Personal Considerations on the 2011 American Thyroid Association and the 2007 Endocrine Society Pregnancy and Thyroid Disease Guidelines

Daniel Glinoer

In the autumn of 2004, while attending the annual American Thyroid Association (ATA) meeting in Vancouver, I was approached by a distinguished colleague, member of both the ATA and The Endocrine Society (TES), who wished to know if I would be interested in being part of an ad hoc committee to be established by TES on guidelines for managing thyroid dysfunction during pregnancy and postpartum. Being aware of my long commitment to clinical research in this field, he asked me to suggest a list of names for the committee and the main topics it should investigate. The committee eventually took shape in January to February of 2005 and adopted the initial list of topics to be discussed. These were thyroid function tests during pregnancy, maternal hypo- and hyperthyroidism and their fetal/neonatal aspects, iodine nutrition, autoimmune thyroid disorders and their potential association with pregnancy morbidity, postpartum thyroid dysfunction, thyroid nodules and thyroid cancer, and the utility of systematic screening in newly pregnant women for thyroid abnormalities.

Officially supported by TES, this international committee comprised 10 members, including endocrinologists and obstetricians. There were representatives from the ATA, American Association of Clinical Endocrinologists, and American Congress of Obstetricians and Gynecologists (ACOG). Nobuyuki Amino represented the Asia and Oceania Thyroid Association; Marcos Abalovich, the Latin American Thyroid Society; and I, the European Thyroid Association. Under the skilled chairmanship of Professor L. DeGroot, we worked very hard for 2 years. The final result of this rather complicated and challenging undertaking was the publication in August 2007 of the first Clinical Practice Guidelines dedicated to the management of thyroid dysfunction during pregnancy and postpartum (1).

What did we achieve? First, we published a comprehensive guideline article—a "premier" in the field— with its main ambition being to help the many health caretakers deal with the varied and complex thyroid problems of women before, during, and after their pregnancies. Second, we presented our clinical recommendations with a grading of their strength, based on evidence from the most pertinent articles in the literature. Third, we tried to identify the main areas of uncertainty and contention to help orient future research.

What did we not achieve? First, we were unable to reach a consensus with our obstetrician colleagues representing ACOG. Therefore, they choose not to be included as authors of the 2007 TES publication (1). Second, it was our feeling that there were several areas where objective knowledge was lacking and, as a consequence, reliable data were not available to formulate answers for some of our most important questions.

Because many questions remained unanswered, it was entirely appropriate for the ATA to establish the present task force, which authored Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum, published in this issue of Thyroid (2). Moreover, it is comforting to know that progress in the field has occurred since the 2007 TES guidelines (1). When asked by the Editor-in-Chief of Thyroid to write an editorial to accompany the publication of present ATA guidelines (2), I pondered before accepting his request because I had been retired from active professional life for 2 years and was uncertain whether I had much to add, having written an exhaustive review on this topic in 1997 (3) and a second such review with two colleagues 13 years later (4). In accepting Dr. Emerson’s request I hoped to help guide Thyroid’s readers by shedding some light on the real advances associated with the new data that have recently become available. Hence, the present editorial will focus on some of the differences between the 2007 TES Guidelines (1) and the 2011 ATA Guidelines (2). The former is referred to here as the 2007 guidelines and the latter as the current guidelines.

Let us start by first examining the literature that each of the guidelines used as a basis for their recommendations. While the 2007 guidelines included 281 references, the current guidelines contain 319 references. It should be noted that the 2011 list of references was not based on the 2007 guidelines—since the ATA task force decided to start from “scratch”— and the 2011 list includes a substantial number of references that were not in the 2007 guidelines. It is most striking that, in such a short time, the authors of the current guidelines were able to add a staggering number of new articles, these becoming available after the 2007 guidelines were formulated. This emphasizes the wealth of scientific information and the rapid development of the thyroid and pregnancy field. It fully
justifies the utility of the current guidelines, published only 4 years after the 2007 guidelines. A scrutiny of these new references indicates that 16 were published in 2007. References 17,28, and 25 were published in the next 3 years, respectively, and three more appeared in the beginning of 2011. Altogether, 28% of the references in the current guidelines were published since the 2007 guidelines. Among the remaining 230 articles, one half were listed in both the 2007 and current guidelines. From a global scrutiny of the evidence reviewed by the authors of the current guidelines, one should logically expect not only to find some of the same basic recommendations when comparing the 2007 and current guidelines, but also significant improvements in some areas in the current guidelines.

In the current guidelines, the first section is dedicated to changes in thyroid function tests during pregnancy; it constitutes a real improvement compared to the 2007 guidelines. Five recommendations (R1 to R5) accurately emphasize the narrowing of the thyrotropin (TSH) reference range in pregnancy compared with the nonpregnant TSH range, the need to establish trimester-specific reference ranges for serum TSH and free thyroxine (FT4) estimates, and also the caution required to correctly interpret the results provided by most commercially available FT4 immunoassays, although the authors admit that such tests perform reasonably well under most circumstances. This is important because they are currently the most commonly used throughout the world.

With regard to maternal hypothyroidism, the current guidelines provide 16 recommendations (R6 to R21) that are basically similar to those proposed in 2007. The main goal is to normalize serum TSH by restoring or maintaining TSH levels below 2.5 mIU/L (first trimester) or 3 mIU/L (second and third trimesters). Among the improvements, it is worth mentioning the position clearly taken by the authors that (a) women with prior hypothyroidism should start their pregnancy with a serum TSH not higher than 2.5 mIU/L (in my opinion, a lower TSH value [<1.5 mIU/L] is even more appropriate); (b) the adjustment of levothyroxine (LT4) dosage in treated hypothyroid pregnant women should be initiated as soon as possible; (c) LT4 treatment is not recommended for isolated hypothyroxinemia; and finally, (d) the risk to benefit comparison does not support routine selenium supplementation during pregnancy.

In the section on thyrotoxicosis, the current guidelines give 14 recommendations (R22 to R35) with an overall content that is essential similar to that proposed in the 2007 guidelines. Some differences deserve a comment. Following a series of studies by the group of Polak (Paris), one is much more aware nowadays of the imperative need to avoid fetal hypothyroidism in the setting of maternal thyrotoxicosis, mainly due to maternal overtreatment with antithyroid drugs, particularly during late gestational stages (5). Also, special attention is given to the importance of prenatal counseling, by insisting on the notion that the optimal time for a hyperthyroid woman to conceive is not until the euthyroid state is achieved. However, it remains common practice—unfortunately—that women do not usually ask their doctor permission to become pregnant and, therefore, the actual usefulness of such a wise recommendation remains to be confirmed. Finally, the most important new issue is the attention recently brought to the hepatotoxic risks associated with the indiscriminate use of propylthiouracil (PTU). This attention, in turn, led to the recommendation in the current guidelines to limit PTU use to the first trimester. The remaining unsettled issue is whether thyrotoxic pregnant women should be switched from PTU to methimazole after the first trimester of pregnancy.

Five recommendations (R36 to R40) are given in the current guidelines for adequate iodine nutrition in pregnancy; they are almost identical to those provided in the 2007 guidelines. The World Health Organization (WHO) recommends 250 µg/d for pregnant and lactating women. In most Western countries, such an intake level can only be achieved by the systematic daily administration of prenatal multivitamins containing 100–150 µg of supplemental iodine (6).

The current guidelines contain a section discussing the association of antithyroid antibodies with pregnancy loss. They propose five recommendations (R41 to R45) whose main characteristic is that, for all of these, the authors were compelled to state that “there is insufficient evidence to recommend for or against ... systematic screening for thyroid autoantibodies ... or treating thyroid antibody-positive euthyroid women with LT4.” Thus, although the association between pregnancy loss (spontaneous, recurrent, or after in vitro fertilization procedures) and thyroid autoimmunity is clearly established, causality is not. Suffice to add that this area remains highly controversial and only future studies may help us unravel this complex topic.

With regard to the section on thyroid nodules and cancer, the current guidelines propose 17 recommendations (R46 to R62). This section is extremely interesting, improves considerably the information provided previously, and therefore, constitutes real progress. Most relevant questions that are important for the clinicians are addressed using recently available information. The current guidelines include an algorithm for the work-up and management of a thyroid nodule detected during pregnancy; each clinician should keep this scheme in mind. The most important “take home” message regarding thyroid nodules in pregnant women is that in those in whom a well-differentiated thyroid cancer is identified during pregnancy, surgery may be generally deferred until postpartum.

With regard to the section on postpartum thyroiditis (PPT), the personal opinion of this writer is that, despite the inclusion of an algorithm, this section is—curiously—less well presented than its counterpart in the 2007 guidelines. Furthermore, an important aspect is the etiological diagnosis of an early thyrotoxic phase during the postpartum period which requires differentiation between Graves’ disease (either new onset or recurrence) and transient thyrotoxicosis due to PPT per se. This paragraph is not found in the PPT section but rather in the section on thyrotoxicosis (see Question 38). This makes reading of the topic somewhat cumbersome. Altogether, the authors propose nine recommendations (R63 to R71) dealing with thyroid function testing and its timing, use of propranolol for transient thyrotoxicosis, and modalities of LT4 administration during the hypothyroid phase of PPT.

The final section of the current guidelines concerns thyroid function screening. It was the authors’ decision to write a relatively lengthy section, presumably because thyroid screening in pregnancy is one of these areas of hot debate that arises at each meeting where the topic is on the program. Therefore, the expectation of this writer was to find new information and, perhaps, novel concepts more
precisely defined than previously. How disappointing then to read this section and realize that not much new has been acquired in the last 4 years. The most disquieting feature was the oral report by Lazarus on the “CATS study” at the 2010 International Thyroid Conference in Paris (7). Although still preliminary, the data showed no difference in IQs between the children (aged 3 years) whose mothers had received LTI treatment (for elevated TSH or low FT4) and the control group. Five recommendations are proposed (R72 to R76) that are broadly equivalent to those presented in the 2007 guidelines. In addition, the authors reiterate the usefulness as well as the limitations (already proposed in the 2007 guidelines) of case-finding screening in high risk women, with the addition to the current list of clinical conditions such as women with morbid obesity, women treated with lithium or amiodarone, and women residing in areas with iodine deficiency and the converse (i.e., women with a recent exposure to excess amounts of iodine). A final comment is that, similar to our failure to convince our obstetrician colleagues to endorse the 2007 guidelines, ACOG and Society for Maternal-Fetal Medicine are not endorsing (personal communication from Editor-in Chief of Thyroid) the current ATA recommendations (2).

To conclude, the members of the present ATA task force should certainly be commended for their timely formulation of the current guidelines (2) and for their efforts to clarify areas that were of necessity too vague in the 2007 guidelines (1). The current guidelines are presented in a “simple question” followed by a “clear answer” mode, which is evidently pleasant to read, although perhaps difficult to remember because of the large number of final recommendations. Although the current guidelines are intended to “sit on their own,” i.e., without being based on the 2007 guidelines, this writer views them as a continuum of all previous efforts. Only the future will tell us when it will be the time, once again, to sit down and rewrite what has presently been achieved. The only thing I can foresee is that it will be without me, although my dearest wish is to remain alert to any progress made in this fascinating field which has kept me quite busy—and most often very happy—for the last 25 years.

References

Address correspondence to:
Daniel Glinoer, M.D., Ph.D.
University of Brussels
Hospital Saint Pierre
322, rue Haute
B-1000 Brussels
Belgium
E-mail: daniel.glinoer@gmail.com
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