ATA Signal

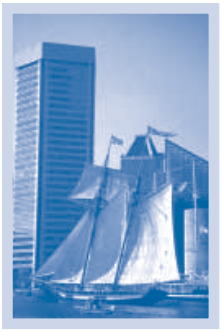
AMERICAN THYROID ASSOCIATION
FOUNDED 1923

VOLUME 8 NO. 1, JANUARY 2005

THE NEWSLETTER OF THE AMERICAN THYROID ASSOCIATION

Thyroid Cancer Is Focus of ATA Spring Meeting in Baltimore

Thyroid cancer will be the focus of the ATA's spring meeting in Baltimore, April 14–17, 2005. **Frontiers in Thyroid Cancer 2005: Clinical Care and Research for the Future** will feature U.S. and international thyroid cancer experts, who will examine important developments in pathogenesis, screening, diagnosis, and treatment.



"The American Thyroid Association is shining a spotlight on thyroid cancer in 2005. In addition to this exciting conference, the ATA will be releasing new thyroid cancer guidelines at the meeting, The topic of thyroid cancer is particularly timely because of heightened public interest due to the unfortunate afflictions of Chief Justice Rehnquist and several athletes and celebrities with thyroid cancer," said James Fagin, MD, meeting co-chair.

The meeting will feature two keynote speakers: Bert Vogelstein, MD, Clayton Professor of Oncology and Professor of Pathology at the Johns Hopkins University School of

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ATA and Sawin Family Establish Clark T. Sawin History Resource Center

The American Thyroid Association is pleased to announce a major endowment to continue the work of Clark T. Sawin, MD, of incorporating a historical perspective into current thyroid disease research, diagnosis and treatment.

Dr. Sawin felt strongly that current practice in treating thyroid disease could be enriched with an understanding of the history of scientific development and practice patterns in the past. Out of this belief, approximately 15 years ago, he developed the concept of historical vignettes as a part of the programming at the ATA Annual Meeting. His enthusiasm, breadth of historical knowledge, and skill as a presenter ensured that his vignettes were well received — becoming a valued portion of the ATA Annual Meeting program.

Leslie Sawin announces the new Sawin Endowment.

Dr. Sawin's family is committed to continuing his historical work

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Important ATA Member Notices

- **Register for Frontiers in Thyroid Cancer 2005, the spring meeting of the ATA (page 13)**
- **Call for nominations for 2005–2006 officers (page 19) and 2005 awards (page 19)**
- **Apply for 2005 Thyroid Research Grants — see page 19.**

President's Message

Our society is in excellent shape, with greatly expanded programs, a more influential voice, growing membership, and sound finances. These successes arise from voluntary commitments of our committees, councilors, and officers, especially Secretary Greg Brent. Our October meeting in Vancouver was widely acknowledged to have been

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Secretary's Report

The Vancouver meeting was a spectacular success with stimulating science, collegiality, and an inspiring venue. Many expressed the hope that we can return to Vancouver for a future meeting. Our program co-chairs, Mary Samuels and Jim Baker, put together an innovative and stimulating program that highlighted the latest in basic and clinical thyroid research. The pre-meeting endocrinology fellows conference, organized and directed by Chip Ridgway, again brought in fellows from across the country for an outstanding program. Many fellows who came to the conference stayed on to attend our Annual Meeting.

An AACE-sponsored ultrasound course and the public education forum conducted by members of the ATA Alliance for Thyroid Patient Education rounded out a broad range of pre-meeting activities. Abstract submissions increased in number and quality, and meeting attendance, including international colleagues, was excellent. We all greatly appreciated Leslie Sawin's participation in the meeting as we honored Clark's many contributions to the ATA. Jerry Hershman presented a moving remembrance of Clark's career, including quotes contributed by his colleagues. Leslie announced a generous endowment to establish an ATA history program in honor of Clark that is described in detail in this *Signal*.

"...This organization is not stagnant but is aggressive and always seeking to improve upon the known and the tried."

Many have worked hard through the years to expand and diversify our membership. Virginia Sarapura, who first chaired the membership committee when Marty Surks was secretary, worked with Marty at that time to simplify the membership application process and create the Associate category for fellows. Virginia has returned as membership chair and welcomed a record number of new members this year. It is our first group with near equal numbers of men and women and several new members from under-represented disciplines.

This change in our new members has paralleled the organization of Women in Thyroidology. This group, initiated by Carole Spencer, Virginia Sarapura, and others at the Los Angeles meeting in 2002, has grown steadily since its inception. It is a great encouragement to see the impact that this group is having on the ATA. We are an organization with a narrow focus that has thrived and grown because we are not just another scientific or professional organization to our members, but a passion. Please continue to encourage your colleagues and fellows to apply for membership.

Program chairs, Steve Sherman and Jim Fagin, have assembled an outstanding group of thyroid cancer experts from around the world for our April Frontiers in Thyroid Cancer meeting. In addition to the core meeting, there will again be a one-day, pre-meeting endocrinology fellows course directed by Chip Ridgway and an advanced ultrasound workshop, directed by Dan Duick and Jack Baskin, focusing on thyroid cancer detection. We will also be inviting endocrine fellows to attend the entire meeting in a "fellows track," under the direction of Mike McDermott and Stephanie Fish. Fellows will attend the core meeting, but will also have special programs with case presentations and other learning experiences.

I am very appreciative of Paul Ladenson's support and leadership in the past year while he served in an expanded president-elect role. Paul brings great enthusiasm and vision as our president and I look forward to a very productive year. Charles Emerson has worked closely with Theresa Ronk to further refine our financial and accounting systems. Bobbi Smith and her staff organized and managed our Annual Meeting while planning for the Frontiers in Thyroid Cancer meeting, scheduled only six months later, with an office move fit in between. Bobbi continues to transform the administration of our organization and has created a highly effective professional team that is a pleasure to work with.

The Council will come together in January for our winter meeting to complete the strategic planning process. As a result of our Council meeting last year, our vision and mission statements were updated and a draft of a five-year plan begun. We shared the draft plan at the Annual Meeting and welcome input from members. Our goal this year is to prioritize the various initiatives and develop a strategy for implementation.

I will close with a quote from a presidential address from more than 50 years ago, but still very relevant as we complete our planning process and look to the future.

"...This organization is not stagnant but is aggressive and always seeking to improve upon the known and the tried. We are a diversified group, working in different fields; but we have never been content with the status quo, and have striven to approach the many problems involved, with an open mind and a progressive cooperative spirit."—*Dr. Claude J. Hunt, President, American Goiter Association, 1953*

Gregory A. Brent, MD
ATA Secretary

AMERICAN THYROID ASSOCIATION
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ATA Signal

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Please notify the ATA of changes in contact information.

ATA Executive Council Highlights

The Westin Bayshore Resort & Marina • Vancouver, BC, Canada

At the ATA Executive Council meeting on Sept. 29, a variety of issues were discussed, covering legislative, regulatory, patient, and clinical issues as well as standard ATA business.

Of priority was finalizing the establishment of the **Sawin Memorial Fund** and the Sawin endowment, initiated by Clark Sawin's wife, Leslie. In addition to the Sawin family's contributions, future funds raised will support projects related to thyroid history, the continuation of the historical vignette, the preservation of Clark's lectures, and the archival of historical materials.

The Council acknowledged the condolences and wonderful remembrances of Clark that the ATA received from around the world.

Dr. Brent reported that the ATA response to the **FDA's approval of generic levothyroxine** as equivalent to branded products in late June was a major focus of ATA activities. The ATA, The Endocrine Society, and AACE coordinated a response to this decision in a joint statement that was posted on all three web sites and in a news release.

In addition, Alan Farwell, with the help of patient group leaders in the **ATA Alliance for Thyroid Patient Education**, provided the patient's perspective on this issue in a web posting. Continued efforts on this issue include Paul Ladenson working with David Orloff at the FDA to develop a scientific workshop on the assessment of thyroxine bioequivalence, and Elliott Levy leading a committee to implement a pharmaco-vigilance program, developed to monitor adverse events associated with switching thyroxine products.

In other business, it was announced that Marty Surks, **Publications** Committee Chair, negotiated an excellent contract with Mary Ann Liebert Publishers to continue publication of *Thyroid*.

In the area of education, it was announced that a series of manuscripts summarizing the January 2004 **ATA/Centers for Disease Control and Prevention conference** is scheduled for publication in the January 2005 issue of *Thyroid*. Joe Hollowell was acknowledged for his enormous efforts to see these papers published. In addition, the proceedings of the one-day CME course "The Impact of Maternal Thyroid Status on Pregnancy and Fetal and Childhood Development," held in April 2004, are available on the ATA web site in streaming video.

Planning for the spring meeting of the ATA, **Frontiers in Thyroid Cancer 2005**, is underway with program chairs Jim Fagin and Steven Sherman. Mike McDermott and Stephanie Fish are co-chairing a fellows "track," providing a special educational opportunity for fellows from around the country to attend these special fellows sessions as well as regular meeting sessions. Dan Duick and Jack Baskin will organize a pre-meeting advanced ultrasound course.

It was also announced that the **ATA** has produced several first-time documents during 2004:

- A membership brochure
- An endowment policy
- Policies and procedures
- A patient fundraising brochure

Treasurer Charles Emerson reported that assets have shown excellent growth but sources of income must continue to be cultivated. The ATA has implemented program-based budgeting and the computerized flow of data entry to summary reports.

Membership Committee chair Virginia Sarapura reported that in 2004, 50 Active, four Corresponding, and 22 Associates were approved for membership. Also in 2004, 30 percent of new members represent expansion beyond adult endocrinologists, including eight general surgeons, three ENT surgeons, one orbital surgeon, five radiologists, two pathologists, one pharmacologist, one pediatric endocrinologist, one oncologist, one occupational medicine practitioner, and one veterinary medicine practitioner. Overall, 33 percent of members are women — who are represented in greater numbers in the Associates category (52 percent) than for Active and Corresponding members (24 percent). The overall growth of membership in 2004 was 10 percent, resulting in 876 members.

Chief Justice Rehnquist's Condition Fosters Awareness and Concern About Thyroid Cancer

The topic of thyroid cancer has been in the media spotlight since the October 25 announcement that Chief Justice William Rehnquist is undergoing treatment for thyroid cancer.

As a result, the ATA has been a primary source of information to the media about thyroid cancer. In fact, ATA members from across the country have been quoted in major newspapers, on TV, and on Internet news sites about the topic. ATA spokespeople — President Paul Ladenson, MD, and ATA Director Steven Sherman, MD, and James Fagin, MD, who are the co-chairs of the upcoming ATA thyroid cancer spring meeting — were quoted extensively in a variety of media outlets, such as *The New York Times, The Washington Post*, *USA Today*, ABCNews.com, and Bloomberg.com. ATA Past President Jerome Hershman, MD, was interviewed for a story on National Public Radio.

...the ATA has been a primary source of information to the media about thyroid cancer.

In addition to using ATA experts as resources, the ATA's patient information material was used in articles, such as *The Washington Post*, to provide background on the incidence, diagnosis, and treatment of thyroid cancer and other thyroid diseases.

The Campaign for Thyroid Discovery Recognizes Its Major Donors

On behalf of ATA members and the scientific community of thyroidologists, Major Donors* to the *Campaign for Thyroid Discovery* are gratefully recognized.

Research by ATA members has led to important breakthroughs that have improved the lives of patients with thyroid diseases. Building an endowment for thyroid research ensures that this exciting and important work will continue in perpetuity.

Anonymous
Lois F. Lunin and David V. Becker, MD
S. Thomas Bigos, MD
Lewis E. Braverman, MD
Gerard N. Burrow, MD
Boris Catz, MD
Rebecca Catz, PhD
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* Major Donors have contributed $1000 or more to the *Campaign for Thyroid Discovery*

Editor's Corner: What's new in thyroidology?

Rebecca S. Bahn, MD, *ATA Signal* Editor

Why do some patients have persistently low TSH after successful treatment for Graves' hyperthyroidism?

In some Graves' disease patients, the TSH levels remain suppressed following antithyroid drug or radioiodine therapy despite clinical euthyroidism and normal T4 and T3 concentrations. Also, a low TSH level following a course of antithyroid drug treatment has been found to be an independent risk factor for recurrence of Graves' hyperthyroidism.

To explain these observations, Drs. Mark Prummel, Wilmar Wiersinga, and colleagues at the Academic Medical Center in Amsterdam hypothesized that thyroid-stimulating immunoglobulins (TSI) might act directly on the pituitary gland to suppress TSH secretion, independent of thyroid status. Of course, this would require that the pituitary have TSH receptors (TSHR).

Prummel and his colleagues undertook a series of studies to investigate this possibility. Using RT-PCR, *in situ* hybridization, and immunocytochemistry, they demonstrated the presence of TSHR mRNA and protein in the human anterior pituitary, and localized it to the folliculo-stellate cells.[1] They also wished to determine whether TSI is in fact capable of down-regulating TSH secretion *in vivo*. Rats were treated with methimazole and thyroxine to inhibit thyroid hormone production while maintaining euthyroidism and normal TSH levels.[2] The animals were then infused either with human TSI or a control IgG preparation. As predicted, lower TSH levels were found in the TSI-treated rats, while T4 and T3 levels were similar between the groups.

Proof of principal in patients was next. Prummel and his colleagues followed a cohort of 45 patients with Graves' disease treated with combined methimazole and thyroxine. After three months on this regimen, 22 patients still had detectable TSI levels. They found that, taken as a group, these patients had a lower mean TSH than did the TSI-negative patients, despite similar levels of T3 and T4.[3]

What might be the physiological role of these extrathyroidal TSHR? Prummel and colleagues hypothesize that thyrotropin secretion may be partially regulated by an ultra-short feedback loop at the pituitary level, as has been shown for other peptides within the hypothalmic-pituitary axis. This would allow for "fine-tuning" of TSH secretion. An elevated TSH levels would be sensed immediately by the pituitary gland, and its effect on the thyroid anticipated. The pituitary could then immediately begin to decrease TSH production, rather than waiting for the signal brought by elevated T4 levels. Such early feedback might help to dampen potential overshoot of thyroid hormone levels.

1. Prummel MF, Brokken LJS, Meduri G, Misrahi M, Bakker O, Wiersinga WM. J Clin Endocrinol Metab 85: 4347-53, 2000.
2. Brokken LJS, Scheenhart JWC, Wiersinga WM, Prummel MF. J Clin Endocrinol Metab 86: 4814-17, 2001.
3. Brokken LJS, Wiersinga WM, Prummel MF. J Clin Endocrinol Metab 88: 4135-38, 2003.

ATA's Efforts Decrying FDA Levothyroxine Decision Make a Media Splash

The ATA and its sister endocrine societies have waged a communications campaign to voice concern about the FDA's decision this past summer to approve generic substitutes for levothyroxine products.

After much futile outreach to the FDA before and after its decision, the ATA — in concert with the American Association of Clinical Endocrinologists, The Endocrine Society, and the ATA Alliance for Thyroid Patient Education — turned to the news media on several occasions for help in alerting the medical community and patients to the potential problems that could arise from generic substitution.

Several media outlets recognized the importance of this story and provided important coverage. Dow Jones News Service was one such conduit on the consumer side, and *The Medical Letter*, which reaches more than 120,000 practicing physicians in every medical specialty, pharmacists, medical educators, interns, residents, and medical and pharmacy students, provided not only highlights of the issue but also its ringing endorsement of the ATA's message.

The Medical Letter concluded in its article: "Levothyroxine has a narrow therapeutic index. Given the multiple sources of variation in the effects of a dose of the drug, there is no good reason to introduce another one by substituting a generic that could be switched without the prescriber's knowledge from one refill to the next. It would be prudent to re-check TSH concentrations 6–8 weeks after any change in formulation."

ATA Welcomes New Members for 2004

The ATA Membership Committee proudly welcomes 76 new members for the year 2004. The ATA extends its appreciation to members who recruited and sponsored applicants for membership as well as to Dr. Virginia Sarapura for her excellent job as the new Membership Committee chair.

Membership application forms can be found in the ATA journal, *Thyroid*, or on the ATA web site at *www.thyroid.org*.

March 2004

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Pamela Schroeder, MD	Paul Ladenson, MD

Corresponding New Members	Sponsors
Elizabeth Chua, PhD	Gregory Brent, MD

Membership Renewal and Dues

ATA members can pay their dues online at *www.thyroid.org*. Please note that the ATA is updating its payment system; to avoid any interruption in the delivery of *Thyroid* and other ATA member services, members are encouraged to renew membership by Jan. 31, 2005.

American Association of Clinical Endocrinologists
American Thyroid Association
The Endocrine Society

Joint Position Statement on the Use and Interchangeability of Thyroxine Products

Recently, the Food and Drug Administration (FDA), approved the use of additional thyroxine products. A press release and notice to the American Association of Clinical Endocrinologists (AACE), The Endocrine Society (TES), and American Thyroid Association (ATA) members followed.

AACE, TES, and the ATA are issuing this joint statement to address the introduction of several generic levothyroxine products to the market that the FDA has deemed to be equivalent to some currently branded preparations.

1) **We are concerned about the FDA's method for determining bioequivalence.**

The FDA had recently acknowledged concerns about its methods for determining bioequivalence. In fact, it made a commitment to address the concerns of AACE, TES, and the ATA by agreeing to hold a workshop in order to do so.

2) **The FDA has failed to satisfactorily address questions relating to the bioequivalence of thyroxine preparations.**

Despite a written commitment to address the concerns of AACE, TES, and the ATA, as organizations that represent those most knowledgeable about caring for patients with thyroid disorders and thyroid hormone metabolism, the FDA proceeded to grant generic status to additional levothyroxine preparations.

3) **Physicians and patients should be educated about our concerns.**

Practicing physicians and patients should be well informed of AACE, TES, and the ATA's scientifically based concerns about the FDA's methodology for establishing generic status. These concerns are the basis for our recommendation not to substitute thyroxine preparations for one another—FDA generic equivalence notwithstanding.

4) **Physicians should become familiar with the historical background and glossary of terms related to the use of thyroxine preparations.**

This will enhance the ability of physicians to educate patients and other health care professionals about the use of thyroxine preparations.

Background[1]:

Thyroid hormone was first used in 1891 by injecting sheep thyroid extract into a patient with myxedema. Kendall discovered thyroxine in 1914 and Harrington established its structure in 1926, and went on to synthesize it. Nevertheless, desiccated thyroid, made from animal thyroid glands, remained the mainstay of therapy until the 1970s. A high-yield synthetic technique was developed in 1949. However, it was not until 1962 that levothyroxine came to market after the realization that sodium L-thyroxine form was much better absorbed than the free acid thyroxine. The FDA did not require a New Drug Application (NDA) for levothyroxine, based on the belief that it was not a new drug.

Subsequently, Adverse Drug Experience Reports, citing serious clinical consequences, brought to light problems with preparation potency (both under and over), stability, and consistency in lot-to-lot bioavailability. In some instances, reformulations with different excipients (including color agents and fillers that were generally thought to be inert) proved to be responsible for some within brand variations.

By 1997, the FDA concluded that no marketed levothyroxine preparation had been shown to have consistent potency and stability and, therefore, could not be recognized by the FDA as "safe and effective." In light of this, the FDA ruled that an NDA would be required in order to market a levothyroxine product after August 14, 2000, and that pre-existing products that were "non-NDA approved" could only be distributed until August 14, 2001.

The FDA has been cognizant of the "narrow toxic to therapeutic ratio with significant clinical consequences of excessive or inadequate treatment," which may have an impact on the heart, bone, and pregnancy status. This is reflected in the shelf life potency requirements that prevent thyroxine preparations from losing more than 20% potency under standard storage conditions. It has continued to use pharmacokinetic methods to establish therapeutic equivalence that are potentially flawed for endogenously-produced substances, and, by its own recent admission, should be subjected to formal review. These methods employ Area Under the Curve [AUC] and maximum concentration [Cmax] determinations in normal subjects with normal thyroid function. **These indices of bioavailabilty are used to establish bioequivalence and, in turn, conclude therapeutic equivalence.** Uncorrected, these methods fail to account for the subjects' own endogenous contribution to thyroxine levels (baseline contribution). In addition, TSH levels, the widely accepted best single laboratory tool for establishing thyroid status, are not part of the FDA's determinations of equivalence.

"Uncorrected," the FDA's methodology may lead to the conclusion that preparations that differ by as much as 33% are equivalent. "Correcting" for baseline values may reduce the difference detected to less than 25% but greater than 12.5%[2]. Even though the FDA has asserted that its current methodology makes it unlikely that generics that differ by 9, 12, or 15% from a branded product will be approved, the sensitivity of their current methodology for detecting differences less than 25% has not been directly demonstrated. Moreover, the FDA recently approved Levothyroxine Sodium-Sandoz as a bioequivalent alternative to Synthroid, even though baseline corrected AUC data between 0 and 48 hours demonstrated that on average the Sandoz product had 12.5% greater bioavailability than Synthroid. It is widely appreciated that in many, if not most, clinical situations, a 33% or 25% difference in thyroxine dose may have a substantial clinical

[1]Hennessey JV. Levothyroxine a New Drug? Since When? How Could That Be? Thyroid. 2003; 13,279-282.

[2] Blakesley V, Awni W, Locke C, Ludden T, Granneman GR, Braverman LE. Are bioequivalence studies of levothyroxine sodium formulations in euthyroid volunteers reliable? Thyroid. 2004;14:191-200.

impact. What is perhaps less well appreciated is that differences less than 25% may not only have a significant impact on serum TSH levels, but in certain clinical settings, such as the elderly with cardiac disease or pregnancy, the impact may be clinically highly significant. In fact, this is the basis for manufacturing multiple thyroxine doses. For example, the difference between 137 mcg of thyroxine and 150 mcg is only 9%.

Not only did the FDA's new ruling have an impact on pharmaceutical companies making levothyroxine preparations, it also had an unintentional impact on patients taking thyroxine preparations as well as physicians caring for them. A confusing array of new levothyroxine preparations came to market. To date, these have included: preparations made by companies that previously did not make thyroxine, reformulation of existing products, and replacement of one company's product with an FDA-approved product made by another company. Most recently, the FDA has granted approval of three preparations as equivalent to longstanding branded products, despite the concerns referred to above. As a result, the following has frequently happened:

a) Patients did not know that their thyroxine preparation was changed.
b) Physicians did not know that a different thyroxine preparation was dispensed to their patients.
c) Pharmacists did not know about formulation changes and, therefore, could not properly counsel patients about their thyroid medication.
d) Physicians were deluged with patients' concerns about the quality of their thyroxine preparations. This was particularly prevalent in 2001 when patients were led to believe that their thyroxine preparations (not yet FDA approved) may be unreliable and potentially hazardous to their health.
e) Physicians and other health care personnel have spent an extraordinary amount of time counseling patients about the use of thyroxine products, and money testing for therapeutic equivalence by employing TSH and other thyroid hormone levels, thereby adding a substantial burden to our health care system.

Conclusion:

Best Physician Practices:

Patients should be maintained on the same brand name levothyroxine product. If the brand of levothyroxine medication is changed, either from one brand to another brand, from a brand to a generic product, or from a generic product to another generic product, patients should be retested by measuring serum TSH in six (6) weeks, and the drug reiterated as needed. Since small changes in levothyroxine administration can cause significant changes in TSH serum concentrations, precise and accurate TSH control is necessary to avoid potential adverse iatrogenic effects.

Best Patient Practices:

Use the same brand of thyroid medication throughout your treatment. Thyroid disease often requires lifelong therapy and is best managed with consistent and precise treatment with the same brand of thyroid hormone. Your doctor may change your dose of thyroid hormone, but the brand of your thyroid hormone medication should always stay the same.

When you go to the pharmacy, do not change the brand of your thyroid medication without checking with your doctor. You should not change from one brand of thyroid medication to another, from your brand of thyroid medication to a generic product, or from one generic product to another without first checking with your doctor. Repeat blood tests and visits to your doctor may be required, and your dose may need to be readjusted if your thyroid medication is changed, or if you switch to a generic product.

Thyroid disease often requires lifelong therapy and is best managed with consistent and precise treatment. Do not change the brand of your thyroid medication without checking with your doctor. If the pharmacist suggests changing brands or recommends a generic product, you should also check with your doctor. Your insurance company or state aid program may not pay for the cost of a brand name drug or charge a higher co-payment if you want a specific brand name drug. Repeat blood tests and visits to your doctor may be required, and your dose may need to be readjusted if your thyroid medication is changed to a different brand, a generic product, or a different generic product.

APPENDIX I: Glossary

Generic Drugs: A generic drug is a copy that is the same as a **brand-name** drug in dosage, safety, strength, how it is taken, performance, and intended use (Source: FDA (cite the URL of the FDA web site). Note: a generic drug, bearing the chemical name of the drug, can only serve as a substitute for the brand(s) to which it was designated to be equivalent. In the case of thyroxine preparations, it requires an AB rating (see below). Until recently (as of 2002), Mylan Pharmaceuticals made the only approved generic levothyroxine, which could only be used as a substitute for Unithroid, a brand of levothyroxine made by Stevens. Recently, the FDA approved a previously NDA approved levothyroxine preparation made by ALARA (Levo-T) and to be distributed by Sandoz that can be substituted for Synthroid made by Abbott Pharmaceuticals as well as Levoxyl made by Jones Pharmaceuticals. It also ruled that the levothyroxine preparation made by Mylan Pharmaceuticals could be substituted for Synthroid and Levoxyl and that Unithroid could be substituted for Levoxyl.

Therapeutic Equivalents (TE): Drugs that are **pharmaceutical equivalents** (identical amounts of the same active drug ingredient, same dosage, same route of administration) and bioequivalent (see below). Drugs can be considered therapeutic equivalents even if they have different release mechanisms. Therapeutic equivalents can be substituted for one another with the expectation that there will be similar clinical effects and that follow-up testing would not be required.

Bioavailability and **Bioequivalence**: Bioavailability refers to the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug product and becomes available "at the site of drug action." Two drugs are considered bioequivalent if they have an "equivalent rate and extent of absorption from these formulations," or, in other words, appear to have comparable bioavailability. The FDA's language (see web site) indicates that the formulations do not have to undergo comparison "at the site of drug action," which would be reflected in a pharmacodynamic parameter, such as serum TSH measurements in the case of levothyroxine. Bioequivalence, in turn, establishes therapeutic equivalence and, therefore, interchangeability. Hence, a generic drug that is demonstrated to be bioequivalent by pharmacokinetic methods along the lines outlined above to the pioneer (innovator) drug, may be marketed as a generic version of that product.

AB: This is one of a number of "Therapeutic Equivalent Evaluation Codes" used by the FDA to denote therapeutic equivalence to other pharmaceutically equivalent drug products, when "actual or potential bioequivalence problems have been resolved with adequate *in vivo* and/or *in vitro* evidence supporting bioequivalence."

Generic levothyroxine preparations have AB codes. Branded levothyroxine preparations that have generic equivalents have AB codes.

The terminology "AB to" or "AB rated to" thereby indicates that two products are considered interchangeable by FDA standards and will be substituted unless the physician designates that they are not (e.g., "NO SUBSTITUTION") to be exchanged.

Note: Drug I may be AB to Drug II and Drug II AB to Drug III. However, this does not mean that Drug I and III are AB to each other. This is because Drug II and Drug III may not have been compared with one another, rather than proven not to be equivalent. This point is illustrated by the following example: Drug I on average is more bioavailable than II but close enough for FDA approval to be considered equivalent. Drug III is less bioavailable than II but close enough to be considered equivalent. However, when Drugs I and III are compared directly to one another, they do not correspond sufficiently to be considered equivalent by the FDA.

AB-#: When more than one drug is listed under the same FDA "reference" (i.e. levothyroxine), and the drugs are not bioequivalent, the FDA employs three character designations: AB1, AB2, AB3, AB4… (See Appendix III from FDA Orange Book description of this designation and Appendix IV for Levothyroxine Sodium update) in order to classify products with identical active ingredients, dosage form, and route of administration. Since Levoxyl, for example, was not AB to Synthroid, we correctly anticipated that the FDA's recent approval of additional generic products would lead to the implementation of three character designations for levothyroxine products.

We believe that multiple character designations make matters even more complex for pharmacists, physicians, and patients. As a result, not only will it continue to be virtually impossible to remain on the same generic product (which is one of our fundamental concerns about generic products), but it will also become increasingly difficult for patients to remain on the same branded product.

BX: This is one of a number of Therapeutic Equivalent Evaluation Codes used by the FDA to denote that a pharmaceutically equivalent drug product is not therapeutically equivalent, because actual or potential bioequivalence problems have not been resolved by adequate evidence of bioequivalence. The BX code is the designation used by the FDA when the data reviewed by the FDA are "insufficient to determine therapeutic equivalence." Currently, branded levothyroxine preparations that do not have generic equivalents, and, therefore, cannot be interchanged with a pharmaceutically equivalent drug product, ***common pharmacy practices notwithstanding,*** have a BX code.

APPENDIX II: Current List and Status of Thyroxine Preparations

Before June 23, 2004, only Unithroid (Stevens) and Levothyroxine (Mylan) were AB rated. Synthroid (Abbott), Levo-T (Alara), Novothyrox (Genpharm), Levoxyl (Jones [related to Monarch and King]), Thyro-Tabs (which has become the new Levothroid preparation made by Lloyd but owned by Forest), and Levolet (Vintage) were all BX rated.

Since June 23, 2004, the FDA deemed Levo-T (ALARA), to be distributed as levothyroxine (Sandoz), to be equivalent to Synthroid and Levoxyl. The makers of Levoxyl are currently contesting this. In addition, levothyroxine (Mylan) was deemed equivalent to Synthroid and Levoxyl, while Unithroid was designated bioequivalent to Levoxyl. The FDA Orange Book should reflect this by changing Levo-T, Synthroid, and Levoxyl from BX to AB and adding the levothyroxine preparation (Sandoz) to its AB listings. Levothyroxine (Mylan) previously was AB to Unithroid, as noted above.

Of especial interest is the fact that the bioequivalence of the designated generic preparations levothyroxine (Mylan) and levothyroxine (Sandoz) have not been compared to one another, and would therefore be considered BX to one another even though each one is designated AB3 to Levoxyl and AB2 to Synthroid.

APPENDIX III (From the FDA Web site [www.fda.gov/cder/ob/docs]) AB, AB1, AB2, AB3… Products meeting necessary bioequivalence requirements

Multisource drug products listed under the same heading (i.e., identical active ingredient(s), dosage form, and route(s) of administration) and having the same strength (see *Therapeutic Equivalence-Related Terms, Pharmaceutical Equivalents)* generally will be coded **AB** if a study is submitted demonstrating bioequivalence.

In certain instances, a number is added to the end of the AB code to make a three-character code (i.e., AB1, AB2, AB3, etc.). Three-character codes are assigned only in situations when more than one reference listed drug of the same strength has been designated under the same heading. Two or more reference listed drugs are generally selected only when there are at least two potential reference drug products which are not bioequivalent to each other. If a study is submitted that demonstrates bioequivalence to a specific listed drug product, the generic product will be given the same three-character code as the reference listed drug it was compared against. For example, Adalat® CC (Miles) and Procardia XL® (Pfizer), extended-release tablets, are listed under the active ingredient nifedipine. These drug products, listed under the same heading, are not bioequivalent to each other. Generic drug products deemed by FDA to be bioequivalent to Adalat® CC and Procardia XL® have been approved. Adalat® CC and Procardia XL® have been assigned ratings of AB1 and AB2, respectively. The generic drug products bioequivalent to Adalat® CC would be assigned a rating of AB1 and those bioequivalent to Procardia XL® would be assigned a rating of AB2. (The assignment of an AB1 or AB2 rating to a specific product does not imply product preference.) Even though drug products of distributors and/or repackagers are not included in the List, they are considered therapeutically equivalent to the application holder's drug product, if the application holder's drug product is rated either with an AB or three-character code or is single source in the List. Drugs coded as AB under a heading are considered therapeutically equivalent only to other drugs coded as AB under that heading. Drugs coded with a three-character code under a heading are considered therapeutically equivalent only to other drugs coded with the same three-character code under that heading.

APPENDIX IV
APPROVED DRUG PRODUCTS with THERAPEUTIC EQUIVALENCE EVALUATIONS
24th EDITION, Cumulative Supplement 6

Prepared By the Office of Pharmaceutical Science; Office of Generic Drugs; Center for Drug Evaluation and Research, FDA

June 2004

1.4 LEVOTHYROXINE SODIUM

Because there are multiple reference listed drugs of levothyroxine sodium tablets and some reference listed drugs' sponsors have conducted studies to establish their drugs' therapeutic equivalence to other reference listed drugs, FDA has determined that its usual practice of assigning two or three character TE codes may be potentially confusing and inadequate for these drug products. Accordingly, FDA provides the following explanation and chart of therapeutic equivalence evaluations for levothyroxine sodium drug products.

Levothyroxine Sodium (Mylan ANDA 76187) tablets have been determined to be therapeutically equivalent to corresponding strengths of Unithroid (Jerome Stevens NDA 21210) tablets.

Levo-T (Alara NDA 21342) and Levothyroxine Sodium (Mylan ANDA 76187) tablets have been determined to be therapeutically equivalent to corresponding strengths of Synthroid (Abbott NDA 21402) tablets.

Levo-T (Alara NDA 21342), Unithroid (Jerome Stevens NDA 21210) and Levothyroxine Sodium (Mylan ANDA 76187) tablets have been determined to be therapeutically equivalent to corresponding strengths of Levoxyl (King/Jones Pharma NDA 21301) tablets.

Novothyrox (Genpharm NDA 21292) requires further investigation and review to establish therapeutic equivalence to corresponding strengths of any other levothyroxine sodium drug products and is rated BX.

Thyro-Tabs (Lloyd NDA 21116) requires further investigation and review to establish therapeutic equivalence to corresponding strengths of any other levothyroxine sodium drug products and is rated BX.

Levolet (Vintage NDA 21137) requires further investigation and review to establish therapeutic equivalence to corresponding strengths of any other levothyroxine sodium drug products and is rated BX.

The chart outlines TE codes for all 0.025mg products with other products being similar. **Therapeutic equivalence has been established between products that have the same AB+ number TE code. More than one TE code may apply to some products. One common TE code indicates therapeutic equivalence between products**.

Trade Name	Applicant	Potency	TE Code	Appl No	Product No
UNITHROID	STEVENS J	0.025MG	AB1	21210	001
LEVOTHYROXINE SODIUM	MYLAN	0.025MG	AB1	76187	001
LEVOXYL	JONES PHARMA	0.025MG	AB1	21301	001
SYNTHROID	ABBOTT	0.025MG	AB2	21402	001
LEVOTHYROXINE SODIUM	MYLAN	0.025MG	AB2	76187	001
LEVO-T	ALARA PHARM	0.025MG	AB2	21342	001
LEVOXYL	JONES PHARMA	0.025MG	AB3	21301	001
LEVO-T	ALARA PHARM	0.025MG	AB3	21342	001
UNITHROID	STEVENS J	0.025MG	AB3	21210	001
LEVOTHYROXINE SODIUM	MYLAN	0.025MG	AB3	76187	001
NOVOTHYROX	GENPHARM	0.025MG	BX	21292	001
THYRO-TABS	LLOYD	0.025MG	BX	21116	001
LEVOLET	VINTAGE PHARMS	0.025MG	BX	21137	001

BASE URL = http://www.fda.gov/cder/orange/supplement/cspreface.htm
URL = http://fda.gov/cder/orange/supplement/cspreface.htm
Modified = DOAC29F6DC74C401B0

APPENDIX V:
THYROXINE PRODUCT STATUS: JUNE 23, 2004

	Synthroid	Levoxyl	Levothroid	Unithroid	LT4-Sandoz	LT4-Mylan	Novothyrox	Levolet
Synthroid(Abbott)	———	BX	BX	BX	**AB2**	**AB2**	BX	BX
Levoxyl(Jones)	BX	———	BX	**AB 3**	**AB3**	**AB3**	BX	BX
Levothroid (Forest: FormerlyLloyd Thyrotabs)	BX	BX	———	BX	BX	BX	BX	BX
Unithroid1(Stevens)	BX	**AB1**	BX	———	BX	**AB1**	BX	BX
LT4-Sandoz	**AB2**	**AB3**	BX	BX	———	**BX**	BX	BX
LT4-Mylan	**AB2**	**AB3**	BX	**AB1**	**BX**	———	BX	———
Novothyrox(Genpharm)	BX	BX	BX	BX	BX	BX	———	BX
Levolet(Vintage)	BX	BX	BX	BX	BX	BX	BX	———

AB1: Product rating using Unithroid as "reference drug,"[2] considered interchangeable with Unithroid. Generic product LT4-Mylan listed may be exchanged with Unithroid.

AB2: Product rating using Synthroid as "reference drug," considered interchangeable with Synthroid. Generic products LT4-Mylan and LT4-Sandoz may be exchanged with Synthroid[3].

AB3: Product rating using Levoxyl as "reference drug," considered interchangeable with Levoxyl. Generic products LT4-Mylan and LT4-Sandoz may be exchanged with Levoxyl[3].

Drugs within a TE rating will likely be interchanged within the same three character products unless prescriber specifies "No Substitution," "Brand Name Necessary," "Dispense as Written," etc.

BX: Not Interchangeable

NOTE1: Lannett is distributing Unithroid (made by Stevens) as a generic product "LT4-Lannett," which the FDA has designated as TE to Levoxyl. This has been omitted from the table, because FDA postings did not cite its three-character designation(s) by the time this document was completed.

NOTE2: When applicable, row titles list "reference drugs" with table columns designating the drug that is being compared to the "reference drug." Examples:

Row 2: Unithroid is "AB3 to Levoxyl"
Row 4: Levoxyl is "AB1 to Unithroid

For completeness we created rows for the "Generic products" (LT4-Sandoz, LT4-Mylan). These are not "reference drugs." Therefore, the respective three character designations listed in their rows are "referenced" to the products appearing in the columns. Examples:

Row 5: LT4-Sandoz is "AB2 to Synthroid"
Row 6: LT4-Mylan is "AB3 to Levoxyl"

NOTE[3]: LT4-Sandoz and LT4-Mylan are both AB2 to Synthroid and AB3 to Levoxyl. However, LT4-Mylan and LT4-Sandoz are not interchangeable (BX) because they have not been evaluated in regard to one another. See Appendix I for explanation.

ATA Receives Award for Web Site Excellence

The ATA is the recipient of the 2004 Aesculapius Award — given by the nonprofit Health Improvement Institute (HII) to promote excellence in health communications — for quality content on *www.thyroid.org*.

The ATA's web site was singled out for the top prize among eight other prestigious groups for excellence in providing patients, the public, and health professionals with timely and accurate information on thyroid diseases and thyroid cancer.

To register, see page 13 or go to www.thyroid.org

Meeting-at-a-Glance

Frontiers in Thyroid Cancer 2005: Clinical Care and Research for the Future

A spring meeting of the American Thyroid Association

Baltimore Waterfront Marriott Hotel

April 14–17, 2005 • Baltimore, Maryland

Time	Thursday 4/14/05	Friday 4/15/05	Saturday 4/16/05	Sunday 4/17/05
6:00	Exhibitors Move-In	CME Symposium 6:30 - 8:00 Thyroid Fellows Track	CME Symposium 6:30 - 8:00 Thyroid Fellows Track ThyCa Workshop 8:00 am - 5:00 pm	CME Symposium 7:30 - 9:00 Thyroid Fellows Track
7:00	8:00 - 11:00 am			
	Endocrine Fellows Conference			
8:00	7:30 am - 5:00 pm	Welcome 8:00 - 8:05	Welcome 8:00 - 8:05	Cancer following Radioiodine Therapy
	ATA Council Meeting	Keynote 8:05 - 8:45	Keynote 8:05 - 8:45	9:00 - 10:00 am
9:00	8:00 - Noon	Epidemiology/genetic epidemiology 8:45 - 9:15 am	Adjuvant Therapy 8:45 - 9:45 am	Tying it all together: Management of the thyroid cancer patient
		Exhibit Booths open 9:00-3:30 pm	Exhibit Booths open 9:00-2:00 pm	10:00 - 11:00 am
10:00		Break in the Exhibit Foyer 9:15 - 9:30	Break in the Exhibit Foyer 9:45 - 10:00	
10:30		Epidemiology/genetic epidemiology 8:45 - 9:15 am	Adjuvant Therapy (continued) 10:00 - 11:00 am	
		Work-up and Diagnosis 11:00 am - Noon	Follow- up and Surveillance 11:00 am - Noon	
11:00	ATA Committees & Council Liaisons	Meet the Professor Luncheons Noon - 1:30	Meet the Professor Luncheons 12:30 - 2:00	
	Luncheon 11:30 - 1:30	Asa / Hay	Kroll / Ain	
12:00	Advanced Ultrasound Workshop	Nikiforov / Grebe	Reddy & Weber / ThyCa MTP	
	Thyroid Cancer 1:00 - 5:30 pm	Francis / Career - Fellows	Mestman / Tuttle - Fellows	
		Surgery 1:30 - 3:00 pm	Exhibit Hall Closes 2:00	
		Break in the Exhibit Foyer and Posters 3:00 - 3:30 pm	Therapy for Advanced Disease 2:00 - 3:00 pm	
1:30	Exhibit Hall open 2:00-8:00 pm	Pathogenesis of Papillary Thyroid Cancer 3:30 - 5:00 pm	Break in the Exhibit Foyer and Posters 3:00 - 3:30 pm	
	Registration open 2:00 -6:00 pm	ATA Annual Business Meeting 5:00 - 6:00 pm ATA Members Only	Targeted Therapies for Thyroid Cancer 3:30 - 5:00 pm	
2:00	ATA Council meeting 1:30 - 5:00 pm		Clinical Trials Poster Session 5:00 - 6:00 pm	
3:00				
3:30	Cmte Chairs Report 2:00-4:00		Historical Vignette 6:00 - 6:30 pm	
	Women in Thyroidology 5:00 - 6:00	CME Symposium 6:00 - 7:30 pm		
5:00	Newcomers' Welcome 6:00 - 7:00			
		Free Evening		
6:00	Welcome Reception		ThyCa Fundraiser	
7:00	7:00 - 8:30			

On April 16 at the Baltimore Waterfront Marriott Hotel, ThyCa is holding a free workshop, **4th Annual Regional Thyroid Cancer Survivors' Spring Workshop,** for thyroid cancer patients, caregivers, and friends.

For information, go to www.thyca.org or call 877-588-7904.

ATA Spring Meeting in Baltimore, *continued from front page*

Medicine, where he holds a joint appointment in Molecular Biology and Genetics, and ATA President-Elect Ernest Mazzaferri, who will discuss the new paradigms in the management of differentiated thyroid cancer.

Other topics covered in the three-day meeting will be genetic epidemiology, work-up and diagnosis, surgery, pathogenesis of papillary thyroid cancer, adjuvant therapy, follow up and surveillance, therapy for advanced disease, and targeted therapies. In addition, there will be meet the professor sessions on a wide variety of topics, including pediatric thyroid cancer, challenges in surgical pathology, pathogenesis of follicular carcinomas, and palliative therapy and cancer. There will also be opportunities to hear about the latest in thyroid cancer research through the clinical trials poster sessions on April 16. Two special CME symposia will explore thyroid hormone suppression therapy and its impact on the cancer, heart, and bone and the roles of recombinant TSH in managing thyroid cancer.

Endocrine fellows are VIPs at this meeting, with a dedicated all-day course on April 14 as well as a special track created for new fellows throughout the meeting. On Thursday there will also be a half-day symposium on advanced ultrasound for 50 participants — registration required — covering topics such as using diagnostic ultrasound for assessing thyroid nodules for sonographically guided fine-needle aspiration and controversies regarding nodule size and criteria for aspiration. In addition, that evening, there will be a Women in Thyroidology meeting, a reception for newcomers, and a welcome reception for all attendees.

"This year's spring meeting will be very special, a 'mini-Annual Meeting,'" said Steven Sherman, MD, co-chair. "Because the fall ATA Annual Meeting is replaced every five years by the International Thyroid Congress, which will be in Buenos Aires in October 2005, this spring meeting will give ATA members an opportunity to hear about the latest in thyroidology and enjoy the collegiality that is always a part of our meetings."

To register, go to *www.thyroid.org*.

REGISTRATION FORM

American Thyroid Association

Frontiers in Thyroid Cancer: Clinical Care and Research for the Future

Baltimore Marriott Waterfront • Baltimore, Maryland • April 14-17, 2005

Deadline for receipt of advance registration is April 7, 2005.

All requested information must be provided to process registration.
All Fees are in US Dollars.

First name

Last name

Nickname for badge

Professional degree(s) (please list one):_____
a. MD b. PhD c. MD, PhD d. RN e. Other

Organization

Address 1

Address 2

City State Zip code + 4

Country If outside the U.S., country/city code

Phone

Fax

E-mail address

1. **I require a CME certificate for my attendance at this meeting.**
The CME form to be completed will be in your registration packet. Please complete and hand in to the CME desk at the meeting to obtain your certificate on-site.

2. **I consider myself primarily** (please list one):_____
a. Clinician b. Educator c. Scientist d. Other e. Exhibitor

3. **My work is best described as** (please list one): _____
a. Adult endocrinology c. Pediatric endocrinology e. Other
b. Basic science d. Internal medicine

4. **My place of work is** (please list one): _____
a. Academic d. Hospital g. Managed care
b. Private practice e. Government/military
c. Administration f. Corporate/industry

5. **Registration fees (please circle applicable fees):**

		Early Bird (received by February 28)	Discounted (received between March 1 and March 31)	Full Fee (received after March 31)
(M)	ATA member	$325	$350	$375
(N)	Non-member	$475	$500	$525
(A)	Fellows/student/RA *Please fax a letter from your program director to 703-998-8893.*	$100	$125	$150
(B)	Baltimore One-day fee Indicate day:	$275 ☐ (F) Frid.	$300 ☐ (S) Sat.-Sun.	$325
(G)	Spouse/guest *Includes welcome reception, Ruth Volpe suite, coffee breaks*	$ 40	$ 40	$ 40

Spouse/guest name:_____

Advanced Ultrasound Course (must be registered for meeting)

(U)	ATA/AACE member	$125	$150	$175
(UN)	Non-member	$200	$225	$275

6. **Meet the Professor Luncheon Workshops**
(Complimentary for Fellows)

Friday, April 15, Noon – 1:30 pm (please circle one) $38/ticket:

a.	Challenges in Surgical Pathology	Sylvia Asa
b.	Future applications of Molecular Diagnostics in FNA	Yuri Nikiforov
c.	Pediatric Thyroid Cancer	Gary Francis
d.	Pathogenesis and Management of Hurthle cell carcinoma	Ian Hay
e.	Thiazolidenediones, PPAR gamma and thyroid cancer	Stefan Grebe

Saturday, April 16, 12:30 – 2:00 pm (please circle one) $38/ticket:

f.	Pathogenesis of follicular carcinomas	Todd Kroll
g.	Coding Issues in Thyroid Cancer Management & Surgery	Sethu Reddy & Randal Weber
h.	Treatment of patients with undifferentiated thyroid cancer	Kenneth Ain
i.	Thyroid Cancer and Pregnancy	Jorge Mestman

7. **Special events** (please circle events that you plan to attend):
(REC) Welcome reception Thursday, April 14 7–8:30 pm No charge

8. **Total fees**
_____ Attendee registration fee
_____ Spouse/guest fee
_____ **Friday, April 15** Meet the Professor Workshop
_____ **Saturday, April 16** Meet the Professor Workshop
_____ Ultrasound Registration (ATA/AACE Members)
_____ Ultrasound Registration (Non-Members)
_____ Donation to Fellows' Travel Fund
_____ **TOTAL**

9. **Submission and payment —**
Checks and money orders for registration payable to the **American Thyroid Association** in U.S. dollars drawn on a U.S. bank.
☐ MasterCard ☐ VISA ☐ American Express

Card number

Expiration date (month/year)

Print cardholder's name

Signature

REGISTER ON-LINE at the secure ATA web site **www.thyroid.org**.

FAX your completed form with credit card payment (no checks or money orders) to 678-341-3081. ***If you FAX,*** *DO NOT MAIL, you risk duplicate charges.*

MAIL your completed registration form with payment to: ATA Registration, c/o QMS, 6840 Meadowridge Court, Alpharetta, GA 30005. Phone 678-341-3056.

REFUND POLICY: Refund requests must be submitted in writing. Requests postmarked before March 11, 2005 will receive a registration refund less a 25% processing fee. Requests postmarked between March 11 and April 5, 2005 will receive a refund less a 50% processing fee. No refunds will be made if postmarked after April 5, 2005. Refunds will be processed 30 days after the meeting.

In case of emergency, please contact:

Name

Daytime Phone

Evening Phone

Please keep a copy of this form.

Highlights of the ATA 76th Annual Meeting

The ATA 76th Annual Meeting, held in Vancouver, British Columbia, Canada, Sept. 29–Oct. 3, 2004, was the place to be to hear the latest research and clinical insights into thyroid diseases while offering a beautiful setting for catching up with old and new friends.

Plan now to attend the ATA's spring meeting, Frontiers in Thyroid Cancer 2005, taking place in Baltimore April 14–17.

Newly elected President-Elect Ernest Mazzaferri and his wife, Florence, catch up with John Lazarus at the Opening Reception.

Attendees gather to kick off the Poster Sessions and discuss new research in thyroid diseases.

ATA member Paul Mystowski and son enjoy the Opening Reception

Vancouver residents listen to a panel of thyroid experts, patient advocates, and thyroid patients at the annual public education forum held on the eve of the meeting.

ATA member Joe DiStefano and his colleague, graduate student Robyn Javier, on trombone, entertained attendees at the opening of the Exhibit Hall.

Registration goes smoothly for the 76th Annual Meeting.

ATA President Paul W. Ladenson, who took office during the Annual Meeting, pauses with the ATA Council.

Elaine Kaptein offers insights about her professional path during the Women in Thyroidology meeting.

ATA member Manisha Shah discusses her experiences in the medical profession at the Women in Thyroidology meeting

John Morris discusses one of the many legislative and regulatory issues monitored by the Public Health Committee, during its meeting, as Richard Robbins looks on.

Secretary Greg Brent, Executive Director Bobbi Smith, and President Paul Ladenson enjoy the Gala.

Jeff Garber and David Sarne chat with colleagues at the President's Reception.

Hugo Niepomniszcze and wife , hosts of the 13th International Thyroid Conference in October 2005, invited Annual Meeting attendees to visit Buenos Aires for the meeting.

ATA staff Bobbi Smith, Patrice Dickens, and Theresa Ronk relax at the end of a successful Annual Meeting.

ATA Announces 2004 Distinguished Award Recipients

At the ATA 76th Annual Meeting in Vancouver, British Columbia, Canada, Sept. 29–Oct. 3, the ATA honored five thyroid specialists with its Distinguished Awards. Three honorees delivered lectures highlighting the work that formed the basis for their distinguished award.

Sandra M. McLachlan, PhD

Sidney H. Ingbar Distinguished Lectureship

Sandra McLachlan receives the Ingbar award from Arthur Schneider.

Dr. McLachlan, Co-Director of the Autoimmune Disease Unit in the Cedars-Sinai Research Institute and a Professor of Medicine at UCLA, was honored with the 2004 Sidney H. Ingbar Distinguished Lectureship for which she presented a lecture on "An Odyssey in Thyroid Autoimmunity." In her lecture, she discussed insights gained from structural studies of the thyroid-stimulating hormone receptor that have increased understanding of the immune processes in Graves' disease.

The Ingbar award recognizes outstanding academic achievements in thyroidology, in keeping with the innovation and vision that epitomized Dr. Ingbar's brilliant investigative career. The Ingbar award is conferred upon an established investigator who has made major contributions to thyroid-related research over many years. The award is endowed by donations made in memory of Dr. Ingbar and is supported in part by an unrestricted educational grant from Abbott Laboratories.

Dr. McLachlan is a Director on the Executive Council; the Council liaison to the Research Committee, of which she previously served as chair; and on the Editorial Board of *Thyroid*.

Antonio C. Bianco, MD, PhD

Van Meter Award

Antonio Bianco proudly displays the Van Meter Award.

Dr. Bianco, Director of Research of the Thyroid Section at Brigham and Women's Hospital and Associate Professor of Medicine at Harvard Medical School, received the 2004 Van Meter Award. Established in 1930, the Van Meter Award honors an investigator who has made outstanding contributions to research on the thyroid gland.

This award is the ATA's oldest and most anticipated because it is kept secret until the recipient presents a major lecture at the ATA Annual Meeting. Dr. Bianco's lecture was titled "Control of Thyroid Hormone Activation by Ubiquitination and Deubiquitination." The award is supported in part by Quest Diagnostics, Inc.

Dr. Bianco's basic research interests have been in the cellular and molecular physiology of the iodothyronine deiodinases and thyroid hormone-induced energy expenditure. He has authored more than 110 scholarly papers, chapters, and review articles in this area.

Paul G. Walfish, MD

Paul Starr Award

Arthur Schneider and Paul Ladenson present Paul Walfish with the Paul Starr Award.

Dr. Walfish received the 2004 Paul Starr Award in recognition of his outstanding contributions to clinical thyroidology. He is Professor Emeritus in the Department of Medicine, Pediatrics and Otolaryngology at the University of Toronto and a Senior Consultant in the Division of Endocrinology & Metabolism and the Head & Neck Oncology Program of Mount Sinai Hospital.

As part of this award, he presented a major lecture titled "Evolving Strategies in the Detection and Management of Thyroid Carcinoma: Past and Future Perspectives." The award is supported by ATA member Boris Catz, MD, and in part by an unrestricted educational grant from Monarch/King Pharmaceuticals.

Dr. Walfish has contributed extensively to the clinical diagnosis and management of thyroid disorders. His clinical focus and scholoarly publications have centered on the early detection and treatment of congenital hypothyroidism by newborn screening, the application of ultrasound and fine-needle biopsy in the detection and management of thyroid cancer, and the recognition of the post-partum thyroiditis syndrome and its underlying autoimmune etiology.

John T. Nicoloff, MD,

Distinguished Service Award

Peter Singer and Carole Spencer accept the Distinguished Service Award, presented by Greg Brent, on behalf of recipient John T. Nicoloff.

Dr. Nicoloff received the 2004 Distinguished Service Award, which honors important and continuing contributions to the ATA. He is Professor of Medicine and Associate Dean for Research at the University of Southern California (USC), Keck School of Medicine.

Dr. Nicoloff is an ATA past president and received the Paul Starr Lecture Award in 1984. Dr. Nicoloff has authored more than 100 research papers, 200 abstracts, and 46 textbook chapters and reviews.

His major areas of research interest include the hormonal factors regulating human pituitary TSH release, the mechanism of nonsuppressible thyroxine secretion, the autoregulation of peripheral thyroxine to triiodothyronine conversion, the alternate routes of T4 and T3 metabolism, and the significance of circulating serum thyroglobulin in the management of neoplastic and other thyroid disease states.

P. Reed Larsen, MD,
Thyroid Pathophysiology Medal

P. Reed Larsen, the recipient of the Thyroid Pathophysiology Medal, is congratulated by Greg Brent and Paul Ladenson.

Dr. Larsen, Professor of Medicine at Brigham and Women's Hospital, Harvard Medical School, received the 2004 Thyroid Pathophysiology Medal. Dr. Larsen is also Chief of the Division of Endocrinology, Diabetes and Hypertension and a Senior Physician at the hospital.

The award recognizes outstanding research contributions to the understanding of thyroid physiology or the pathophysiology of thyroid disease. Dr. Larsen was honored with this award for the impact of his research in thyroid physiology and pathophysiology on subsequent research and clinical practice in thyroid disorders.

Dr. Larsen is an ATA past president and serves on the Editorial Board of *Thyroid*. In addition, he is a recipient of several ATA awards, including the Distinguished Service Award, the Van Meter Award, and the Parke-Davis Distinguished Lectureship.

Dr. Samuel Alonzo Wells, Jr. Honored By Light of Life Foundation for Thyroid Cancer

The Light of Life Foundation for Thyroid Cancer — a member of the ATA Alliance for Thyroid Patient Education — awarded Dr. Samuel Alonzo Wells, Jr., of Duke University its distinguished annual Light of Life Award on Dec. 2, 2004. Dr. Wells was honored for his outstanding contributions to molecular characterization, surgical management, and the conduct of clinical trials for patients with medullary thyroid carcinoma.

Each year, The Light of Life Foundation seeks out individuals who have made seminal contributions to thyroid cancer medicine. Following the award dinner, Dr. Wells presented the Sonenberg Annual Lecture on "The Multiple Endocrine Neoplasia Syndromes" to the Department of Medicine at Memorial Sloan-Kettering Cancer Center.

President's Message, *continued from front page*

among the best ever, thanks to the imagination and dedication of Co-chairs Mary Samuels and Jim Baker. Of course, all of the association's achievements depend on the professionalism and ingenuity of our administrative staff, particularly Executive Director Bobbi Smith. Congratulations and thanks to all!

"Thyroid Cancer 2005" will be the theme for the coming year. Paradoxically, our relative success in treating most thyroid cancer patients has slowed investment and advances in understanding thyroid cancer biology and clinical medicine — leaving many patients with no truly effective treatment. A series of coordinated activities and events will punctuate this year-long focus on thyroid cancer. Public awareness of thyroid cancer has already been heightened by its apparent sharply rising incidence, the unfortunate affliction of prominent persons, and an elegant print and broadcast campaign instigated by Joan Shey of the Light of Life Foundation.

Our Clinical Affairs Committee, chaired by David Cooper, is revising our thyroid nodule and cancer practice guidelines. In April, a special "Frontiers in Thyroid Cancer" symposium will describe the state-of-the–art and chart a course for future research priorities. The meeting agenda and presenters, which have been planned by Co-chairs Jim Fagin and Steve Sherman, are absolutely outstanding. The meeting will also be an exciting substitute for the regular ATA Annual Meeting, which, by tradition, is not held during the year of the International Thyroid Congress. I know most ATA members will want to attend this special thyroid cancer meeting in Baltimore April 14–17, 2005.

The second half of the year will be highlighted by another dedicated Thyroid Cancer Awareness month in September, which will be sponsored by ThyCa: Thyroid Cancer Survivors Association. Under their board chair Gary Bloom's leadership, ThyCa has been a generous supporter of thyroid cancer research, with peer review orchestrated by the ATA.

The ATA has been the epicenter of many other initiatives in recent months. We continue to strengthen our ties with patient education and advocacy organizations and to define our own strategy for direct involvement with lay persons committed to supporting our mission. We issued a joint statement with AACE and The Endocrine Society expressing concern about differences in the potencies of approved levothyroxine products, and collaborated with the FDA in planning for a thyroxine bioequivalence workshop. In addition, we are preparing to launch our own thyroid pharmacovigilance program, about which you will hear more in coming months.

Like many ATA presidents before, I am deeply honored and very grateful for this chance to lead an organization that has played such an important role in my life and especially during such exciting times.

With best wishes for the New Year,

Paul W. Ladenson, MD
ATA President

ATA Speaks Out About Misleading Information From Government on KI and Nuclear Preparedness

In a Dec. 15, 2004, letter to Robert G. Claypool, MD, Deputy Chief Medical Officer of the Department of Health and Human Services (DHHS), ATA President Paul W. Ladenson, MD, strongly urged DHHS to rethink and revise the draft guidelines recently released for review. These guidelines are intended to advise state and local governments on stockpiling, distributing, and using KI in the event of a nuclear accident or terrorism.

The guidelines — titled "Federal Guidelines for Requesting Potassium Iodide (KI) from the Strategic National Stockpile" — would appear to have the potential effect of interfering with, rather than assisting and encouraging, states and localities in obtaining KI as a preparedness measure, emphasized Dr. Ladenson in the letter.

He encouraged DHHS to take another look at the guidelines in consultation with appropriate local agencies, as called for by Public Health Security and Bioterrorism Preparedness and Response Act of 2002, as well as with knowledgeable professional organizations, such as the National Academy of Sciences and the ATA. "This issue is of the utmost importance if our citizens are to be protected in the event of a nuclear incident arising from terrorism or accident," said Dr. Ladenson.

For a copy of the letter, go to the ATA web site, *www.thyroid.org*.

Clark T. Sawin History Resource Center, *continued from front page*

and furthering his vision of bringing an appreciation of history to current thyroid research and clinical practice. Working closely with the ATA leadership, his family has established The Clark T. Sawin History Resource Center. The goal for the center will be —

- To continue presentation of the historical vignettes as part of the ATA Annual Meeting,
- To develop electronic mechanisms to make his slides, photos, and papers available to others via the ATA web site, on CD-ROM, and other electronic media, and
- To work together with ATA leadership to identify and support colleagues who are interested in history and would like to present and publish historical work in the area of thyroid disease, research, and treatment.

The endowment will also include the donation of thyroid-related personal items from Dr. Sawin to the ATA, including historical material documenting past meetings and other ATA history.

Leslie and Clark Sawin in Palm Beach, Fla., at the 2003 ATA Annual Meeting

Separate from the endowment, Dr. Sawin had a large personal library in the field of endocrinology. This library, his historical papers, historical background materials, and personal papers will be made available to potential physician–historians to form the basis of an ongoing program of historical research and a fellowship to support endocrine research. All materials pertaining to thyroid disease, research, and treatment will be jointly owned by the ATA and The Endocrine Society.

The ATA and the Sawin family strongly encourage ATA members interested in the history of thyroid practice and research to contact Marguerite Hays, Chair of the ATA History and Archives Committee, at *ritahays19@yahoo.com* to get involved in this important work. To volunteer for the committee, please contact the ATA office.

Contributions to the Sawin endowment should be sent to the ATA headquarters or e-mail Bobbi Smith at *bsmith@thyroid.org* for more information.

Upcoming Meetings

AAAS Annual Meeting
Feb. 17–21, 2005, Washington, D.C.

Clinical Endocrinology 2005
March 28–April 1, 2005, Boston

Frontiers in Thyroid Cancer 2005
A spring meeting of the ATA, April 14–17, 2005, Baltimore

AACE 14th Annual Meeting and Clinical Congress
May 18–22, 2005, Washington, D.C.

ENDO 2005: 87th Annual Meeting
June 4–7, 2005, San Diego

Annual Meeting, American Society for Bone and Mineral Research
September 22–26, 2005, Nashville, Tennessee

13th International Thyroid Congress
Oct. 30–Nov. 4, 2005, Buenos Aires, Argentina

For more information visit www.thyroid.org.

Call for Nominations for 2005–2006 ATA President-Elect and Council Directors

The ATA Nominating Committee is soliciting nominations from the membership for candidates for the offices of president-elect and directors to serve on the ATA Executive Council. Two candidates will be on the ballot for president-elect and four candidates can run for two director positions.

The president-elect serves a one-year term, followed by a one-year term as president (2006–2007) and another year as a director on the Executive Council (2007–2008). Two directors will each serve a four-year term (2005–2009).

This will be the third year of competitive elections for the offices of president and directors. In accordance with the ATA Bylaws, the Nominating Committee evaluates all nominations and proposes the election slate to the Executive Council for approval. A ballot of nominees will be sent by mail in August 2005. The election results will be announced at the ATA Membership Meeting in Buenos Aires and in the *Signal*.

To nominate a candidate, go to the ATA web site, *www.thyroid.org*, for a nomination form. All nominations must be submitted to the ATA secretary by letter, fax, or e-mail by March 31, 2005.

Call for Nominations for the ATA 2005 Awards

The ATA is now accepting nominations for its 2005 distinguished awards: the Van Meter Award, the Distinguished Service Award, and the Pathophysiology Award. The deadline for nominations is Feb. 1, 2005.

To nominate a candidate, go to the ATA web site, *www.thyroid.org*, for a nomination form, or contact the ATA at *admin@thyroid.org* or at 703-998-8890. Nominators must submit the following information:

1. Completed nomination form;
2. Curriculum vitae of nominee with publications, excluding abstracts;
3. Letter stating nominee's qualifications, noting the significance and quality of research; and
4. Reprints or copies of up to four selected publications by the nominee.

Apply for 2005 Thyroid Research Grants

The ATA research grant program is now accepting proposals for 2005 research grants. Proposals for research in thyroid disease, pathophysiology, and thyroid cancer are due Jan. 31, 2005. The ATA Research Committee will rank proposals according to their scientific merit. Authors of selected proposals will be asked to submit full grant applications.

ATA Research Grants support a limited number of research projects in thyroid function and disease. Topics include, but are not limited to, clinical thyroidology, thyroid cancer, thyroid autoimmunity, thyroid and the brain, thyroid hormone action and metabolism, and thyroid cell biology. Research grants, up to $25,000 annually, will be awarded for two-year terms, based on receipt and review of a satisfactory progress report from funded investigators in the fourth quarter of the first year.

In addition, the ATA is excited to announce that ThyCa: Thyroid Cancer Survivors' Association, Inc. is once again supporting a Thyroid Cancer Research Grant of up to $25,000. ThyCa will be funding a thyroid cancer research project through the ATA for the third year in a row.

Research awards are targeted for funding new investigators. The focus of these awards is to allow the gathering of preliminary data for submission of a more substantial application to the National Institutes of Health, or other granting organization. Detailed guidelines on applicant eligibility and use of research funds can be found on the ATA web site, *www.thyroid.org*.

Proposals should be submitted electronically through the Research Grant Application feature on the ATA web site. A hard copy should also be sent to James Fagin, MD, Chair of the ATA Research Committee, in care of the ATA headquarters at 6066 Leesburg Pike, Suite 550, Falls Church, VA 22041.

Authors of selected proposals will be notified by late February and invited to submit detailed grant applications that are due by April 1, 2005.

ATA Signal

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

American Thyroid Association
6066 Leesburg Pike, Suite 550
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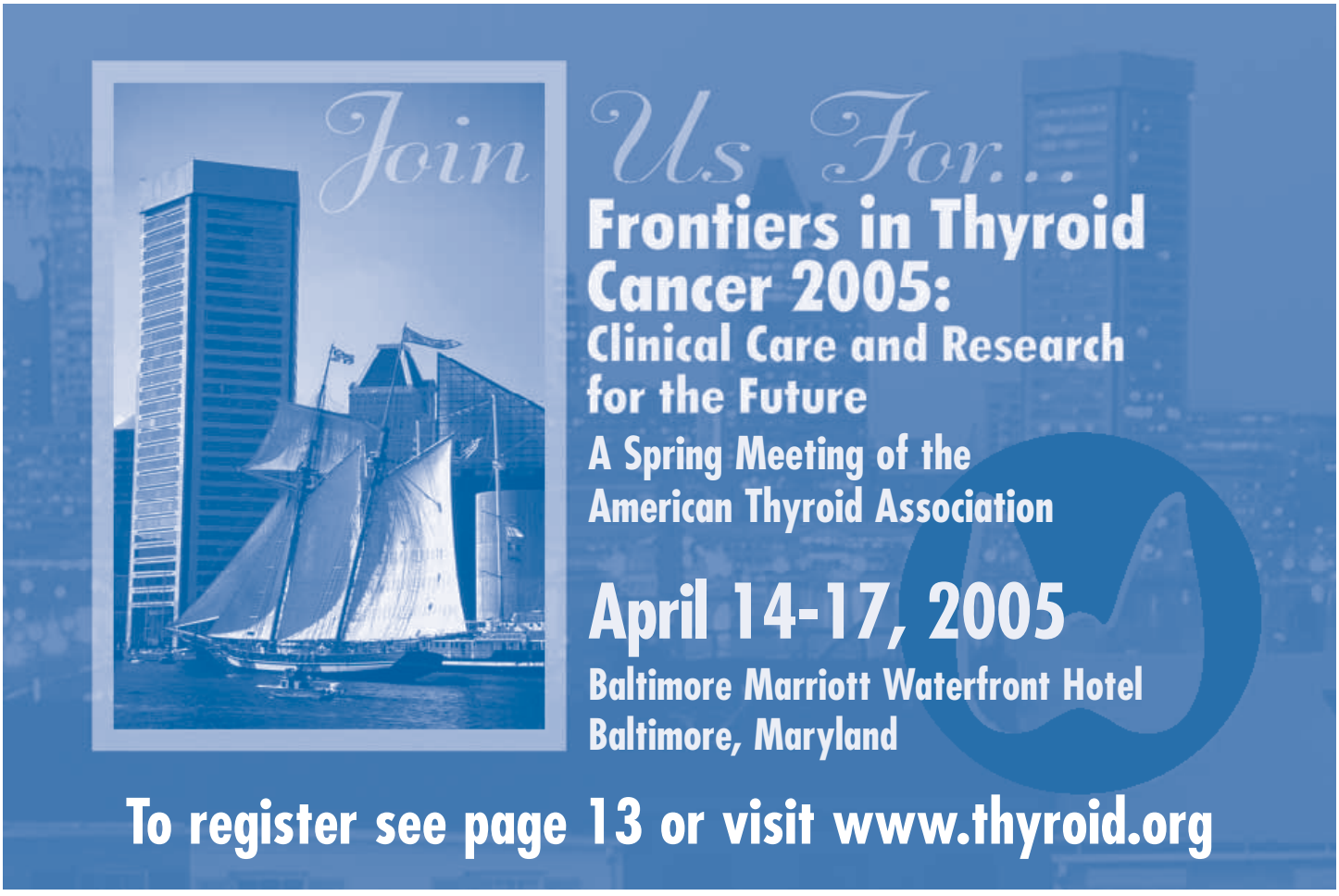

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