Clinical THYROIDOLOGY FOR THE PUBLIC

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EDITOR'S COMMENTS2

Screening the general population for thyroid disease is controversial. A study published 10 years ago by USPSTF concluded that there was no benefit to screening for thyroid dysfunction. The current follow-up study re-examines the evidence regarding screening for thyroid disease in the general population.

Rugge JB et al. Screening and treatment of thyroid dysfunction: an evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 2015;162:35-45.

THYROID AND PREGNANCY5 Diagnosing mild thyroid problems in early pregnancy and defining its impact on complications of pregnancy needs to be revisited

Hypothyroidism in the mother during early pregnancy is associated with adverse outcomes, but not consistently across studies. This study examined whether adding serum thyroidfunction tests to the routine screening for chromosomal abnormalities between 9 and 14 weeks of pregnancy predicts adverse pregnancy outcomes.

Ong GS et al. Does the thyroid-stimulating hormone measured concurrently with first trimester biochemical screening tests predict adverse pregnancy outcomes occurring after 20 weeks gestation? J Clin Endocr Metab 2014;99:E:2663-72.

Selenium is important for thyroid function as the major enzyme that activates thyroid hormone contains selenium. Selenium supplementation has been shown in some studies to decrease TPO antibody levels and reduce the risk of thyroid function abnormalities after pregnancy. This study sought to determine whether supplementation with a lower dose of selenium in pregnant women would show similar findings.

Mao J et al. Effect of low-dose selenium on thyroid autoimmunity and thyroid function in UK pregnant women with mild-to-moderate iodine deficiency. Eur J Nutr., 2014 Dec 19. [Epub ahead of print].

thyroid cancer is associated with delayed time to child-bearing and with decreased fertility in older women

Side effects of radioactive iodine therapy for thyroid cancer are infrequent but can be significant and can include a short-lived disruption of the menstrual cycle in the first year after treatment and a slightly earlier onset of menopause. The aim of this study was to evaluate the frequency of non-cancerous complications and the effect of radioactive iodine therapy on childbearing in female thyroid cancer survivors.

Wu JX et al. Reproductive outcomes and non-oncologic complications after radioactive iodine ablation for well-differentiated thyroid cancer. Thyroid 2015;251:133-8.

Radioactive iodine therapy is frequently used in the treatment of thyroid cancer. Radioactive iodine is also taken up in some of the cells in the tear ducts and the nasal area. About 10% of thyroid cancer patients may develop eye problems after radioactive iodine therapy, although this is usually mild. This study looked at the nasal and tear duct function in patients with thyroid cancer treated with radioactive iodine.

Jonklaas J et al. Nasal symptoms after radioiodine therapy: a rarely described side effect with similar frequency to lacrimal dysfunction. Thyroid. September 8, 2014 [Epub ahead of print].

Up to 30% of patients with thyroid cancer will have spread of the cancer outside of the thyroid at the time of surgery, with most of this spread to the lymph nodes in the central neck around the thyroid. It is controversial whether the surgeon should try to remove all lymph nodes in the central neck at the time of surgery. The aim of this study was to evaluate the clinical implications of prophylactic central-neck dissection performed at the same time as a total thyroidectomy.

Viola D et al Prophylactic central compartment lymph node dissection in papillary thyroid carcinoma: clinical implications derived from the first prospective randomized controlled single institution study. J Clin Endocrinol Metab. January 15, 2015 [Epub ahead of print].



www.thyroid.org

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CLINICAL THYROIDOLOGY FOR THE PUBLIC

A publication of the American Thyroid Association

VOLUME 8 • ISSUE 5 • MAY 2015

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 presented 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 <u>@thyroidfriends</u> 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.

May is <u>International Thyroid Awareness Month</u>. May 25 is World Thyroid Day and May 25–31 is International Thyroid Awareness week.

In this issue, the studies ask the following questions:

- 1. Is it worthwhile to screen for thyroid disease?
- 2. Is it worthwhile to screen for thyroid disease in pregnancy?
- 3. Does selenium supplementation affect pregnancy outcomes?
- 4. Does radioactive iodine therapy for thyroid cancer affect fertility in women?
- 5. What are the complications of radioactive iodine therapy?
- 6. Is there a reason to perform prophylactic central-neck dissections for papillary thyroid cancer?

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

— Alan P. Farwell, MD



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A publication of the American Thyroid Association

HYPOTHYROIDISM



BACKGROUND

Screening the general population for thyroid disease is controversial. Based on NHANES III data (a survey of health parameters in the United States), about 5% of the U.S. population has subclinical thyroid dysfunction and 1.2% has overt thyroid dysfunction. The majority of thyroid dysfunction is hypothyroidism. The current study was commissioned by the U.S. Preventive Services Task Force (USPSTF) in order to determine whether screening the population for thyroid disease would have clinical benefit. The study was a follow-up to one published 10 years ago by USPSTF, which concluded that there was no benefit to screening for thyroid dysfunction. The current study focused on answering four questions: (1) Does screening for thyroid dysfunction reduce morbidity and mortality? (2) What are the harms of screening? (3) Does treating screen-detected overt or subclinical thyroid dysfunction improve: (a) mortality and morbidity? or (b) intermediate outcomes? and (4) What are the harms of treating thyroid dysfunction detected by screening?

THE FULL ARTICLE TITLE

Rugge JB et al. Screening and treatment of thyroid dysfunction: an evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 2015;162:35-45.

SUMMARY OF THE STUDY

The major databases for published clinic studies (Medline and Cochrane databases) were reviewed for relevant articles from 2002 to mid-2014 on subclinical hypothyroidism and hyperthyroidism. Studies were included if they compared screening versus no screening or compared treatment versus no treatment. Cardiac outcomes, fractures, changes in bone mineral density, quality of life, and cognitive function were examined.

One study of treatment of subclinical hypothyroidism showed a reduction of cardiac events and all-cause mortality in those who were treated with levothyroxine versus those who had no treatment. Review of several studies of cholesterol showed that treatment of subclinical hypothyroidism with levothyroxine lowered total cholesterol and LDL levels significantly. There was no evidence of harm due to therapy for subclinical hypothyroidism.

In general, there was no significant improvement in quality of life due to treatment of subclinical hypothyroidism versus no treatment. Based on two studies of cognitive function with treatment versus no treatment of subclinical hypothyroidism, the review concluded that there was no benefit of therapy.

The first two questions concerning reduction of morbidity and mortality and harms of screening could not be addressed in a satisfactory manner because no study compared those screened versus those not screened.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

It is clear that screening for thyroid disease will identify individuals with TSH levels above or below the normal range, with most of these individuals having normal thyroid hormone levels other than the TSH. What is unclear is a definite benefit to identifying and treating these individuals. There does appear to be a benefit of treating hypothyroidism in reducing cardiac risk factors (elevated cholesterol) and possibly cardiac events. However, this benefit is not strong enough on its' own to recommend screening. Not enough data is available to determine effects on quality of life or mortality or morbidity. At this point, rather than recommending against screening, the authors conclude that "more research is needed to determine the clinical benefits associated with thyroid screening."

— Alan. P. Farwell, MD

ATA THYROID BROCHURE LINKS

Hypothyroidism: <u>http://www.thyroid.org/</u> what-is-hypothyroidism



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HYPOTHYROIDISM, continued



ABBREVIATIONS & DEFINITIONS

NHANES: The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations.

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

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

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

Levothyroxine (T_4) : the major hormone produced by the thyroid gland and available in pill form as Synthroid[™], Levoxyl[™], Tyrosint[™] and generic preparations.

Cognitive function: this refers to brain functions such as memory, ability to concentrate and understand concepts.

International Thyroid Awareness Month



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THYROID AND PREGNANCY

Diagnosing mild thyroid problems in early pregnancy and defining its impact on complications of pregnancy needs to be revisited

BACKGROUND

Thyroid hormone is essential for the normal growth and development of the baby during pregnancy. Hypothyroidism in the mother during early pregnancy is associated with adverse outcomes, but not consistently across studies. Many studies show that screening for thyroid disease during pregnancy does identify a lot of mild thyroid problems, mainly mild hypothyroidism. While it is clear that severe hypothyroidism in the mother results in complications in the baby, it is much less certain that mild hypothyroidism has significant effects on the baby. Further, it is completely unclear whether treating mild hypothyroidism in the mother has any effect in preventing any adverse outcomes. This study examined whether adding serum thyroid-function tests to the routine screening for chromosomal abnormalities between 9 and 14 weeks of pregnancy predicts adverse pregnancy outcomes.

THE FULL ARTICLE TITLE

Ong GS et al. Does the thyroid-stimulating hormone measured concurrently with first trimester biochemical screening tests predict adverse pregnancy outcomes occurring after 20 weeks gestation? J Clin Endocr Metab 2014;99:E:2663-72.

SUMMARY OF THE STUDY

A group of 2411 women in Western Australia with pregnancies with a single baby were studied. The investigators evaluated the association between TSH and FT_4 and a variety of adverse pregnancy events.

A TSH >2.15 mU/L in the first trimester (97.5th percentile)

was found in 133 women (5.5%), including 22 (1%) with TSH >4 mU/L and 5 (0.2%) >10 mU/L. Adverse pregnancy outcomes occurred in 327 women (15%). TSH and FT_4 did not differ significantly between women with or without adverse pregnancy events. The mother's TSH >2.15 mU/L was not a predictor of adverse pregnancy outcomes.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that screening for TSH as part of firsttrimester screening does not predict adverse pregnancy outcomes. However, a major limitation of this study is that no information was provided as to any medications that the mothers may have been on during the pregnancy. Specifically, it is not known whether any mothers were already on thyroid hormone, either before or after the screening took place. In fact, the relatively low rate of elevated TSH levels suggests that some of these mothers were indeed treated with thyroid hormone. In any event, despite many studies in this area, no clear conclusions can be made on the role of screening for or treating mild thyroid dysfunction in the mother during pregnancy.

— Alan P. Farwell, MD

ATA THYROID BROCHURE LINKS

Thyroid and Pregnancy: <u>http://www.thyroid.org/</u> <u>thyroid-disease-and-pregnancy</u> Thyroid Function Tests: <u>http://www.thyroid.org/</u> <u>blood-test-for-thyroid</u> Hypothyroidism: <u>http://www.thyroid.org/</u>

what-is-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.

Thyroxine (T_4) : the major hormone produced by the

thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

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

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A publication of the American Thyroid Association

THYROID AND PREGNANCY

Selenium supplementation during pregnancy

BACKGROUND

Selenium is a mineral known to be involved in the regulation of immune and thyroid function. Selenium is important for thyroid function as the major enzyme that activates thyroid hormone contains selenium. Autoimmune thyroid disease is the most common cause of hypo- and hyperthyroidism and is characterized by positive antithyroid antibodies, most commonly anti-TPO antibodies. People with high anti-TPO antibodies are at increased risk of developing hypothyroidism. Women with positive TPO antibodies have been shown to have an increased risk of pregnancy complications, including miscarriage and preterm labor. Researchers have been interested in determining whether reducing TPO antibody levels during pregnancy could improve pregnancy outcomes. Selenium supplementation has been shown in some studies to decrease TPO antibody levels and in one study selenium use during pregnancy decreased TPO antibodies and reduced the risk of thyroid function abnormalities after pregnancy. This study sought to determine whether supplementation with a lower dose of selenium in pregnant women would show similar findings. The current study examined the effect of selenium supplementation on TPO antibody levels and thyroid function in pregnant women.

THE FULL ARTICLE TITLE

Mao J et al. Effect of low-dose selenium on thyroid autoimmunity and thyroid function in UK pregnant women with mild-to-moderate iodine deficiency. Eur J Nutr., 2014 Dec 19. [Epub ahead of print].

SUMMARY OF THE STUDY

This study was part of the SPRINT Study (Selenium in PRegnancy INTervention), which is a study of pregnant women treated with either no selenium or selenium 60 micrograms per day starting at 12-14 weeks of pregnancy and continuing through delivery. These investigators examined the effect of selenium supplementation

on thyroid function tests (TSH and thyroid hormone levels) as well as TPO antibody levels during pregnancy. A total of 230 women were included in the study, with 115 women receiving selenium. Selenium use did not change TPO antibody levels during pregnancy. Overall, TSH increased and free T4 decreased during pregnancy. They analyzed the results comparing women who were TPO antibody positive or negative. Women with positive TPO antibodies had higher TSH values than those who were antibody negative and showed reduced TSH and free T4 levels during pregnancy with selenium treatment compared to women who took the placebo. Unlike the earlier study, this study did not show that selenium use reduced TPO antibody levels during pregnancy. This study differed from the earlier study in that it used a lower dose of selenium in a smaller study group of women who tended to be more iodine deficient.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that selenium in low doses did not alter TPO antibody levels but altered thyroid function, primarily reducing free T4 levels, in women with positive TPO antibodies. The long term effects of this are unknown.

This study is important for patients in that it demonstrates that additional research on the role of selenium supplementation during pregnancy is needed and that routine addition of selenium supplements during pregnancy cannot be recommended at this time. Future studies are needed to draw conclusions about the effect of selenium on thyroid function, thyroid antibody levels and outcomes during pregnancy.

- Whitney Woodmansee, MD

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

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).



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THYROID AND PREGNANCY, continued

TPO antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States. Selenium: a mineral found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. It is needed in small amounts by the body.

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 March is **International Thyroid Awareness Month** and a bracelet is available through the <u>ATA</u> <u>Marketplace</u> to support thyroid cancer awareness and education related to thyroid disease.









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THYROID CANCER

Radioactive iodine therapy for women with thyroid cancer is associated with delayed time to child-bearing and with decreased fertility in older women

BACKGROUND:

Radioactive iodine therapy for thyroid cancer is a very effective therapy for moderate to high risk thyroid cancer patients. Side effects of radioactive iodine therapy are infrequent but can be significant and include the development of other cancers and non-cancerous complications such as decreased saliva, dry mouth, dental cavities, dry eyes and tear duct obstruction. Limited data is available regarding the reproductive complications associated with radioactive iodine therapy. It has been reported that the radioactive iodine therapy can result in a short-lived disruption of the menstrual cycle in the first year after treatment and a slightly earlier onset of menopause. Prior smaller studies have suggested that the radioactive iodine therapy does not result in decreased fertility. The aim of this study was to evaluate the frequency of non-cancerous complications and the effect of radioactive iodine therapy on childbearing in female thyroid cancer survivors.

THE FULL ARTICLE TITLE:

Wu JX et al. Reproductive outcomes and non-oncologic complications after radioactive iodine ablation for well-differentiated thyroid cancer. Thyroid 2015;251:133-8.

SUMMARY OF THE STUDY:

This study used the California Cancer Registry (CCR) and the California Office of Statewide Health Planning and Development (OSHPD) database. A total of 25,233 patients with papillary or follicular thyroid cancer were identified in the database between 1999 and 2008. Among these, 13,211 patients received radioactive iodine therapy. The patients who received radioactive iodine therapy were younger, had larger cancers, higher rates of spread of the cancer outside of the thyroid disease and fewer associated health issues. The patients who received radioactive iodine therapy were also more likely to develop nasal and tear-duct obstruction than those who did not receive this treatment. The radioactive iodine therapy was not associated with a higher risk of any other non-cancerous complications. age with thyroid cancer followed for an average period of 4 years. Among these, 9,883 (52.4%) patients received radioactive iodine therapy. Women who received radioactive iodine therapy were younger, had higher socioeconomic status, tended to be married and had larger cancers than women who did not receive this treatment. There were 104 pregnancies at the time of the cancer diagnosis that resulted in live birth. A total of 1,179 live births occurred during the follow-up period. Overall, there was no difference in the birth rates between women who received and those who did not receive radioactive iodine therapy treatment in the entire group. However, women 35 years of age or older who received radioactive iodine therapy had lower birth rates than those who did not receive this treatment (11.5 vs. 16.3 births per 1000 person-years). The average time to the first delivery after diagnosis was longer in women who received than those who did not receive radioactive iodine therapy (34.5 months vs. 26.1 months).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is the largest published population-based study examining the fertility rates in patients who receive treatment for thyroid cancer. In this study, radioactive iodine therapy was associated with a delayed time to child-bearing and with a decreased birth rate in women over 35 years of age. The study showed that the severity of the disease did not affect the birth rate. Further studies are needed to evaluate whether the decrease in birth rate in older women who receive radioactive iodine therapy reflects their choice or decreased fertility. Women of child bearing age with thyroid cancer should be advised regarding the potential of the radioactive iodine therapy to affect their reproductive capacity.

— Alina Gavrila, MD, MMSC

ATA THYROID BROCHURE LINKS

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

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

The database included 18,850 women of childbearing

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THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer.

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

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-I3I is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer.



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THYROID CANCER

Radioactive iodine treatment in patients with thyroid cancer can damage the nasal area

BACKGROUND

After surgery for thyroid cancer, radioactive iodine therapy is an option to destroy any remaining thyroid cancer cells. It is effective because thyroid cells actively take up and trap iodine within the cell. Radioactive iodine is also taken up in some of the cells in the tear ducts and the nasal area but is not trapped. Even so, some patients may suffer damage to these cells as a side effect of the radioactive iodine therapy. About 10% of thyroid cancer patients may develop eye problems after radioactive iodine therapy, although this is usually mild. This study looked at the nasal and tear duct function in patients with thyroid cancer treated with radioactive iodine at Georgetown Medical Center between 2008 and 2012.

THE FULL ARTICLE TITLE

Jonklaas J et al. Nasal symptoms after radioiodine therapy: a rarely described side effect with similar frequency to lacrimal dysfunction. Thyroid. September 8, 2014 [Epub ahead of print].

SUMMARY OF THE STUDY

A total of 411 patients were reviewed for symptoms such as dry eyes, excessive tearing, "generalized nasal discomfort," dry nose, and nose bleeds that appeared after the first treatment with radioactive iodine. The time of appearance of symptoms after radioactive iodine was estimated and possible contributing factors such thyroid hormone withdrawal or rhTSH stimulation, age, sex, weight, body-mass index, previous eye or nasal problems or head and neck irradiation, autoimmune disease and medication was analyzed. Out of 411 patients about 10% had a nasal side effect and 10% had eye symptoms. The average dose of radioactive iodine was 109 mCi. The analyses showed that higher doses of radioactive iodine increased the risk of both nasal and eye symptoms. The nasal symptoms appeared about 11 days after the radioactive iodine was given, whereas eye symptoms appeared about 300 days after radioactive iodine therapy. No patient had nasal symptoms during the 3 to 12 months of follow-up. Patients with higher body-mass index were at higher risk to develop both side effects. In addition, patients prepared with rhTSH for radioactive iodine had a lower risk of side effects than patients after thyroid hormone withdrawal.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Nasal and eye symptoms each develop in about 10% of patients with thyroid cancer after radioactive iodine therapy and about half of patients had both symptoms. Nasal symptoms occurred early within 1 to 2 weeks, but eye symptoms appeared about one year after radioactive iodine therapy. The risk of these side effects was lower in patients who had been prepared with rhTSH. The results of this study indicate that both nasal and eye symptoms should be considered as potential risks of radioiodine therapy.

— Jamshid Farahiti, MD

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-I3I is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the 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).

mCi: millicurie, the units used for I-131.



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THYROID CANCER, continued

Recombinant human TSH (rhTSH): human TSH that is produced in the laboratory and used to produce high levels of TSH in patients after an intramuscular injection. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan. The brand name for rhTSH is Thyrogen[™].

Thyroid Hormone Withdrawal (THW): this is used to produce high levels of TSH in patients by stopping

thyroid hormone pills and causing short-term hypothyroidism. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan.

Body-mass index (BMI): a standardized measure of obesity calculated by dividing the weight in kilograms by the square of the height. A normal BMI is 18.5-24.9, overweight is 25-30 and obese is >30.



A publication of the American Thyroid Association

THYROID CANCER

No clinical advantage to prophylactic central-neck dissection for papillary thyroid cancer

BACKGROUND

Thyroid surgery is the first treatment for thyroid cancer and usually involves a total thyroidectomy. Up to 30% of patients with thyroid cancer will have spread of the cancer outside of the thyroid at the time of surgery. Most of this spread is to the lymph nodes in the central neck around the thyroid. It is controversial whether the surgeon should try to remove all lymph nodes in the central neck at the time of surgery (prophylactic central-neck dissection) or only remove the abnormal-looking lymph nodes. Patients undergoing central neck dissection have higher rates of complications but a possible reduction in cancer recurrence rates. The aim of this study was to evaluate the clinical implications of prophylactic central-neck dissection (both advantages and disadvantages) performed at the same time as a total thyroidectomy.

THE FULL ARTICLE TITLE

Viola D et al Prophylactic central compartment lymph node dissection in papillary thyroid carcinoma: clinical implications derived from the first prospective randomized controlled single institution study. J Clin Endocrinol Metab. January 15, 2015 [Epub ahead of print].

SUMMARY OF THE STUDY

A total of 181 patients with papillary thyroid cancer and no clearly abnormal lymph nodes in the central neck had either total thyroidectomy alone (n = 88) or total thyroidectomy with prophylactic central-neck dissection (n = 93). The patients had no preoperative imaging or surgical findings of suspicious or enlarged lymph nodes. The authors determined the rate of cure and the rate of recurrent or persistent disease at 5 years. Surgical complications were assessed, especially hypoparathyroidism due to damage of the parathyroid glands at the time of surgery.

Almost half (46%) of the patients who had a central neck dissection had positive lymph nodes. The rate of persistent cancer in the group with thyroidectomy

alone was 8.0%, versus 7.5% in the group undergoing central-neck dissection. The thyroidectomy alone group were more likely to require multiple doses of radioactive iodine therapy and had a lower rate of permanent hypoparathyroidism than the group undergoing central-neck dissection. There was not a significant increase in recurrent laryngeal nerve injury between groups.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Overall, a similar outcome was found between groups in terms of cancer recurrence rate and recurrent laryngeal nerve paralysis. The prophylactic central neck dissection group had a higher rate of permanent hypoparathyroidism but a lower rate of needing repeated doses of radioiodine. The authors concluded that there was no clinical advantage to performing a prophylactic central-neck dissection in patients with papillary thyroid cancer.

The most striking finding from this study is the remarkably high rate of permanent hypoparathyroidism (19.4%) that followed the performance of a prophylactic central-neck dissection. This sobering finding alone, must be balanced against the potential benefits of the procedure when making decisions about the extent of surgery. The chief limitation of this study is the small sample size.

Regardless, prophylactic central-neck dissection in patients with papillary thyroid cancer is performed by some experts and at high-volume centers, and debate over its usefulness is expected to continue.

- Ronald B. Kuppersmith, MD, FACS

ATA THYROID BROCHURE LINKS

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

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



A publication of the American Thyroid Association

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer.

Total thyroidectomy: surgery to remove the entire thyroid gland.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-I3I is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid.

Lymph node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells. Central neck compartment: the central portion of the neck between the hyoid bone above, and the sternum and collar bones below and laterally limited by the carotid arteries.

Prophylactic central neck dissection: careful removal of all lymphoid tissue in the central compartment of the neck, even if no obvious cancer is apparent in these lymph nodes.



A publication of the American Thyroid Association

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 towards the improvement of thyroid education and resources for patients.

WHO WE ARE (in alphabetical order)

- American Thyroid Association
- Bite Me Cancer
- Graves' Disease and Thyroid Foundation
- Light of Life Foundation
- ThyCa: Thyroid Cancer Survivors' Association, Inc.
- Thyroid Cancer Canada
- Thyroid Federation International

AMERICAN THYROID ASSOCIATION

www.thyroid.org

ATA Patient Resources: http://www.thyroid.org/patients/ Find a Thyroid Specialist: www.thyroid.org Phone (toll-free): I-800-THYROID e-mail: thyroid@thyroid.org

ATA Mission: The ATA leads in promoting thyroid health and understanding thyroid biology. **ATA Vision:** The ATA is the leading organization focused on thyroid biology and the prevention and treatment of thyroid disorders through excellence and innovation in research, clinical care, education, and public health. **ATA Values:** The ATA values scientific inquiry, clinical excellence, public service, education, collaboration, and collegiality.

To further our mission, vision and values the ATA sponsors "Friends of the ATA" online to advance the information provided to patients and the public such as this publication, *Clinical Thyroidology for the Public*. We welcome your support.

continued on next page





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ATA Alliance for Thyroid Patient Education



BITE ME CANCER

http://www.bitemecancer.org

Bite Me Cancer was formed as a nonprofit foundation in September, 2010, by Nikki Ferraro, who was 17-years old at the time. Nikki was diagnosed with a rare form of thyroid cancer in April 2010 when she was a junior at Chantilly HS in Virginia. Nikki was determined to lead a Relay for Life team just two weeks after her diagnosis. She named the team Bite Me Cancer and experienced immediate success. When Nikki decided to create a foundation a few months later, she wanted to continue the legacy of her team name and thus her foundation became the Bite Me Cancer Foundation.

e-mail: info@bitemecancer.org

GRAVES' DISEASE AND THYROID FOUNDATION

www.gdatf.org

Phone (toll-free): I-877-NGDF-123 or 643-3123 e-mail: Gravesdiseasefd@gmail.com

Founded in 1990, the Graves' Disease Foundation offers support and resources to Graves' disease patients, their families, and health care professionals. Their mission is to find the cause of and the cure for Graves' thyroid disease through research, to improve the quality of life for persons with Graves' disease and their caregivers and to educate persons with Graves' disease, their caregivers, healthcare professionals, and the general public about Graves' disease and its treatment. The web site features a monitored bulletin board.

LIGHT OF LIFE FOUNDATION

www.checkyourneck.com

email: info@checkyourneck.com

The Light of Life Foundation, founded in 1997, is a nonprofit organization that strives to improve the quality of life for thyroid cancer patients, educate the public and professionals about thyroid cancer, and promote research and development to improve thyroid cancer care.

continued on next page

THYROID ASSOCIATION

www.thyroid.org



A publication of the American Thyroid Association

ATA Alliance for Thyroid Patient Education

Continued...

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

www.thyca.org

Phone (toll-free): 877 588-7904 e-mail: thyca@thyca.org

ThyCa: Thyroid Cancer Survivors' Association, Inc., founded in 1995, is an international nonprofit organization, guided by a medical advisory council of renowned thyroid cancer specialists, offering support and information to thyroid cancer survivors, families, and health care professionals worldwide.

THYROID CANCER CANADA

www.thyroidcancercanada.org Phone: 416-487-8267 Fax: 416-487-0601 e-mail: info@thyroidcancercanada.org

Thyroid Cancer Canada is a non-profit organization founded in 2000. The organization works towards creating an environment in which people who are dealing with thyroid cancer, especially the newly diagnosed, are met with support and information. Their goals & objectives include facilitating communication among thyroid cancer patients, providing credible information about the disease, providing emotional support, and assisting thyroid cancer patients with voicing their needs to health care professionals and those who are responsible for health care policy.

THYROID FEDERATION INTERNATIONAL

http://www.thyroid-fed.org/

e-mail: tfi@thyroid-fed.org

Thyroid Federation International (TFI) was established in Toronto in 1995. Thyroid Federation International aims to work for the benefit of those affected by thyroid disorders throughout the world by providing a network of patient support organizations.









American Thyroid Association Supports *World Thyroid Day* May 25, 2015

The American Thyroid Association (ATA) supports and celebrates the 8th Annual **World Thyroid Day, May 25, 2015.** The American Thyroid Association <u>www.thyroid.org</u>, in cooperation with sister international thyroid societies, the European Thyroid Association <u>www.eurothyroid.com</u>, the Asia & Oceania Thyroid Association <u>www.aothyroid.org</u>, and the Latin American Thyroid Society <u>www.lats.org</u>, recognizes the 8th Annual World Thyroid Day, May 25, 2015.

Established in 2008, World Thyroid Day highlights five major goals to:

- Increase awareness of thyroid health,
- Promote understanding of advances made in treating thyroid diseases,
- Emphasize the prevalence of thyroid diseases,
- Focus on the urgent need for education and prevention programs, and
- Expand awareness of new treatment modalities.

Tens of millions of people worldwide are affected by diseases of the thyroid. The thyroid gland, butterfly-shaped and located in the middle of the lower neck, produces hormones that influence every cell, tissue and organ in the body. The thyroid hormones regulate the body's metabolism— the rate at which the body produces energy from nutrients and oxygen—and affects critical body functions, such as energy level and heart rate.

Iodine Deficiency

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 IODINE DEFICIENCY?

lodine is an element that is needed for the production of thyroid hormone. The body does not make iodine, so it is an essential part of your diet. Iodine is found in various foods (see *Table 1*). If you do not have enough iodine in your body, you cannot make enough thyroid hormone. Thus, iodine deficiency can lead to enlargement of the thyroid (goiter – see *Goiter brochure*), hypothyroidism (see *Hypothyroidism brochure*) and to mental retardation in infants and children whose mothers were iodine deficient during pregnancy.

Before the 1920s, iodine deficiency was common in the Great Lakes, Appalachian, and Northwestern U.S. regions and in most of Canada. Treatment of iodine deficiency by the introduction of iodized salt has virtually eliminated the "goiter belt" in these areas. However, many other parts of the world do not have enough iodine available through their diet and iodine deficiency continues to be an important public health problem globally. Approximately 40% of the world's population remains at risk for iodine deficiency.

HOW DO YOU DIAGNOSE IODINE DEFICIENCY?

lodine deficiency is diagnosed across populations and not specifically in individuals. Since iodine is released from the body through the urine, the best way to determine iodine deficiency across a large population is to measure the amounts of iodine in urine samples. Iodine deficiency is defined as a median urinary iodine concentration less than 50 μ g/L in a population (see *Table 2*).

In the United States, iodine status has remained generally adequate in the last 2 decades although studies have shown that urinary iodine levels dropped by about half between the early 1970s and the early 1990s. However, iodine deficiency is a major issue in other parts of the world, including parts of Europe, Africa and Asia.

WHAT ARE THE SOURCES OF IODINE?

lodine is present naturally in soil and seawater. The availability of iodine in foods differs in various regions of the world. Individuals in the United States can maintain

adequate iodine in their diet by using iodized table salt (unless they have to restrict the amount of salt in their diet), by eating foods high in iodine, particularly dairy products, seafood, meat, some breads, and eggs, and by taking a multivitamin containing iodine (see below). However, the amount of iodine in foods is not listed on food packaging in the U.S., and it can be difficult to identify sources of iodine in foods.

TABLE 1: COMMON SOURCES OF **DIETARY IODINE** Cheese Cows milk Eggs Frozen Yogurt Ice Cream lodine-containing multivitamins lodized table salt Saltwater fish Seaweed (including kelp, dulce, nori) Shellfish Soy milk Soy sauce Yogurt

WHAT ARE THE SYMPTOMS OF IODINE DEFICIENCY?

All of the symptoms of iodine deficiency are related to its effect on the thyroid:

GOITER – Without adequate iodine, the thyroid progressively enlarges (develops a goiter) as it tries to keep up with demand for thyroid hormone production. Worldwide, iodine deficiency is the most common cause of thyroid enlargement and goiter (see *Goiter brochure*). Within a goiter, nodules can develop. Patients with a large goiter may experience symptoms of choking, especially when lying down, and difficulty swallowing and breathing.

HYPOTHYROIDISM – As the body's iodine levels fall, hypothyroidism may develop, since iodine is essential for making thyroid hormone. While this is uncommon in the United States, iodine deficiency is the most common cause of hypothyroidism worldwide (see *Hypothyroidism brochure*).

Iodine Deficiency

PREGNANCY-RELATED PROBLEMS – Iodine deficiency is especially important in women who are pregnant or nursing their infants. Severe iodine deficiency in the mother has been associated with miscarriages, stillbirth, preterm delivery, and congenital abnormalities in their babies. Children of mothers with severe iodine deficiency during pregnancy can have mental retardation and problems with growth, hearing, and speech. In the most severe form, an underactive thyroid can result in cretinism (a syndrome characterized by permanent brain damage, mental retardation, deaf mutism, spasticity, and short stature), though this is not seen in the United States. Congenital hypothyroidism due to iodine deficiency is the most common preventable cause of mental retardation in the world. Even mild iodine deficiency during pregnancy, which may be present in some women in the United States, may be associated with low intelligence in children.

HOW IS IODINE DEFICIENCY TREATED?

There are no tests to confirm if you have enough iodine in your body. When iodine deficiency is seen in an entire population, it is best managed by ensuring that common foods that people eat contain sufficient levels of iodine. Since even mild deficiency during pregnancy can have effects on delivery and the developing baby, all pregnant and breastfeeding women should take a multivitamin containing at least 150 µg iodine per day. The RDA is 220 µg iodine per day for pregnant women and 290 µg iodine per day for breastfeeding women. Because the effects of iodine deficiency are most severe in pregnant women and their babies, the American Thyroid Association has recommended that all pregnant and breastfeeding women in the U.S. and Canada take a prenatal multivitamin containing 150 µg iodine per day.

ARE THERE PROBLEMS WITH TAKING TOO MUCH IODINE?

Taking too much iodine can also cause problems. This is especially true in individuals that already have thyroid problems, such as nodules, hyperthyroidism and autoimmune thyroid disease. Administration of large amounts of iodine through medications (ie Amiodarone), radiology procedures (iodinated intravenous dye) and dietary excess (Dulce, kelp) can cause or worsen hyperthyroidism and hypothyroidism.

In addition, individuals who move from an iodinedeficient region (for example, parts of Europe) to a region with adequate iodine intake (for example, the United States) may also develop thyroid problems since their thyroids have become very good at taking up and using small amounts of iodine. In particular, these patients may develop iodine-induced hyperthyroidism (see *Hyperthyroidism brochure*).

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HOW IS IODINE DEFICIENCY PREVENTED?

As with many diseases, it is better to prevent the problem rather than have to treat it. Over the last 80 years, world-wide efforts have been made to eliminate iodine deficiency. Indeed, elimination of iodine deficiency has been a major goal of the World Health Organization. Iodized salt has been the mainstay of treatment for iodine deficiency worldwide, including in the United States. Injections of iodized oil are occasionally used in regions of the world where widespread iodized salt use is not possible. Iodination of water supplies also has been effective in some places.

UNITED STATES RECOMMENDATIONS – The Institute of Medicine has set the Recommended Dietary Allowance (RDA)

for iodine in adult men and women at 150 µg per day. Individuals who add tablet salt to their food regularly should use iodized salt. One teaspoon of iodized salt contains approximately 400 µg iodine. Most iodine-containing multivitamins have at least 150 µg iodine, but only about half of the types of multivitamins in the U.S. contain iodine.

TABLE 2. MEDIAN POPULATION URINARY IODINE VALUES AND IODINE NUTRITION

| MEDIAN URINARY IODINE CONCENTRATION (µg/L) | CORRESPONDING IODINE INTAKE (µg/day) | IODINE NUTRITION |
|---|---|---------------------|
| <20 | <30 | SEVERE DEFICIENCY |
| 20-49 | 30-74 | MODERATE DEFICIENCY |
| 50-99 | 75-149 | MILD DEFICIENCY |
| 100-199 | 150-299 | OPTIMAL |
| 200-299 | 300-449 | MORE THAN ADEQUATE |
| >299 | >449 | POSSIBLE EXCESS |

[From WHO, UNICEF and ICCIDD 2001 Assessment of the lodine Deficiency Disorders and monitoring their elimination. A guide for programme managers. WHO publ., Geneva. WHO/NHD/01.1]



FURTHER INFORMATION

This page and its contents are Copyright © 2014 the American Thyroid Association 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*.