Clinical THYROIDOLOGY FOR PATIENTS

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

VOLUME 5 • ISSUE 10 • 2012

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A publication of the American Thyroid Association

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EDITOR'S COMMENTS

Welcome to Clinical Thyroidology for Patients, bringing to you, the patients, the most up-to-date, cutting edge thyroid research. What you read here as research studies will likely become the accepted practice in the future. *Clinical Thyroidology for Patients* is published on a monthly basis and includes summaries of research studies that were discussed in a recent issue of *Clinical Thyroidology*, a publication of the American Thyroid Association for physicians. This means that you, the patients, are getting the latest information on thyroid research and treatment almost as soon as your physicians.

The Calendar of Events highlights educational forums and support groups that are organized around the country by members of the Alliance for Thyroid Patient Education. The Alliance member groups consist of: the *American Thyroid Association*, the *Graves' Disease and Thyroid Foundation*, the *Light of Life Foundation* and *ThyCa: Thyroid Cancer Survivors Association*.

Follow us on Twitter at @thyroidfriends. Get the most up-to-date thyroid news fast and easy! Be the most informed thyroid patient in the waiting room. Please feel free to submit questions as well as suggestions as to how we can better serve thyroid patients.

Check us out on Facebook: www.facebook.com/thyroidassociation.

In this issue, the studies ask the following questions:

- Is the brain development in pre-term infants affected by hypothyroidism in the mother?
- Can thyroid hormone prevent abnormal brain development if hypothyroidism in the mother is diagnosed during the pregnancy?
- Is methimazole taken during pregnancy associated with birth defects?
- Is kidney disease associated with autoimmune thyroid disease?
- What is the best to prepare patients for whole body scans to diagnose spread of 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.

Have a happy and healthy fall season!

— Alan P. Farwell, MD

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THYROID AND PREGNANCY

Brain development in pre-term infants born of mothers with hypothyroidism

BACKGROUND

Thyroid hormone is essential for normal brain development in the baby during pregnancy. Mild abnormalities in thyroid function tests in pregnant women have been reported to be related to poor mental development of children, but most studies did not focus on outcomes of pre-term infants. These infants, born before 34 weeks of pregnancy, often have lower thyroid hormone levels that full-term babies and are more likely to have brain abnormalities. The aim of this study was to examine the relationship between the thyroid hormone levels in pregnant women at the time of delivery of pre-term infants and the future mental development of the children.

THE FULL ARTICLE TITLE

Williams F et al Mild maternal thyroid dysfunction at delivery of infants born ≤34 weeks and neurodevelopmental outcome at 5.5 years. J Clin Endocrinol Metab. April 4, 2012 [Epub ahead of print]. doi:10.1210/jc.2011-2451.

SUMMARY OF THE STUDY

The Millenium study enrolled women and infants between 1998 and 2001 in Scotland. Pre-term infants born on or before 34 weeks of pregnancy were enrolled from Scottish neonatal intensive care units. The investigators measured levels of TSH, T_4 and FT_4 in women within one hour of delivery of the infant. At age 5 ½ years, the children had their mental development tested using the McCarthy Scale. In statistical analyses adjusted for important risk factors, decreasing TSH measurements in mothers were associated with decreases in various scores within the McCarthy Scale in these children. However, decreasing free T_4 measurements were associated with increases in various scores of the McCarthy Scale.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The main conclusion of the authors was that higher levels of TSH in the mother at delivery of pre-term infants was associated with lower mental development scores of the children at 5 ½ years. These findings reinforce the importance for women with hypothyroidism to have their TSH measurements closely followed in pregnancy and thyroid hormone doses adjusted as needed to avoid TSH elevations.

— Anna Sawka, MD

ATA THYROID BROCHURE LINKS

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

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

Thyroid Function Tests: http://www.thyroid.org/blood-test-for-thyroid

ABBREVIATIONS & DEFINITIONS

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

Thyroxine (T_4): the major hormone secreted by the thyroid gland. Thyroxine is broken down to produce Triiodothyronine which causes most of the effects of the thyroid hormones.

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

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THYROID AND PREGNANCY

Maternal hypothyroidism during pregnancy is not associated with severe brain abnormalities in the baby if treated with thyroid hormone prior to the third trimester

BACKGROUND

Thyroid hormone is essential for normal brain development in the baby during pregnancy. All babies are screened for congenital hypothyroidism at birth to identify and treat patients to avoid severe lifelong developmental disabilities. Early on in pregnancy the thyroid hormone in the baby comes from the mother, thus hypothyroidism in the mother should be avoided during pregnancy. Thus, hypothyroidism in either the mother or baby can be associated with impaired brain development if left untreated. One rare form of severe hypothyroidism is caused by TSH receptor-blocking antibodies, which can cross from the mother to the baby during pregnancy and cause hypothyroidism in the baby. Some pregnant women with newly detected severe hypothyroidism have expressed a desire to terminate their pregnancies due to fears of brain abnormalities in their unborn child. This study reports on the brain development of 3 children born to mothers with severe hypothyroidism detected during pregnancy and aggressively treated with thyroid hormone.

THE FULL ARTICLE TITLE

Downing S et al. Severe maternal hypothyroidism corrected prior to the third trimester is associated with normal cognitive outcome in the offspring. Thyroid. 22(6): 625-630. 2012.

SUMMARY OF THE STUDY

This study examined brain function and IQ tests in 3 children born to mothers with severe hypothyroidism due to TSH receptor blocking antibodies. The women were diagnosed during pregnancy and were aggressively treated with thyroid hormone with the goal to normalize thyroid hormone and TSH levels prior delivery of the child. All 3 children had evidence of congenital hypothyroidism at birth due to these antibodies and were treated with thyroid hormone. A variety of tests, including IQ tests, were performed when the children were between 5 and 6 years old. All 3 children had average or above average scores on the tests – none showed any significant impairment. Additionally, these 3 children were each compared to one of their siblings. All the mothers had normal thyroid function during the pregnancy of the sibling. On some tests the children born when the mother had hypothyroidism during pregnancy did better and on some the sibling performed better. The main finding was that these 3 children exposed to maternal hypothyroidism during pregnancy that was treated early with thyroid hormone demonstrated average or above average brain development.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors conclude that if maternal hypothyroidism is treated early in pregnancy, severe brain dysfunction can be prevented and early termination of pregnancy due to fears of impaired brain development is not warranted. Although this study reports on only 3 children born to mothers with severe hypothyroidism, it provides some reassuring information for mothers with hypothyroidism detected during pregnancy that severe brain dysfunction in their child is unlikely if they receive prompt and appropriate therapy with thyroid hormone.

— Whitney Woodmansee MD

ATA THYROID BROCHURE LINKS

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

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

continued on next page

THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

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

Congenital: condition that exists at birth.

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.

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal. The goal of treatment is a TSH in the normal range and is the usual therapy.

TSH Receptor Blocking Antibodies: these are antibodies that block the TSH signaling pathway. TSH normally signals the thyroid gland to secrete thyroid hormones. TSH blocking antibodies prevent TSH from transmitting its signal to the thyroid cells, thus, the cells stop producing thyroid hormone, producing hypothyroidism.

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THYROID AND PREGNANCY

Higher risk of birth defects in women treated with methimazole vs. propylthiouracil during pregnancy

BACKGROUND

Hyperthyroidism due to Graves' disease is relatively common in women of childbearing years. Because of this, women may become pregnant during medical therapy for Graves' disease or, less commonly, develop Graves' disease during pregnancy. The two most common medications for the treatment of hyperthyroidism are methimazole and propylthiouracil (PTU), with methimazole the drug of choice according to the recent American Thyroid Association (ATA) guidelines for the management of hyperthyroidism. Some studies have suggested that using methimazole during early pregnancy may be associated with extremely rare congenital problems in the newborn baby. Indeed, the ATA guidelines recommend switching from methimazole to PTU during the first half of pregnancy. This study is now the largest one ever done to closely examine the association of methimazole and PTU with congenital abnormalities.

THE FULL ARTICLE TITLE:

Yoshihara A et al. Treatment of Graves' disease with antithyroid drugs in the first trimester of pregnancy and the prevalence of congenital malformation. J Clin Endocrinol Metab. April 30, 2012 [Epub ahead of print]. doi: 10.1210/jc.2011-2860.

SUMMARY OF THE STUDY

This is a study based on the medical records over 10 years (1999-2010) of almost 6000 Japanese pregnant women with Graves' disease, the most common cause of hyperthyroidism. During the first trimester of pregnancy, 1426 women were treated with methimzole alone and 1578 with PTU alone; 2065 women were not hyperthyroid and received no medication. The overall rate of congenital abnormalities was 2.5% (152 of 5997 infants). The rate of congenital abnormalities in infants born to the women in the methimazole group was 4.1% (50 of 1231 infants) as compared with 1.9% (26 of 1399) in the PTU group and 2.1% (40 of 1906 infants) in the patients without hyperthyroidsm. Thus, women who took methimazole during the first trimester of pregnancy had double the risk of birth defects, compared to women who took PTU or neither medication. Some of the birth defects included a skin disorder on the scalp and problems with development of the stomach and intestines.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study confirms that methimazole use during the first trimester of pregnancy should be avoided if possible. PTU use is preferred, especially during the 1st trimester. Pregnant mothers with Graves' disease should consult with their physician to discuss the best treatment recommended for both mother and baby.

— Angela Leung, MD

ATA THYROID BROCHURE LINKS

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

Graves' Disease: http://www.thyroid.org/what-is-graves-disease

ABBREVIATIONS & DEFINITIONS

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Congenital: a condition that exists at birth.

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.

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

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AUTOIMMUNE THYROID DISEASE

Several forms of kidney disease may be associated with autoimmune thyroid disease

BACKGROUND

Hashimoto's thyroiditis, the most common cause of hypothyroidism in the United States, is an autoimmune disease that is characterized by high blood levels of antibodies against different thyroid proteins that attack the thyroid and destroy the gland. However, many patients with Hashimoto's thyroiditis will only have partial thyroid destruction and not develop hypothyroidism. It is known that patients with Hashimoto's thyroiditis have a higher risk to develop other autoimmune diseases, including type 1 diabetes and adrenal insufficiency. While there are several forms of autoimmune diseases that affect the kidneys, only a few isolated patients with Hashimoto's thyroiditis who also had kidney disease have been previously reported. The aim of this study was to evaluate the frequency and further characterize the renal disease in a group of patients with Hashimoto's thyroiditis.

THE FULL ARTICLE TITLE

Kocak G et al. Coexistent findings of renal glomerular disease with Hashimoto's thyroiditis. Clin Endocrinol (Oxf) 2012;76:759-62.

SUMMARY OF THE STUDY

This is a study of 28 patients with Hashimoto's thyroiditis who were evaluated for glomerular kidney disease in a kidney clinic between 2007 and 2011. No association was found between the blood antithyroid antibody or thyroid hormone level and kidney function. The study showed significantly decreased renal function in patients with long-standing Hashimoto's thyroiditis compared to recent-onset (less than 12 months) Hashimoto's thyroiditis. Twenty patients underwent kidney biopsies, while eight patients had transient kidney abnormalities and did not require biopsy. The frequency of different glomerular kidney diseases diagnosed on the biopsy was similar in patients with and without Hashimoto's thyroiditis. A total of 7 out of 20 patients who underwent kidney biopsy required immunosuppressive therapy for their kidney disease. The response of the kidney disease to treatment did not differ in patients with or without Hashimoto's thyroiditis.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is the largest published study evaluating patients diagnosed with both Hashimoto's thyroiditis and kidney disease. The fact that long-standing Hashimoto's thyroiditis was associated with more severe decrease in kidney function is suggestive of a possible relationship between the two diseases. These findings will need to be confirmed by further research in this area.

— Alina Gavrila, MD

ATA THYROID BROCHURE LINKS

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

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).

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

Immune system: a system of organs, tissues and cells in our body that has the role to recognize potentially harmful foreign substances and organisms as well as abnormal body cells and produce antibodies to destroy these factors.

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

Autoimmune disorders: A diverse group of disorders that are caused by antibodies that get confused and attack the body's own tissues. The disorder depends on what tissue the antibodies attack. Graves' disease and Hashimoto's thyroiditis are examples of autoimmune thyroid disease. Other autoimmune disorders include: type 1 diabetes mellitus, Addison's disease (adrenal insufficiency), vitiligo (loss of pigment of some areas of the skin), systemic lupus erythematosus, pernicious anemia (B12 deficiency), celiac disease, inflammatory bowel disease, myasthenia gravis, multiple sclerosis and rheumatoid arthritis.

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THYROID CANCER

Use of thyroid hormone withdrawal before radioactive iodine whole body scans for metastatic thyroid cancer is superior to recombinant TSH in detecting tumor sites

BACKGROUND

Patients with thyroid cancer are treated with surgery, which is often followed by radioactive iodine therapy to destroy any remaining thyroid cancer cells. When there is concern that the cancer has spread, radioactive iodine scans are used to detect the cancer. These scans are done in the presence of elevated TSH levels to increase the radioactive iodine uptake into thyroid cancer cells allowing for the detection and treatment of thyroid tumors. Elevated TSH levels can be achieved by stopping thyroid hormone therapy (thyroid hormone withdrawal, THW) or by injections of TSH in the form of recombinant human TSH (rhTSH, ThyrogenTM). While both methods are approved for preparation for the initial radioactive iodine therapy, rhTSH preparation is not FDA approved for the scanning or treatment of metastatic thyroid cancer. This is because the ability of rhTSH preparation to achieve a sufficient concentration of radioactive iodine in such tumors has not been proven. This study compared the results of radioactive iodine whole body scans after both rhTSH and THW in patients suspected to have persistent thyroid cancer.

THE FULL ARTICLE TITLE

Van Nostrand D et al. Recombinant human thyroid-stimulating hormone versus thyroid hormone withdrawal in the identification of metastasis in differentiated thyroid cancer with ^{131}I planar whole-body imaging and 124I PET. J Nucl Med. 2012;53:359-62. Epub February 7, 2012.

SUMMARY OF THE STUDY

A total of 40 patients with suspected recurrent or metastatic thyroid cancer had radioactive iodine whole body scans after either rhTSH (24 patients) or THW preparation (16 patients). The number of metastatic lesions that concentrated iodine was then counted by two physicians independently.

Far more lesions (2-10-fold more) were detected on the radioactive iodine scans in patients who were prepared with THW rather than rhTSH.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that THW is superior to rhTSH preparation in the detection of metastatic thyroid cancer. However, more studies are needed to determine whether THW is superior to rhTSH preparation in the treatment of metastatic thyroid cancer.

— Mona Sabra, MD

ATA THYROID BROCHURE LINKS

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

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

Thyroid Surgery: http://thyroid.org/patients/patient_brochures/surgery.html

ABBREVIATIONS & DEFINITIONS

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).

Diagnostic radioactive iodine whole body scans: these radioactive iodine scans are performed under TSH stimulation, either after thyroid hormone withdrawal or after injections of recombinant human TSH (Thyrogen). The scan identifies any remaining thyroid cells in the body and determines if there is any evidence of metastatic thyroid cancer.

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.

AMERICAN THYROID ASSOCIATION
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www.thyroid.org

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.

WHO WE ARE

AMERICAN THYROID ASSOCIATION

www.thyroid.org
ATA Patient Resources: http://www.thyroid.org/patients/
Find a Thyroid Specialist: www.thyroid.org
Phone (toll-free): 1-800-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 Patients*. We welcome your support.

GRAVES' DISEASE AND THYROID FOUNDATION

www.gdatf.org
Phone (toll-free): 1-877-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.

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.

AMERICAN THYROID ASSOCIATION
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www.thyroid.org

ATA Alliance for Thyroid Patient Education
CALENDAR OF EVENTS

Educational forums, patient support groups and other patient-oriented meetings

ATA Conferences www.thyroid.org

Nothing is scheduled at this time. Please visit the website for updates.

Graves' Disease Conferences www.gdatf.org

October 26- 28, 2012 - San Diego, CA
Patient & Family Conference at the beautiful Kona Kai Resort & Spa. Details at www.gdatf.org

Light of Life Foundation www.checkyourneck.com

Ongoing — www.checkyourneck.com
Thyroid Cancer Awareness campaign with Cindy Crawford and Brooke Shields

June 12, 2010 — a previous symposium available online at:
http://www.checkyourneck.com/About-Thyroid-Cancer/Thyroid-Cancer-Symposium-Presentations

Thyroid Cancer Symposium Presentations: What's New in Thyroid Cancer?
A Day for Patients and Their Families

Please visit the Light of Life Foundation website to view the Patient Educational Symposium which took place in NYC in 2010. As part of the Patient Educational Program these online presentations provide valuable information in hopes that patients everywhere can gain further information and support about their disease.

November 17, 2012 — New York, NY
Annual Light of Life Foundation Patient Symposium. Details at www.checkyourneck.com

ThyCa Conferences www.thyca.org

Every Month
ThyCa Support Group Meetings around the United States and in Canada, Costa Rica, and Philippines. Complete list of groups, meetings, and contacts at www.thyca.org/sg/local

September 2012 — **Thyroid Cancer Awareness Month**
Worldwide observance sponsored by ThyCa: Thyroid Cancer Survivors' Association, Inc., with many partnering organizations. Details at www.thyca.org

October 19–21, 2012 — Chicago, Illinois. **The 15th International Thyroid Cancer Survivors' Conference** Sponsored by ThyCa: Thyroid Cancer Survivors' Association, Inc. Details at www.thyca.org

October 20, 2012 — Chicago, Illinois
The 10th Annual Dinner/Auction Fundraiser for Thyroid Cancer Research, in conjunction with the 15th International Thyroid Cancer Survivors' Conference
Sponsored by ThyCa: Thyroid Cancer Survivors' Association, Inc. Details at www.thyca.org