Clinical THYROIDOLOGY

JULY 2012
VOLUME 24 • ISSUE 7

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

Clinical
THYROIDOLOGY

VOLUME 24 • ISSUE 7 JULY 2012

Neuropsychological Development in Children of Mothers with Hypothyroidism Is Normal When Euthyroidism Is Achieved after Conception

Downing S, Halpern L , Carswell J , Brown RS. Severe early maternal hypothyroidism corrected prior to the third trimester associated with normal cognitive outcome in the offspring. Thyroid 2012;22:625-30. Epub May 10, 2012.

SUMMARY

Background

Concern about potential harmful effects of early maternal hypothyroidism (MH) on fetal brain development has led to calls for universal screening early in, or even before, pregnancy. However, evidence in humans that adverse effects are irreversible if thyroid-hormone replacement is initiated after the first trimester is limited. The authors sought to determine the outcome if treatment is given in early pregnancy.

Methods

The authors identified three women who had TSH receptor blocking antibody-induced MH during pregnancy and were treated with levothyroxine (L-T_4), starting at 27 weeks, 5 weeks, and the first month of gestation. The corresponding pretreatment serum TSH levels in the 2 women in whom data were available were 68 mU/L at 25 weeks of gestation and 65 mU/L at 24 weeks of gestation, falling, in each case to 6 mU/L. The third woman with MH required 0.5 mg of L-T_4 to normalize her thyroid hormone levels by 4 months of gestation. Their infants were also treated with L-T_4 after neonatal screening identified congenital hypothyroidism (CH). A battery of neuropsychological tests was administered to assess intelligence, language, memory, and visual-motor performance. All testing of these three infants at 5.4 years of age (range, 5.1 to 6.1) and of three sibling controls at 6.8 years (range, 9.1 to 3.0) was performed by two experienced pediatric clinical psychologists who had no knowledge of the maternal thyroid function during pregnancy.

Results

Children born to women with MH had average or above average results on all parameters. Comparative scores of the neuropsychological tests in sibling

continued on next page

Back to Contents

pairs for full-scale IQ and performance IQ were variable; some scores were higher and some lower in children with CH.

Conclusions

Although the findings do not exclude a subtle impact of MH on intellectual function during early gestation, the normal cognitive outcome despite overt MH should provide data with which to counsel mothers who have overt hypothyroidism early in pregnancy. Aggressive thyroid-hormone replacement as soon as possible is important, but early termination of the pregnancy because of fear that the baby will have significant cognitive delay is not warranted.

ANALYSIS AND COMMENTARY

Low intelligence quotient (IQ) scores in children of pregnant women with poorly treated hypothyroidism have been of great concern to health care professionals and to the lay population. Very early reports of cretinism in infants of women with hypothyroidism were related to severe iodine deficiency and/or maternal hypothyroidism (1). In 1999, Haddow et al., in a retrospective study, found that a group of children born to women with untreated hypothyroidism had a 7-point deficit in their IQ at 7 to 9 years of age as compared with matched children from mothers whose serum TSH levels were within reference range (2). However, the deficit was only 4 points (not statistically significant) when children of mothers with treated and untreated hypothyroidism were compared with controls. Hypothyroidism is not uncommon in pregnancy; the prevalence of newly diagnosed hypothyroidism in pregnancy is 2% to 4%. In addition, the incidence of hypothyroidism diagnosed in pregnancy in women undergoing L-T_4 therapy antedating pregnancy has been reported to be between 20% and 40% at the first obstetrical visit (3). Therefore, it has been recommended to advise women on L-T_4 therapy to add two extra tablets per week of the usual L-T_4 dose when pregnancy is confirmed (4), or as an alternative, to have a serum TSH <1.2 mIU/L before planning pregnancy (5). Since the placental transfer of maternal thyroid hormones to the embryo in early pregnancy is very well accepted (6), the question of diagnosing hypothyroidism via universal screening in early pregnancy became a heated argument in the medical community, although recent guidelines by the ATA (7) and the Endocrine Society (8) recommend selective screening in women considered to be at risk, supporting early statements by the American College of Obstetricians and Gynecologists (9). As mentioned by Downing et al., every health care professional caring for pregnant women affected by hypothyroidism had the experience of a patient requesting an early termination of pregnancy. Several publications in the past few months brought some good news for children from mothers with hypothyroidism. Lazarus et al., in a large study of mothers with subclinical hypothyroidism, in which half of them received L-T_4 replacement therapy and the other half served as controls, concluded that antenatal screening (at a median gestational age of 12 weeks 3 days) with treatment of the women for hypothyroidism did not result in improved cognitive function in children at 3 years of age (10). In other studies from Japan, the children of mothers with hypothyroidism whose L-T_4 treatment was started after the second half of pregnancy had neurodevelopment cognitive scores similar to their siblings who were born when their mothers were euthyroid throughout pregnancy (11, 12). As stated by Downing et al., "Although further data are required to exclude a more subtle impact on cognitive function, the present findings, together with other studies in the medical literature, do not support widespread concern that affected infants whose mothers are treated after the first trimester of pregnancy will have significant intellectual delay as long as maternal thyroid function is normalized before the third trimester. Larger randomized control trials of patients with early MH are necessary to exclude a more subtle impact on neurocognitive function."

— Jorge H. Mestman, MD

References

1. Pharoah PO, Connolly KJ, Ekins RP, Harding AG. Maternal thyroid hormone levels in pregnancy and the subsequent cognitive and motor performance of the children. Clin Endocrinol (Oxf) 1984;21:265-70.
2. Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999;341:549-55.
3. Cleary-Goldman J. Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, Luthy D, Gross S, Bianchi DW, D'Alton ME. Maternal thyroid hypofunction and pregnancy outcome. Obstet Gynecol 2008;112:85-92.
4. Yassa L, Marqusee E, Fawcett R, et al. Thyroid hormone early adjustment in pregnancy (the THERAPY) trial. J Clin Endocrinol Metab 2010; 95:3234-41. Epub May 12, 2010.
5. Abalovich M, Alcaraz G, Kleiman-Rubinsztein J, et al. The relationship of preconception thyrotropin levels to requirements for increasing the levothyroxine dose during pregnancy in women with primary hypothyroidism. Thyroid 2010;20:1175-8.
6. Calvo RM, Jauniaux E, Gulbis B, et al. Fetal tissues are exposed to biologically relevant free thyroxine concentrations during early phases of development. J Clin Endocrinol Metab 2002;87:1768-77.
7. Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011;21:1081-125. Epub July 25, 2011.
8. De Groot LJ, Abalovich M, Alexander E, et al. Endocrine Society guidelines on management of thyroid disease during pregnancy and postpartum. J Clin Endocrinol Metab. in press.
9. Committee on Patient Safety and Quality Improvement, Committee on Professional Liability. ACOG Committee Opinion No. 381: subclinical hypothyroidism in pregnancy. Obstet Gynecol 2007;110:959-60.
10. Lazarus JH, Bestwick JP, Channon S, et al. Antenatal thyroid screening and childhood cognitive function. N Engl J Med 2012;366:493-501.
11. Liu H, Momotani N, Noh JY, Ishikawa N, Takebe K, Ito K. Maternal hypothyroidism during early pregnancy and intellectual development of the progeny. Arch Intern Med 1994;154:785-7.
12. Momotani N, Iwama S, Momotani K. 2012 Neurodevelopment in children born to hypothyroid mothers restored to normal thyroxine (T_4) concentration by late pregnancy in Japan: no apparent influence of maternal T_4 deficiency. J Clin Endocrinol Metab 2012;97:1104-8. Epub February 8, 2012.

Clinical THYROIDOLOGY
AMERICAN THYROID ASSOCIATION FOUNDED 1923

Exposure to Methimazole during the First Trimester of Pregnancy Increases the Risk of Congenital Anomalies

Yoshihara A, Noh, J, Yamaguchi T, Ohye H, Sato S, Sekiya K, Kosuga Y, Suzuki M, Matsumoto M, Kunii Y, Watanabe N, Mukasa K, Ito K, Ito K. 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

Background

Several reports have suggested that propylthiouracil (PTU) may be safer than methimazole (MMI) for treating thyrotoxicosis during pregnancy because congenital malformations have been associated with the use of MMI during pregnancy. The authors investigated whether infants exposed in utero to antithyroid drugs had a higher rate of major malformations than infants born to a control group of pregnant women.

Methods

The authors reviewed the records of 6941 women with Graves' disease who became pregnant between January 1, 1999, and December 31, 2010; the pregnancy outcome of 6744 (97%) women was known. The diagnosis of Graves' disease was based on the clinical examination and laboratory data. There were 5967 live births, 30 perinatal losses, 657 miscarriages, and 90 abortions. All of the deliveries were attended by obstetricians. During each mother's first visit after delivery, a physician interviewed her about the congenital malformations diagnosed by the obstetricians. If a malformation was reported, the doctor corresponded with the gynecologist to determine whether there were any life-threatening anomalies in the fetus. The authors classified mothers and infants into three groups according to whether the mothers received treatment with MMI only, PTU only , or no medication (control group) in the first trimester of pregnancy (0 to 12 weeks' gestation). FT_4 was evaluated during the first trimester of pregnancy.

Results

During the first trimester of pregnancy, 1426 women were treated with MMI alone and 1578 with PTU alone; 2065 women received no medication and served as the control group. The remaining 1675 women had been treated with potassium iodide (394 women), levothyroxine (838), or more than one drug during the first trimester (443). Of the 2065 women in the control group, 1695 were in remission after treatment with antithyroid drugs for Graves' disease before their pregnancy, and the rest had received radioiodine ablation therapy. The mean (±SD) dose of MMI was 5.0±8.1 mg/day and PTU 100±113 mg/day. The overall rate of congenital malformation was 2.5% (152 of 5997 infants). The rate of malformed infants born to the women in the MMI 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 control group. The overall rate of major malformations in the MMI group was significantly higher than in the control group (P = 0.002, Fisher's exact test), but there was no increase in the overall rate of major anomalies in the PTU group as compared with the control group (P = 0.709). The dosage of the antithyroid drug did not differ significantly according to whether or not the mothers delivered a child with a congenital malformation. With multivariate logistic-regression analysis, the mothers treated with MMI during pregnancy had higher odds of giving birth to an infant with a congenital malformation (odds ratio [OR], 2.28; 95% confidence interval [CI], 1.54 to 3.33; P = 0.0002) than mothers who did not receive any medication for the treatment of Graves' disease. On the other hand, no increased risk of giving birth to an infant with a congenital malformation was found among the mothers treated with PTU (OR, 0.66; 95% CI, 0.41 to 1.03; P = 0.079). Aplasia cutis congenita, omphalocele, or omphalomesenteric duct anomaly were reported in

continued on next page

20/1231 babies from mothers being treated with MMI and in none from mothers treated with PTU or in those from the control group. Two mothers whose infants were born with an omphalocele took MMI up to 7 weeks' gestation, one mother switched to PTU and the other to potassium iodide. One mother who switched to PTU at 9 weeks' gestation delivered a baby with aplasia cutis congenita and omphalomesenteric anomaly. Multivariate analysis, which included maternal treatment during the first trimester of pregnancy, maternal thyroid status, and maternal age, showed that maternal thyroid status had no effect on the rate of giving birth to an infant with a congenital malformation (OR, 0.86; 95% CI, 0.63 to 1.1; P = 0.28).

Conclusions

Exposure to MMI during the first trimesterof pregnancy increased the risk of congenital anomalies, including the risk of the rare anomalies aplasia cutis congenita, omphalocele, and a symptomatic omphalomesenteric duct anomaly. It seems preferable to treat Graves' disease with PTU because it appears to be safer to use during the childbearing years; however, the reported risk of hepatotoxicity in both the mother and the child is a concern.

ANALYSIS AND COMMENTARY

For many years and without good scientific evidence, PTU was considered to be the drug of choice in the management of hyperthyroidism in pregnancy. Risk of a rare skin lesion, aplasia cutis congenita (1), and less maternal transplacental passage to the fetus favored PTU over MMI. However, studies comparing the two drugs showed an equal therapeutic response (2, 3). The overall incidence of congenital malformations due to MMI is very low, and some authors even suggested that poorly treated maternal hyperthyroidism could be the culprit for these abnormalities (4). Nevertheless, a specific methimazole embryopathy has been described, and reports with a few cases are published regularly. Recently, severe liver toxicity due to PTU administration, including hepatic coma, death, and the need for liver transplantation, has been revisited (5). The ATA (6) has strongly recommended limiting the use of PTU to special circumstances, such as thyroid storm, allergy to MMI, and the first trimester of pregnancy. Some physicians are reluctant to switch from MMI to PTU during early pregnancy and then back to MMI because of the potential difficulty of maintaining maternal euthyroidism, in view of the uncertainty of the equivalence in potency between PTU and MMI. Yoshihara et al. reported from Japan the largest series of pregnant women with hyperthyroidism who were exposed to either PTU or MMI in the first trimester of pregnancy and compared the rate of congenital malformations with a control group of euthyroid women with Graves' disease who were receiving no antithyroid drug therapy. This is an important study because in a 10-year period almost 6000 pregnant women from one institution were studied, and the investigators were able to obtain information on drug exposure and congenital anomalies in the offspring. Their results confirmed the reported specific anomalies in infants exposed to MMI in the first trimester of pregnancy; the reported high incidence of aplasia cutis congenita is of interest because some studies showed an incidence similar to that in the general population (7). The low incidence of choanal atresia and esophageal atresia (one infant) in their population is explained by the authors as the result of a low frequency of these anomalies in Japan. Another interesting observation is the lack of correlation between thyroid status in the first trimester of pregnancy and congenital abnormalities; this obser-

continued on next page

vation is pertinent because of a recent publication of neonatal dysplasia of the hip in infants born from mothers with hyperthyroidism, irrespective of the cause (8). In summary, Yoshihara et al. present strong evidence for using PTU as the antithyroid drug of choice in the first trimester of pregnancy.

— Jorge H. Mestman, MD

References

1. Mandel SJ, Brent GA, Larsen PR. Review of antithyroid drug use during pregnancy and report of a case of aplasia cutis. Thyroid 1994;4:129-33.
2. Wing DA, Millar LK, Koonings PP, Montoro MN, Mestman JH. A comparison of propylthiouracil versus methimazole in the treatment of hyperthyroidism in pregnancy. Am J Obstet Gynecol 1994;170:90-5.
3. Chattaway JM, Klepser TB. Propylthiouracil versus methimazole in treatment of Graves' disease during pregnancy. Ann Pharmacother 2007;41:1018-22. Epub May 15, 2007.
4. Barbero P, Valdez R, Rodríguez H, Tiscornia C, Mansilla E, Allons A, Coll S, Liascovich R. Choanal atresia associated with maternal hyperthyroidism treated with methimazole: a case-control study. Am J Med Genet A 2008;146A:2390-5.
5. Cooper DS, Rivkees SA. Putting propylthiouracil in perspective. J Clin Endocrinol Metab 2009;94:1881-2. Epub April 28, 2009.
6. Bahn R, Burch H, Cooper D, Garber J, Greenlee C, Klein IL. The role of propylthiouracil in the management of graves' disease in adults: report of a meeting jointly sponsored by the American Thyroid Association and the Food and Drug Administration. Thyroid 2009;19:673-4.
7. Van Dijke CP, Heydendael RJ, De Kleine MJ. Methimazole, carbimazole, and congenital skin defects. Ann Intern Med 1987;106:60-1.
8. Ishikawa N. The relationship between neonatal developmental dysplasia of the hip and maternal hyperthyroidism J Pediatr Orthop 2008;28:432-4.

Clinical THYROIDOLOGY
AMERICAN THYROID ASSOCIATION FOUNDED 1923

Several Forms of Renal Disease May Be Associated with Thyroid Autoimmune Disease

Kocak G, Huddam B, Azak A, Ortabozkoyun L, Duranay M. Coexistent findings of renal glomerular disease with Hashimoto's thyroiditis. Clin Endocrinol (Oxf) 2012;76:759-62.

SUMMARY

BACKGROUND

The coexistence of Hashimoto's thyroiditis and Graves' disease (1) with other autoimmune diseases (AID) is well established and possibly more frequent in adolescent and young adults than in later life (2). Furthermore, most textbooks mention the association with adrenal insufficiency, disseminated lupus, psoriasis, type 1 diabetes and other AID. Occasionally, the coexistence of thyroid AID with renal disease has been reported. Yet all these associations are rare events, perhaps with the exception of the association of type 1 diabetes with thyroid autoimmune disease. The present article reports on an unusually large series of cases of renal involvement in Hashimoto's thyroiditis.

METHODS AND RESULTS

From 2007 to 2011, 28 patients with Hashimoto's disease were referred to the department of nephrology in an Ankara hospital because of unexplained hematuria, proteinuria, or renal impairment. Patients with a history of kidney stones, systemic vasculitis, connective-tissue disease, or diabetes mellitus were excluded from the present study. Renal biopsies were performed in 20 patients. In 8 patients, the renal abnormalities were transient and did not need to be biopsied. The mean (±SD) age of patients was 46±17 years; 18 women and 10 men were affected. The glomerular filtration rate (GFR) was below 60 ml/min/1.73 m2 of body-surface area in 43% of the patients. Hematuria was found in 39% and proteinuria in 86%. Hypertension was present in 57% of patients. There was a significant difference in GFR between recent-onset Hashimoto's thyroiditis (<12 months) and long-standing disease. In early Hashimoto's thyroiditis, the mean GFR was 83 ml/min/1.73 m2, in long-standing disease 55 ml/min/1.73 m2. In 15 to 20% of the patients, renal biopsies showed either focal or membranous glomerulonephritis, immunoglobulin A nephritis, or minimal change disease. There was one case of amyloidosis. Most importantly, there was no correlation between renal function and thyroid antibodies (antithyroglobulin and or anti-TPO antibodies). Sixteen patients (57%) received either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Four patients did not receive antihypertensive treatment because of hypotension or absence of proteinuria. Nevertheless, in 7 of 20 patients, immunosuppressive therapy had to be introduced. The success of treatment was variable but within the frame of treatment responses observed in similar cases of renal diseases without Hashimoto's thyroiditis.

CONCLUSIONS

The study reported on 28 patients with concomitant Hashimoto's thyroiditis and renal glomerular disease. There was no association between thyroid antibody titer and renal function. This is a novel and important finding because so far only sporadic isolated cases have been described. The response of the glomerular disease to therapeutic interventions did not differ from that in patients without Hashimoto's thyroiditis. No data concerning a possible link between thyroid antibody immune complexes and glomerular disease are available. The authors do not comment on possible intrarenal immune complexes with antithyroglobulin or anti-TPO antigenicity. It is not clear whether they tested this possibility. Apparently, the treatments for the renal disease did not differ from those in patients without Hashimoto's thyroiditis.

continued on next page

ANALYSIS AND COMMENTARY

The association between Hashimoto's thyroiditis and renal glomerular disease was first recognized a few years ago. It is, however, most difficult to obtain quantitative information about the frequency of this association. Even the present article leaves this question open, since the patients were probably referred from many centers.

The value of this article lies in the large number of cases and in the facts that these were not adolescents or young adults and that there was no correlation between antibody titer and renal involvement. The latter point has to be interpreted cautiously, since antibody titers can fluctuate greatly over time. The finding that long-standing hypothyroidism was associated with more severe renal involvement may hint at a possible causal relationship. Despite the relatively large number of cases, little can be said about the therapeutic response, particularly since the data relating to the response is difficult to understand.

The clinician must realize that a causal relationship between renal disease and Hashimoto's thyroiditis is, at present, no more than an unproven hypothesis, since statistical proof is lacking. Nevertheless, it makes sense to follow the decrease of serum creatinine after starting thyroxine treatment in Hashimoto's thyroiditis, and particularly in cases of coexisting hypertension, to look for any form of renal disease.

— Albert G. Burger, MD

REFERENCES

1. Chakera A, Paul HJ, O'Callaghan CA. Reversible renal impairment caused by thyroid disease. Scand J Urol Nephrol 2010;44:190-2.
2. Agras PI, Kinik ST, Cengiz N, Baskin E, Saatci U. Autoimmune thyroiditis with associated proteinuria: report of two patients. J Pediatr Endocrinol Metab 2005;18:319-22.

Clinical THYROIDOLOGY
AMERICAN THYROID ASSOCIATION FOUNDED 1923

A 1.1 GBq (30 mCi) dose of ^{131}I Is Sufficient for Ablation in the Management of Low-Risk Thyroid Cancer

Schlumberger M, Catargi B, Borget I, Deandreis D, Zerdoud S, Bridji B, Bardet S, Leenhardt L, Bastie D, Schvartz C, Vera P, Morel O, Benisvy D, Bournaud C, Bonichon F, Dejax C, Toubert ME, Leboulleux S, Ricard M, Benhamou E; Tumeurs de la Thyroïde Refractaires Network for the Essai Stimulation Ablation Equivalence Trial. Strategies of radioiodine ablation in patients with low-risk thyroid cancer. N Engl J Med 2012;366:1663-73.

SUMMARY

Background

The optimal strategy for ablation of thyroid remnants after thyroidectomy for differentiated thyroid carcinoma is still debatable. The current paper is a French multicenter, randomized, controlled trial comparing four methods for ablation of thyroid remnants in patients with low-risk thyroid carcinoma who have tumors 1 to 4 cm or positive lymph nodes. Essentially, this is a comparison of 30 mCi (1.1 GBq) versus 100 mCi (3.7 GBq) for ablation in either the hypothyroid state or the euthyroid state facilitated by using rhTSH.

Methods

Each patient had total thyroidectomy. Lymph-node dissection was performed in those with evidence of lymph-node involvement and in some patients with no evidence of lymph-node involvement, depending on local practice Patients with aggressive histologic subtypes and those with posttherapy scans that showed disease outside the neck were excluded. The investigators enrolled 752 patients who were randomly assigned to one of the four treatment strategies: 1.1 GBq given with rhTSH, 3.7 GBq given with rhTSH, 1.1 GBq given during hypothyroidism, and 3.7 GBq given during hypothyroidism. Hypothyroidism was induced by withdrawal of levothyroxine for 28 days or triiodothyronine for 14 days.

The number of dropouts in each group was similar, and the number of patients who could be evaluated in each group varied from 166 to 177. The primary outcome was thyroid ablation assessed at 8 months after radioiodine ablation through the use of neck ultrasonography and determination of the level of rhTSH–stimulated serum thyroglobulin or a diagnostic ^{131}I total-body scan in patients with detectable antithyroglobulin antibody. The criteria for completeness were negative ultrasound, stimulated Tg <1 ng/ml, and negative radioiodine scan in those with positive antibody levels. Secondary outcomes were assessment of hypothyroidism and quality of life using quantitative scales. TNM staging was similar in the four groups. About 18% had positive nodes and another 12% had tumors larger than 2 cm.

Results

Thyroid ablation was considered complete in 92% of the 684 patients. There was no difference in the rates of complete ablation among the four groups.

In regard to secondary outcomes, thyroid hormone withdrawal at the time of ablation was associated with symptoms of hypothyroidism and a poorer quality of life, but there was no difference in these assessments between the groups when analyzed 3 months after ablation when all patients were taking levothyroxine.

Conclusions

The use of a low dose, 1.1 GBq (30 mCi) ^{131}I, is probably sufficient for ablation in the management of low-risk thyroid cancer.

continued on next page

A 1.1 GBq (30 mCi) dose of ^{131}I Is Sufficient for Ablation in the Management of Low-Risk Thyroid Cancer

ANALYSIS AND COMMENTARY

This excellent study shows that 30 mCi ^{131}I is as successful as 100 mCi for ablation of residual thyroid tissue. A major factor that contributes to the success of the low dose is the surgical procedure of complete thyroidectomy. This could account for the higher ablation rate of 92% in this study as compared with lower rate of approximately 80% in older studies (1).

Not surprisingly, hypothyroid symptoms and reduced quality of life occurred in the hypothyroid state, as previously reported (2), but these were reversible with levothyroxine therapy. After preparation with rhTSH, 58.5% had serum Tg ≤1 ng/ml; after thyroid hormone withdrawal, only 38% had Tg ≤1 ng/ml. This finding suggests to me that the stimulatory effect of thyroid hormone withdrawal on residual thyroid cells is much more potent than that of rhTSH, suggesting that there is an advantage to the therapy after withdrawal of thyroid hormone. This must be balanced against the disadvantage of more radiation toxicity related to a higher total body dose for similar ^{131}I doses in patients prepared with thyroid hormone withdrawal as compared with rhTSH (3,4).

Unfortunately the paper does not state whether patients were on a low-iodine diet, a practice that is followed routinely in the United States.

— Jerome M. Hershman, MD

References

1. Hackshaw A, Harmer C, Mallick U, Haq M, Franklyn JA. ^{131}I activity for remnant ablation in patients with differentiated thyroid cancer: a systematic review. J Clin Endocrinol Metab 2007;92:28-38. Epub October 10, 2006.
2. Schroeder PR, Haugen BR, Pacini F, et al. A comparison of short-term changes in health-related quality of life in thyroid carcinoma patients undergoing diagnostic evaluation with recombinant human thyrotropin compared with thyroid hormone withdrawal. J Clin Endocrinol Metab 2006;91:878-84. Epub January 4, 2006.
3. Rosario PW, Borges MA, Purisch S. Preparation with recombinant human thyroid-stimulating hormone for thyroid remnant ablation with ^{131}I is associated with lowered radiotoxicity. J Nucl Med 2008;49:1776-82. Epub October 16, 2008.
4. Hanscheid H, Lassmann M, Luster M, et al. Iodine biokinetics and dosimetry in radioiodine therapy of thyroid cancer: procedures and results of a prospective international controlled study of ablation after rhTSH or hormone withdrawal. J Nucl Med 2006;47:648-54.

Clinical THYROIDOLOGY
AMERICAN THYROID ASSOCIATION FOUNDED 1923

Core Needle Biopsy Is Useful for Diagnosis of Thyroid Nodules after Previous FNA Biopsy was Nondiagnostic

Samir AE, Vij A, Seale MK, Desai G, Halpern E, Faquin WC, Parangi S, Hahn PF, Daniels GH. Ultrasound-guided percutaneous thyroid nodule core biopsy: clinical utility in patients with prior nondiagnostic fine-needle aspirate. Thyroid 2012;22:461-7. Epub February 3, 2012.

SUMMARY

Background

Ultrasound-guided FNA of thyroid nodules is nondiagnostic in 5 to 20% of cases, resulting in uncertainty about the presence of malignancy. Core needle biopsies have been used in other areas, but have not been recommended for thyroid nodules that are nondiagnostic on FNA. The current study explores the clinical utility of combined ultrasound-guided thyroid FNA and core needle biopsy (CB) in patients with prior nondiagnostic FNA.

Methods

Records were reviewed for all patients who had combined FNA and CB from 2006 through 2008 at Massachusetts General Hospital. During this 3-year period, 762 (14%) of FNAs were nondiagnostic. Ninety combined FNAs and CBs were performed in 82 patients with nondiagnostic FNAs. The procedures were performed by staff interventional radiologists. For FNA, 25-gauge needles were used. For CB, 20-gauge 6-cm needles with 10- or 20-mm needle throw were used. Preparation included the administration of 5 to 10 ml of subcutaneous and perithyroidal lidocaine. Four to 6 FNAs and 2 to 4 CBs were performed on each nodule. CB samples were placed in formalin and then embedded into paraffin blocks and cut into 5-mm sections.

Results

Nodules ranged in maximal dimension from 0.6 to 4.4 cm, with a mean of 2 cm, but only three nodules were less than 1 cm. There were no reported complications.

The combined procedure yielded a diagnostic result in 87% of the 90 nodules. Both FNA and CB were diagnostic in 37% of nodules; in 40% of nodules, CB was diagnostic when FNA was not; in 10% of nodules, FNA was diagnostic when CB was not. For the combined procedure, the diagnosis was benign in 40%, follicular lesion of undetermined significance in 10%, follicular neoplasm in 31%, suspicious for malignancy or malignant in 5.5% (all of these were determined to be malignant as judged by surgical pathology), and nondiagnostic in 13%.

Twenty-two of the 28 patients with the diagnosis of follicular neoplasm underwent surgery; 2 were malignant, 18 were benign follicular adenomas, and 2 were nodular Hashimoto's thyroiditis. Of the 13% of patients who had nondiagnostic pathology with the combined procedure, 5 had surgery and had benign pathology; the others had stable nodule size on follow-up.

Conclusions

Combined FNA and CB of thyroid nodules is safe and clinically useful in selected patients when a prior FNA reading is nondiagnostic; it should be considered as an alternative to surgery in patients with two prior nondiagnostic FNAs.

continued on next page

ANALYSIS AND COMMENTARY

Core needle biopsy of palpable thyroid nodules was performed in the 1950s and 1960s, usually by trained thyroid surgeons, because of the fear of bleeding complications if a large vessel was lacerated (1). The procedure was not adopted by endocrinologists and was fortunately supplanted by FNA in the 1970s. Refinement of the needles to smaller diameters and the use of ultrasound guidance has now made CB more feasible. Potential advantages of CB are that it can provide more tissue and preserve the cellular architecture. Interventional radiologists have the most experience with CB and performed the procedure in this study. Aside from its technical difficulty, CB has not been widely used because earlier comparative studies of FNA and CB showed no diagnostic advantage for CB (2,3).

In the same issue of Thyroid, a paper from a group in Korea compared the use of CB and FNA for evaluation of 149 nodules that were nondiagnostic or follicular lesion of undetermined significance (FLUS) (4). They used an 18-gauge spring-activated needle and lidocaine anesthesia. They reported that the diagnostic sensitivity of CB was higher than that of FNA in the FLUS category, but this was not statistically significant in the 45 patients who had prior nondiagnostic FNA. They noted no major complications of CB, but there were perithyroidal hematomas in 3.6% and mild transient parenchymal edema in 2.3%. They concluded that CB is more useful than repeat FNA in patients with inconclusive diagnostic results.

The pendulum seems to be swinging back to reconsideration of core biopsy for patients with inconclusive diagnostic results. However, the decision to use CB must be based on multiple factors: the suspicion of malignancy on ultrasound and other clinical features, the availability of expertise in performing CB of thyroid nodules, the need to discontinue anticoagulation, and the potential benefit to the patient.

— Jerome M. Hershman, MD

References

1. Wang C, Vickery AL Jr, Maloof F. Needle biopsy of the thyroid. Surg Gynecol Obstet 1976;143:365-8.
2. Silverman JF, West RL, Finley JL, Larkin EW, Park HK, Swanson MS, Fore WW. Fine-needle aspiration versus large-needle biopsy or cutting biopsy in evaluation of thyroid nodules. Diagn Cytopathol 1986;2:25-30.
3. Khoo TK, Baker CH, Hallanger-Johnson J, Tom AM, Grant CS, Reading CC, Sebo TJ, Morris JC 3rd. Comparison of ultrasound-guided fine-needle aspiration biopsy with core-needle biopsy in the evaluation of thyroid nodules. Endocr Pract 2008;14:426-31.
4. Na DG, Kim JH, Sung JY, Baek JH, Jung KC, Lee H, Yoo H. Core-needle biopsy is more useful than repeat fine-needle aspiration in thyroid nodules read as nondiagnostic or atypia of undetermined significance by the Bethesda system for reporting thyroid cytopathology. Thyroid 2012;22:468-75.

Clinical THYROIDOLOGY
AMERICAN THYROID ASSOCIATION FOUNDED 1923

More Foci of Thyroid Cancer Metastases Are Identified by Thyroid Hormone Withdrawal than by Use of Recombinant Human TSH

Van Nostrand D, Khorjekar GR, O'Neil J, Moreau S, Atkins FB, Kharazi P, Mete M, Chennupati SP, Burman KD, Wartofsky L. 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 ^{124}I PET. J Nucl Med. 2012;53:359-62. Epub February 7, 2012.

SUMMARY

Background

Recombinant human TSH is approved for diagnostic studies of recurrent thyroid cancer and for preparation for radioiodine ablation of thyroid remnants after thyroidectomy. In some patients with metastatic disease, it has been used as preparation for therapy with ^{131}I, but there have been no studies of its efficacy compared with that of thyroid hormone withdrawal in a substantial number of patients. The purpose of this study was to compare these two methods of preparation for detection of metastatic foci in patients with a high suspicion of metastatic differentiated thyroid cancer (DTC).

Methods

During the period 2006–2010, patients at the Washington Hospital Center who had high suspicion of recurrent or metastatic DTC, based on an enlarging mass or elevated serum Tg, who were candidates for ^{131}I therapy were prepared with either thyroid hormone withdrawal (THW) or two injections of 0.9 mg rhTSH. Patients were eating low-iodine diets for 2 weeks, including the time of testing. All patients underwent ^{131}I whole-body scans 48 hours after receiving 2 mCi ^{131}I and ^{124}I PET/CT scans 48 hours after receiving 1.7 mCi ^{124}I. All foci of uptake were categorized by two physicians as physiologic uptake, artifact, or positive for functioning metastases.

Results

Forty patients were evaluated; 24 were prepared with rhTSH and 16 with THW. The mean age, serum Tg, type of cancer, and previous ^{131}I doses (usually 2) and total gigabecquerels of ^{131}I did not differ between the two groups. One of 24 patients (4%) had positive foci detected on rhTSH ^{131}I scans, and 10 of 16 (63%) had positive foci detected on THW ^{131}I scans ($P<0.02$). The number of positive foci detected on the rhTSH ^{131}I and THW ^{131}I scans were 2 and 58, respectively ($P<0.05$). Seven of 24 patients (29%) had positive foci detected on rhTSH ^{124}I scans, and 10 of 16 (63%) had positive foci detected on THW ^{124}I scans ($P<0.03$). The number of positive foci detected on the rhTSH ^{124}I and THW ^{124}I scans were 17 and 117, respectively ($P<0.03$).

Conclusions

Significantly more foci of DTC metastases can be identified in patients prepared with THW than in patients prepared with rhTSH.

ANALYSIS AND COMMENTARY

This study corroborates the concept that more sustained elevation of serum TSH is necessary to activate the uptake of radioiodine in DTC tissue as compared with the amount of TSH needed for activating normal thyroid tissue. Although the levels of elevated TSH after injection of recombinant TSH are substantial and persist for several days, the pharmacodynamic area under the TSH curve is likely to be much less than that achieved after withdrawal of thyroid hormone for 2 weeks in the case of T_3 or 4 to 6 six weeks in the case of T_4 withdrawal. Aside

continued on next page

from economic considerations, it would be preferable to use rhTSH in order to avoid symptomatic hypothyroidism. However, this is worthwhile only if the stimulation of rhTSH is effective for activation of thyroid uptake in metastatic tissue. By two methods, this study showed that rhTSH is much less effective than thyroid hormone withdrawal. In a study of lesion dosimetry using ^{123}I in 4 patients with metastatic DTC, Pötzi et al reported that all patients had lesser uptake of ^{123}I under rhTSH stimulation than after hormone withdrawal (1), in agreement with the results of this study.

One criticism of the study is that it was not randomized, although demographic and clinical data in the two groups were very similar. Another criticism is that a tracer dose larger than 2 mCi might have been more effective in showing positive foci with the rhTSH preparation. One could also criticize it because there were no outcome data with regard to the efficacy of radioiodine therapy for elimination of metastases. However, uptake of tracer radioiodine is essential to determine the need for subsequent ^{131}I therapeutic doses.

The study reinforces my practice of using thyroid hormone withdrawal, rather than rhTSH, for preparation for radioiodine scans when there is a strong suspicion of recurrent disease; the withdrawal also prepares the patient for the therapeutic dose.

— Jerome M. Hershman, MD

Reference

1. Pötzi C, Moameni A, Karanikas G, et al. Comparison of iodine uptake in tumour and nontumour tissue under thyroid hormone deprivation and with recombinant human thyrotropin in thyroid cancer patients. Clin Endocrinol (Oxf) 2006;65:519-23.

Clinical THYROIDOLOGY
AMERICAN THYROID ASSOCIATION FOUNDED 1923

Stimulating the Uptake of ^{131}I in Multinodular Goiter by Pretreatment with Recombinant Human TSH Improves Patient Outcomes at 5 Years

Fast S, Nielsen VE, Grupe P, Boel-Jørgensen H, Bastholt J, Andersen PB, Bonnema SJ, Hegedüs L. Prestimulation with recombinant human thyrotropin (rhTSH) improves the long-term outcome of radioiodine therapy for multinodular nontoxic goiter. J Clin Endocrinol Metab. May 10, 2012 [Epub ahead of print]. doi:10.1210/jc.2011-3335.

SUMMARY

BACKGROUND

If obstructive signs or symptoms develop in a patient with multinodular goiter (MNG)—and the surgical risk is deemed acceptable—surgery at a major referral hospital is the treatment of choice (hyperthyroidism, if present, is usually treated first). If surgery is not feasible, ^{131}I can be given to reduce goiter size somewhat, although it initially may cause thyroid swelling and increase the release of thyroid hormone, potentially significant side effects. If the goiter is very large or its uptake is low, large doses of ^{131}I may be required, increasing whole-body radiation and possibly involving the expense of hospitalization. To try to enhance the effectiveness of ^{131}I, a number of centers have tried recombinant human TSH (rhTSH) on an experimental basis. It is given a day before ^{131}I treatment, which increases the uptake of ^{131}I in areas of the gland where uptake is low, makes the radiation more uniform, and increases the retention of ^{131}I in the thyroid. It also increases long-term hypothyroidism. The current paper reports 5-year outcome data from two previously published randomized, double-blind, placebo-controlled studies on selected patients with MNG from an area of Denmark where iodine intake is moderately deficient (1,2).

METHODS

One of the two earlier papers addressed the effects of rhTSH on patients with goiters <100 ml (measured by ultrasound), while the other paper focused on patients with goiters >100 ml (by MRI). Half the patients in both studies received an injection of 0.3 mg of rhTSH 24 hours before ^{131}I was given, while the other half received a placebo injection. The inclusion and exclusion criteria between the two studies differed substantially, as did the ^{131}I doses given. In the first study (1), out of 712 consecutive patents seen from 2002 to 2004 who had "nontoxic" MNG, 57 patients met a variety of inclusion criteria, including having an ^{131}I uptake of 20% or greater, whereas 99 patients with uptakes less than 20% were excluded. Almost half the patients in this study were subclinically hyperthyroid (TSH <0.1 mU/ml). The ^{131}I dose was calculated based on the estimated thyroid volume and the effective ^{131}I half-life: the median dose was 14 mCi in the placebo group and 15.7 mCi in the rhTSH group (the highest dose permitted was 16.2 mCi). After 1 year, the goiters in the placebo group had shrunk by 46%, while those in the rhTSH group had shrunk by 62% (P<0.002). The incidence of hypothyroidism was 5 times greater in the latter patients, who also had 3 times as many adverse events, especially transient hyperthyroidism and cervical discomfort or pain. In the second study, 29 patients with very large nodular goiters who could not or would not undergo surgery were studied (2). Five of the patients had frank hyperthyroidism and were given methimazole until 8 days before the ^{131}I treatment. The patients' mean baseline 24-hour ^{131}I uptake was about 35%, and the mean TSH was about 0.2 mU/L. The median ^{131}I treatment dose was 41 mCi in the placebo group and was 37 mCi in the rhTSH group. (Two patients in the latter group had their ^{131}I doses restricted to 100 mCi.) After 1 year, the goiters in the placebo group had shrunk from

continued on next page

170 ml to 121 ml, while those in the rhTSH group had shrunk from 151 ml to 72 ml. Two patients given rhTSH required 25 mg of prednisolone for thyroid swelling and tenderness, and one was admitted to the hospital for stridor. Only 2 of 14 in the rhTSH group had no adverse events, whereas 7 of 15 in the placebo group had no adverse events. Hypothyroidism had developed in 1 of 15 patients given placebo and in 3 of 14 patients given rhTSH.

RESULTS

Follow-up data were available on 80 of the 86 patients from the two studies. When the data were combined, the placebo groups' goiters had shrunk another 13% and the rhTSH groups' goiters had shrunk another 10% after 5 years. "Treatment failures" (cases in which patients required subsequent thyroid surgery or additional ^{131}I treatment) were twice as common in the patients with the large goiters as in those with goiters <100 ml. In the combined placebo groups, 20% (9 of 44) needed additional treatment (surgery in 6, and additional ^{131}I in 3), whereas in the rhTSH groups, only 5% (2 of 42) needed surgery (P<0.02). Since more of the patients receiving placebo needed additional therapy, their mean follow-up period was slightly shorter (65 months) than that for the rhTSH groups (73 months). On a yes/no question concerning overall satisfaction with the initial therapy: 90% of those who had been given rhTSH and 69% of those given placebo answered "yes"(P = 0.025).

CONCLUSIONS

Five years after treating two highly selected groups of patients with ^{131}I, patients with MNG who were also given rhTSH had fewer goiter-related symptoms, fewer of them needed additional therapy, and their satisfaction with the initial therapy was higher. The goiter shrinkage remained superior, but the incidence of hypothyroidism was much greater in those who received rhTSH.

ANALYSIS AND COMMENTARY

The title of the article indicates that only patients with "nontoxic" MNGs were studied, but many patients had subclinical or frank hyperthyroidism. All the patients had a basal ^{131}I uptake of 20% or greater, so their autonomous nodules probably were more active than those in patients with a lower ^{131}I uptake. However, there are many patients with MNG with a ^{131}I uptake less than 20%, so it would be interesting to know whether such patients would also respond to rhTSH in this Danish population. Although the data do not address that question directly, several recent smaller studies from Brazil—where iodine intake from 1998 to 2003 was excessive—obtained similar results. These studies used substantially lower doses of rhTSH (≤0.1 mg), and the patients' ^{131}I uptakes were below 20%, even after being on low-iodine diets. A study of 28 patients with MNG (average volume >100 ml by helical CT) who had subclinical hyperthyroidism were treated with methimazole for 3 months (3). The methimazole was discontinued 2 weeks before measuring the basal RAI uptake (which generally remained under 20%), and methimazole was discontinued again for 2 weeks preceding the dose of 30 mCi ^{131}I. The decrease in thyroid volume was about 40% at 2 years, as compared with a 15% decrease (statistically insignificant) in patients receiving placebo. A different study on 22 patients with MNG who were euthyroid (none with basal TSH levels below 0.21 mU/ml), who ate a low-iodine diet for 2 weeks before getting 30 mCi ^{131}I, obtained similar results (4). After 1 year, the goiters had shrunk almost 40%, either with a dose of 0.01 mg or 0.1 mg of rhTSH.

Overall, giving rhTSH to patients with MNG seems to double the 24-hour uptake of ^{131}I, regardless of whether the rhTSH dose is 0.01 mg or 0.9 mg. In

continued on next page

contrast, both thyroid swelling and thyroid-hormone levels increase as the rhTSH dose increases from 0.1 mg to 0.9 mg in normal subjects (5). Indeed, a more recent study from the same Danish group did use a lower dose of rhTSH (0.1 mg) and showed that it enhances the efficacy of ^{131}I in shrinking goiters more than threefold (6). Given that there is continuing restriction in the availability of rhTSH, and recognizing that it is about 10,000 times more valuable than gold, it would seem appropriate on both clinical and financial grounds to use a smaller dose than the 0.3 mg used in the pair of studies analyzed by the current study. A recent study showed that if rhTSH is reconstituted in PBS containing BSA, its in vitro biologic activity is stable for at least 6 months (7).

It is also worth noting that several other ways to increase the ^{131}I uptake/retention in MNG have been reported. These include: (1) pretreating patients with methimazole to raise TSH levels, then discontinuing the methimazole before the ^{131}I treatment, as mentioned above; (2) giving lithium before and after ^{131}I (8,9); and (3) giving nonradioactive ^{127}I after ^{131}I treatment (10).

— Stephen W. Spaulding, MD

REFERENCES

1. Nielsen VE, Bonnema SJ, Boel-Jørgensen H, Grupe P, Hegedüs L. Stimulation with 0.3-mg recombinant human thyrotropin prior to iodine 131 therapy to improve the size reduction of benign nontoxic nodular goiter: a prospective randomized double-blind trial. Arch Intern Med 2006;166:1476-82.
2. Bonnema SJ, Nielsen VE, Boel-Jørgensen H, Grupe P, Andersen PB, Bastholt J, Hegedüs L. Improvement of goiter volume reduction after 0.3 mg recombinant human thyrotropin-stimulated radioiodine therapy in patients with a very large goiter: a double-blinded, randomized trial. J Clin Endocrinol Metab 2007;92:3424-8. Epub June 12, 2007.
3. Cubas ER, Paz-Filho GJ, Olandoski M, Goedert CA, Woellner LC, Carvalho GA, Graf H. Recombinant human TSH increases the efficacy of a fixed activity of radioiodine for treatment of multinodular goitre. Int J Clin Pract 2009;63:583-90. Epub September 18, 2008.
4. Albino CC, Graf H, Paz-Filho G, Diehl LA, Olandoski M, Sabbag A, Buchpiguel C. Radioiodine plus recombinant human thyrotropin do not cause acute airway compression and are effective in reducing multinodular goiter. Braz J Med Biol Res 2010;43:303-9.
5. Fast S, Nielsen VE, Bonnema SJ, Hegedüs L. Dose-dependent acute effects of recombinant human TSH (rhTSH) on thyroid size and function: comparison of 0.1, 0.3 and 0.9 mg of rhTSH. Clin Endocrinol (Oxf) 2010;72:411-6. Epub June 8, 2009.
6. Fast S, Hegedüs L, Grupe P, Nielsen VE, Bluhme C, Bastholt L, Bonnema SJ. Recombinant human thyrotropin-stimulated radioiodine therapy of nodular goiter allows major reduction of the radiation burden with retained efficacy. J Clin Endocrinol Metab 2010;95:3719-25. Epub June 2, 2010.
7. Lin R, Hogen V, Cannon S, Marion KM, Fenton MS, Hershman JM. Stability of recombinant human thyrotropin potency based on bioassay in FRTL-5 cells. Thyroid 2010;20:1139-43.
8. Płazińska MT, Królicki L, Bąk M. Lithium carbonate pre-treatment in 131-I therapy of hyperthyroidism. Nucl Med Rev Cent East Eur 2011;14: 3-8.

continued on next page

9. Martin NM, Patel M, Nijher GM, Misra S, Murphy E, Meeran K. Adjuvant lithium improves the efficacy of radioactive iodine treatment in Graves' and toxic nodular disease. Clin Endocrinol (Oxf). March 24, 2012 [E-pub ahead of print]. doi:10.1111/j.1365-2265.2012.04385.x.

10. Rogowski F, Abdelrazek S, Szumowski P, Zonenberg A, Parfienczyk A, Sawicka A. The influence of non-radioactive iodine (^{127}I) on the outcome of radioiodine (^{131}I) therapy in patients with Graves' disease and toxic nodular goitre. Nucl Med Rev Cent East Eur 2011;14:9-15.

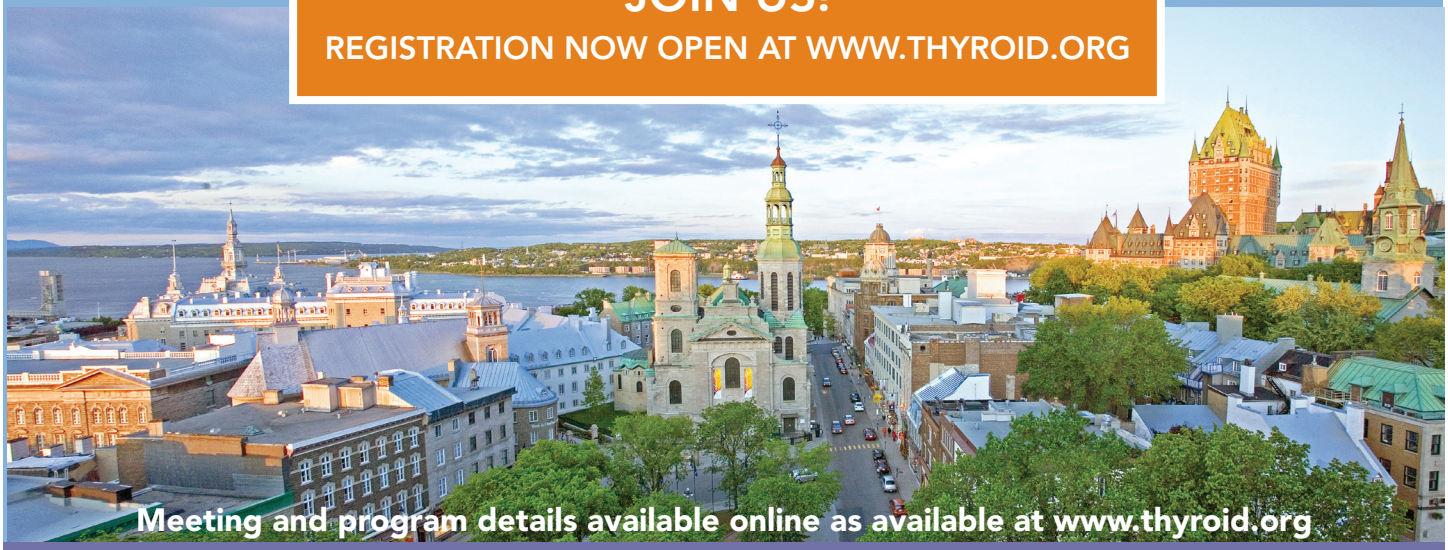
82nd Annual Meeting of the American Thyroid Association

SEPTEMBER 19-23, 2012

Hilton Québec and the QC Convention Centre Québec City, Canada

JOIN US!

REGISTRATION NOW OPEN AT WWW.THYROID.ORG



You Are Invited to the 82nd Annual Meeting of the ATA! All Those Interested in the Thyroid:

Endocrinologists, internists, surgeons, basic scientists, nuclear medicine scientists, pathologists, fellows, nurses, and other health care professionals who wish to broaden and update their knowledge of the thyroid gland and related disorders are invited to attend. Endocrine and surgical fellows will have a customized educational track to enhance their meeting experience.

The American Thyroid Association (ATA) is the leading worldwide organization dedicated to the advancement, understanding, prevention, diagnosis and treatment of thyroid disorders and thyroid cancer. Attend the meeting and earn CME credits, hear innovative talks on clinical and basic science topics, participate in interactive sessions, develop professionally with state of the art information, and renew collegial friendships.

Exhibitor and sponsorship/advertising opportunities available at www.thyroid.org.

AMERICAN THYROID ASSOCIATION®
FOUNDED 1923

American Thyroid Association – *Dedicated to scientific inquiry, clinical excellence, public service, education and collaboration.*

IMPORTANT MEETING DEADLINES:

- ☆ Regular Call Abstract Site Opens – March 7, 2012
- ☆ Regular Call Abstract Site Closes – May 30, 2012
- ☆ Regular Call Acceptance Notification – June 27, 2012
- ☆ Early Bird Registration Deadline: July 1, 2012
- ☆ Fellows Grant Application Deadline: July 12, 2012
- ☆ Short Call Abstract site Opens – July 25, 2012
- ☆ Fellows Grant Application Acceptance Notification: on or about July 25, 2012
- ☆ Short Call Abstract Site Closes – August 8, 2012
- ☆ Short Call Abstract Acceptance Notification – August 15, 2012
- ☆ Discount Registration Deadline: August 20, 2012
- ☆ Hotel Rooming Block Reservation Deadline: August 24, 2012

We look forward to seeing you in Québec City!

www.thyroid.org

American Thyroid Association
Short Call for Abstracts

www.thyroid.org

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

Call for Abstracts Submission Deadlines

- Short call: Site opens – Wednesday, July 25, 2012
  Site closes – Wednesday, August 8, 2012
  Acceptance notification – Wednesday, August 15, 2012

Short Call Abstracts

- Short Call Abstracts are reserved for the presentation of the very latest, important thyroid-related research with high impact. Submission of a Short Call Abstract does not guarantee acceptance for presentation. (Please note that regular research reports should be submitted by the Regular Abstract deadline.)
- Only Six (6) Short Call Abstracts will be selected for 10-minute oral presentations during a special symposium. All other submissions will not be published.
- Acceptance notices for those selected will be e-mailed on or before August 15, 2012. Online confirmation is required.

ATA Abstract Submission Policy and Responsibilities of the Author: The ATA requests submission of abstracts for consideration at ATA scientific meetings to feature new data presented as posters or oral presentations. The ATA goal is to provide the audience and the media with new data that are unpublished (in print or electronic) which are being publicly presented for the first time. Authors are asked to strictly comply with this requirement; data that are to become available to the public ***in the setting of a national or international meeting*** before their presentation at the ATA meeting are not eligible for presentation at the ATA meeting. Data may be submitted for publication before or after abstract submission to the ATA. However, data accepted for publication prior to the ATA meeting would REQUIRE the authors to request the publisher to embargo their publication (electronic and print) until ***8:00 am local time the first day of the meeting***, or would REQUIRE the authors to withdraw their abstract from the ATA meeting. Many editors are favorable to embargo requests because of the attention that may be drawn to the publication after original presentation of the data at a major meeting. Further, the authors are welcome to announce the date and place of their anticipated publication if known. Authors that do not comply with this policy may be restricted from future abstract submissions for a term to be determined by the ATA Executive Committee. Arbitration, if needed, will occur via the ATA Board of Directors. **Abstracts are reviewed in confidence by the ATA program committee with possible ad hoc members.**

Additional policies:

- **CHARACTER LIMIT:** There is a limit of 2,245 characters (approx. 300 words) for the text of your submission.
- Scientific materials presented at the ATA Annual Meeting must not have been submitted for publication at the time of abstract submission or presented at a scientific meeting before the 82nd Annual Meeting of the ATA (local and regional meetings excluded).
- All abstracts must be filed electronically via the American Thyroid Association website *www.thyroid.org*. Submissions will not be accepted by fax or mail.
- All materials must arrive on or before the abstract deadlines noted above.
- Authorship on multiple abstracts is permitted.

Stay Informed About Thyroid Disease — Become a Friend of the ATA

Let your patients know that they can become Friends of the ATA by signing up to get the latest thyroid health information and to be among the first to know the latest cutting-edge thyroid research of importance to patients, their families and the public.

As a Friend of the ATA we will send you:

- *Clinical Thyroidology for Patients* -- This publication is a collection of summaries of recently published articles from the medical literature covering the broad spectrum of thyroid disorders.
- The Calendar of Events highlights educational forums and support groups that are organized by members of the Alliance for Thyroid Patient Education. The Alliance member groups consist of: the *American Thyroid Association,* the *Graves' Disease Foundation,* the *Light of Life Foundation* and *ThyCa: Thyroid Cancer Survivors' Association, Inc*.
- *Friends of the ATA e-news*, providing up-to-date information on thyroid issues, answers to thyroid questions from leading thyroid experts, 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 for patients and the public.

AMERICAN THYROID ASSOCIATION® FOUNDED 1923

The American Thyroid Association (ATA) is a nonprofit medical society composed of physicians and scientists who specialize in the research and treatment of thyroid diseases. Dedicated to improving the lives of the millions of Americans of all ages living with thyroid problems, we are strongly committed to serving as a resource for these patients and the public and to promoting the prevention, treatment, and cure of thyroid-related diseases.

With extensive online resources for thyroid patients, families, and the general public at *www.thyroid.org*, each year we reach thousands of people who have come to rely on us for health information they can trust.

- Answers to frequently asked questions, or FAQs;
- Brochures on specific thyroid diseases;
- A database of ATA members called "Find a Thyroid Specialist";
- A toll-free telephone number with referrals to patient education materials and support groups; and
- Links to the ATA Alliance for Patient Education: organizations that provide support for understanding and coping with thyroid disease and its treatments.

Visit *www.thyroid.org* and become a *Friend of the ATA*.