerous cells if they are present. If there is fluid in the nodule, a syringe may be used to drain it.

Once the biopsy is completed, pressure will be applied to the neck. The procedure usually lasts less than 30 minutes.

### WHAT SHOULD YOU EXPECT AFTER THE PROCEDURE?

The procedure is usually performed using a local anesthetic and no medications are used that affect consciousness or thinking. After the procedure, you may be asked to sit up slowly to prevent you from getting lightheaded. Most patients typically leave feeling well. There are very few, if any, restrictions on what you can do after a thyroid biopsy. Because of this, it is not generally necessary to bring a companion to help or drive you home.

Some neck discomfort at the site of the biopsy is expected following the procedure. Tylenol® and ice compresses can be used to relieve discomfort.

### WHAT HAPPENS TO THE BIOPSY MATERIAL AFTER THE PROCEDURE?

The biopsy samples may be used to make slides immediately and/or collected in a solution to wash excess blood. Specially trained doctors, cytopathologists, then make slides from the material and examine them under a microscope to make a diagnosis.



# Fine Needle Aspiration Biopsy of Thyroid Nodules

## *Procedure and interpretation of results*

### HOW LONG DOES IT TAKE FOR THE RESULTS TO RETURN?

Generally, it can take anywhere from a few days to 2 weeks for the result to return.

### WHAT ARE THE POSSIBLE RESULTS?

Please note that different institutions and centers will have different rates of results depending on their specific populations.

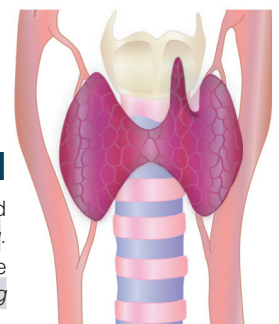
- 1. Benign** – This accounts for up to 70% of biopsies when using the Bethesda System (one of the most common ways that cytopathologists classify nodule biopsy specimens). The risk of malignancy in this group is typically less than 3%. These nodules are generally monitored with a follow up ultrasound within 18 months and if needed, periodically after that.
- 2. Malignant (cancer)** – This accounts for 3-7% of all biopsy specimens. The most common type of thyroid cancer seen in these biopsies is papillary thyroid cancer. When a biopsy comes back as malignant, there is a 97-99% chance that it is truly a cancerous lesion. Almost all of these nodules will go to surgery (thyroidectomy).
- 3. Suspicious for malignancy** – When a biopsy result returns as suspicious for malignancy, there is a 60-75% chance of cancer. The cytopathologist will see features that are worrisome, but not diagnostic of a malignant or cancerous lesion. The treatment is typically surgery.
- 4. Atypia of Undetermined Significance (AUS) or Follicular Lesion of Undetermined Significance (FLUS)** – These categories may be alternatively called “indeterminate.” These specimens have some features that are worrisome and some features that look more benign. This diagnosis carries a 5-15% risk of malignancy, although there is some variability among institutions. A repeat biopsy and/or genetic testing may be useful in these cases.
- 5. Follicular Neoplasm or ‘Suspicious for follicular neoplasm’** – This category carries a 15-30% risk of malignancy. It is difficult to tell if the nodules are a benign condition called follicular adenoma or a malignant nodule unless it is taken out. Generally, at least half of the thyroid is removed (the side with the nodule) for diagnosis and treatment.

- 6. Non-diagnostic** – This means that there are not enough cells in the sample to make a diagnosis. Despite our best efforts and even when we can see that the needle was in the nodule during the biopsy, the specimen sometimes does not have enough thyroid follicular cells to make a proper diagnosis. Non-diagnostic samples can also occur when only cyst fluid is taken out, and for other reasons, such as the presence of too much blood. In these cases, the biopsy should be repeated, and if non-diagnostic a second time, consideration is given to a third biopsy, monitoring, or surgery.

For more detailed information about FNA results, please see the [Thyroid Nodules](#) brochure.

### WHAT GENETIC TESTS ARE USED FOR THYROID BIOPSIES OF NODULES?

Within the past few years, several molecular tests have become available to help determine whether some nodules are cancerous or benign. These tests look at many genes within the thyroid nodule’s genetic make-up (DNA). They are being used when a nodule biopsy comes back with a diagnosis of ‘indeterminate’. Sometimes, the person doing the biopsy will perform an additional pass of the needle to obtain material for such a test. This may be done on the first biopsy or at the time of a repeat biopsy.



### 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](http://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](http://www.thyroid.org)